ACEM PRIMARY 2008/2 PATHOLOGY VIVA Thursday 18th September Session (am) ***Candidate Number*****…… AGREED MARK……**

TOPIC	QUESTION	KNOWLEDGE	PASS CRITERIA
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
Question 2: Type 2 (Antibody mediated) hypersensitivity	1. Give some examples of Antibody-mediated (Type 2) hypersensitivity.	**1.Examples**: 1. *Transfusion reaction;2. Erythroblastosis fetalis;3. certain drug reactions; 4. Autoimmune haemolytic anaemia, thrombocytosis & agranulocytosis; 5. Myaesthenia gravis; 6. Grave's Disease; 7. Pemphigus vulgaris; 8. Glomerulonephritis (some forms); 9. vascular rejection in organ grafts*	3 to pass
	2. By what mechanisms is Type 2 hypersensitivity mediated? Prompt: More detail	**2a. Opsonisation & Complement- and Fc Receptor-mediated Phagocytosis:** Cells are coated (*opsonized*) with molecules attractive to phagocytes. *Complement* activation resulting in by-products (C3b and C4b). *Phagocytosis* results *Antibody-dependent cellular cytotoxicity (ADCC)*: no complement activation, leucocyte driven. **2b. Complement- and Fc Receptor-mediated inflammation**: Extracellular tissue inflammation - mainly antibody deposited activation of complement (by-products C5a; lesser C4a and C3a), which recruit neutrophils and monocytes. Fc receptors also bind the antibodies releasing enzymes and oxygen intermediates **2c. Antibody mediated cellular dysfunction**: antibodies against *cell-surface receptors* impair or dysregulate function ***without*** causing cell injury or inflammation	2 groups to pass
3. Tuberculosis	Describe the **pathogenesis** of tuberculosis in a previously **unexposed immunocompetent** person Prompt if doesn't mention airborne.	**Infection by M. tuberculosis airborne** • M. tuberculosis usually person to person airborne droplet spread **M tuberculosis enters alveolar macrophages and replicates** • Enters alveolar macrophages and replicates by blocking phagosome/lysosome fusion leading to bacteraemia (person generally asymptomatic or mild flu like illness **Immunity through T cell mediated delayed type hypersensitivity reaction that also causes hypersensitivity and tissue destruction- in particular granuloma formation and caseation** • About 3 weeks later T cell activation via MHC antigens on macrophages and IL-2 leading to macrophage becoming bactericidal (thru IFN-γ) This macrophage response also causes tuberculin positivity and formation of granuloma and caseation by recruiting monocytes ("epithelioid histiocytes") **Re- exposure or reactivation causes heightened immune reaction as well as tissue destruction** • Infection may be contained or may progress and may reactivate with immunosuppression from any cause	Highlighted

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4. Calcific Aortic stenosis	1. What are the causes of Aortic valve stenosis?	Postinflammatory scarring (Rheumatic fever) Senile calcific Ao Stenosis Calcification of congenitally deformed valve	2/3 to pass
	2. What is calcific aortic stenosis?	Ao Stenosis most common valvular abnormality **Wear and tear** => calcification on normal or cong bicuspid valves Clinical attention in 6-7th decade in bicusid valves, 8-9th decade in prev. normal valves Heaped up **calcified masses within cusps**=> protrude through to outflow tracts. Functional valve area decreased.	Highlighted
	3. What are the consequences of calcific aortic stenosis?	**LV outflow obstruction**=> increased pressure gradient over valve. (severe when valve area 0.5-1cm^2) CO maintained by concentric **LVH**. Hypertrophied myocardium ischaemic. Impaired systolic and diastolic function. Decompensation => angina, CCF, syncope	Highlighted
5.Thyrotoxicosis	1.What is thyrotoxicosis?	Hypermetabolic state caused by elevated circulating levels of T_3 and T_4	Need to know
	2. What are the clinical features of thyrotoxicosis?	**Cardiac** – inc HR, dysrhythmias, CCF Neuromusc – tremor, prox myopathy **Ocular** – wide staring gaze, lid lag, proptosis CNS – anxiety, emotional lability, insomnia Skin – warm, flushed, inc sweating **Heat intolerance** **Thyroid storm** – fever, tachycardia, arrhyth., may be fatal if not treated promptly	Highlighted
	3. What are the main causes of thyrotoxicosis?	**Diffuse toxic hyperplasia (Graves disease)** Toxic multinodular goitre Toxic adenoma/carcinoma Neonatal from maternal Graves dis Non-hyperthyroidism – thyroiditis, etc	Highlighted + 1 other

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TOPIC	QUESTION	KNOWLEDGE	PASS CRITERIA
1. Role of complement in inflammation	1. What is the complement system?	**Plasma protein system involved in immunity** against microbes. Complement proteins numbered C1-9 are present in plasma in inactive forms.	Highlighted
	2. Describe the main pathways by which complement activation occurs.	1. **Classical pathway:** involving an antigen-antibody complex 2. **Alternate pathway:** triggered by microbial surface molecules (e.g. endotoxin). No antibody involvement. 3. Lectin pathway: plasma mannose-binding lectin binds to carbohydrate on microbe All pathways result in cleavage and activation of C3 (most important and abundant complement component)	Highlighted & way activated
	3. How do activated complement products mediate acute inflammation?	1. **Vascular effects**: increased permeability; vasodilatation (via C3a, C5a mediated histamine release from mast cells) 2. Leucocyte adhesion, chemotaxis and activation: via C5a 3. Phagocytosis: C3b acts as opsonin on microbe and leads to phagocytosis 4. Cell lysis by the membrane attack complex (MAC) – composed of multiple C9 molecules	Vascular and one other
2. Local and Systemic influences on wound healing	1. Describe the factors that affect wound healing Prompt: Outline how they affect the healing process	**(Table 3-5) Local:** blood supply, denervation, local infection, FB, haematoma, mechanical stress, necrotic tissue, protection, surgical technique, tissue type **Systemic:** Age, anaemia, drugs, genetic disorders, hormones, diabetes, malignant disease, malnutrition, obesity, systemic infection, temperature, trauma, hypovolaemia, hypoxia, uraemia, vitamin deficiency (C), trace metal deficiency (Cu, Zn)	At least 3 local and 3 systemic. Must describe effect to pass.
	2. Describe the effect of an additional local/systemic factor.		If < 3 factors described in a group.
3. Malaria	1. What micro-organisms cause malaria?	Parasitic protozoa **Plasmodium falciparum**, vivax, ovale, malarie	Falciparum +1
	2. How does Plasmodium falciparum infection differ from other forms of malaria? Prompts: How does it compare clinically? By what mechanism?	All do: sporozoite→liver→merozoites formed → release & bind to RBC→ Hb hydrolysed → trophozoite→ schizont → merozoite/gametocyte *P. falciparum:* **infects RBCs of any age**, causing **clumping/rosetting** so ischemia, high cytokine production, **high level parasitemia**, severe anemia, cerebral symps, renal failure, pul oedema, death *Others*: infect only new or old RBCs, P vivax & ovale form latent hynpnozoites (relapses), low parasitemia, mild anemia, rarely splenic rupture, nephrotic synd	2/3 Highlighted and 1 clinical feature
	3. What factors can make people less susceptible to malaria?	**Inherited alterations in RBCs: HbS** trait, HbC, Duffy Ag neg Repeated exposure stimulates immune response: Ab and T lymphocytes (P falc avoids this), HLAB53	Highlighted

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4. Pericarditis	1. What are the causes of acute pericarditis?	**Infectious**; **viral**, pyogenic bacteria Immune mediated(presumed); Rheumatic fever, SLE, Scleroderma, post cardiotomy. Post MI (Dressler's), Drug hypersensitivity reaction. Other; AMI, uraemia, post cardiac surgery, neoplastic, trauma, radiation	Need viral and three others
	2. What types of pericardial fluid exudate occur?	1. Serous; usually non-infectious inflammation, RF, SLE, uraemia, tumours 2. Fibrinous/serofibrinous; (most common) post MI, Dressler's, trauma, post surgery but also as in 1. 3. Purulent/suppurative; almost always bacterial invasion from local infection, lymphatic or blood seeding, or at operation 4. Haemorrhagic 5. Caseous	2/5 to pass
	3. Describe the clinical features of pericarditis	Pericardial rub (may be absent if large effusion). Pain, fever (chills and rigors if suppurative), signs of cardiac failure,	Rub, pain,fever required
Question 5: Pathogenesis of Type 1 Diabetes Mellitus	1. What is the pathogenesis of Type 1 Diabetes Mellitus	1. Genetic predisposition 2. Precipitating event 3. Autoimmune destruction of islet cells 4. Subclinical leading to overt DM	3 to pass
	2. What environmental factors may contribute to the development of Type I Diabetes Mellitus?	1. Infections (group B coxsackieviruses; mumps; measles; CMV; rubella; EBV): may induce tissue damage and inflammation, leading to the release of B-cell antigens. ***OR*** the viruses produce antigens which mimic self-antigens with the immune response cross-reacting with self-tissue.	
	3. How does genetic susceptibility contribute to the development of Type I DM?	2. Complex pattern of genetic associations: putative susceptibility genes mapped to at least 20 loci. Most important is ***class II MHC (HLA) locus → 50% of total*** genetic susceptibility: on chromosome 6p21 (HLA-D) 95% Caucasians with type I DM have HLA-DR3, DR4 or both. ***DQB1*0302 allele considered the primary determinant of genetic susceptibility***. **Non-MHC genes**: the first disease-associated non-MHC gene to be identified was *insulin*. Tandem repeats in the promoter region being associated with disease susceptibility. • **mechanism of association is unknown**: maybe the disease associated polymorphism makes the protein less functional or stable OR may influence the level of expression of insulin in the thymus, so altering negative selection of insulin-reactive T cells Another gene recently shown to be associated: encoding for the T-cell inhibitory receptor CTLA-4	

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TOPIC	QUESTION	KNOWLEDGE	PASS CRITERIA
1: Cellular changes in inflammation	Describe the sequence of cellular events in acute inflammation Prompts: • What cells are involved in acute inflammation? • How do these cells get from the blood vessels to the inflammatory site?	**Leucocytes are the major cell type involved. In first 6-24 hours neutrophils, and monocytes/macrophages in 24-48 hours** • Leucocytes line endothelial wall – margination **First stasis of blood flow leading to increased leucocytes along endothelial wall** **Then leucocyte adhesion to endothelial wall and diapedesis or transmigration across into interstitium – extravasation** • Adhesion and transmigration and recruitment are mediated by various mediators such as histamine, PAF cytokines and various attraction molecules – variously called immunoglobulins, integrins, selectins, mucin-like glycoproteins **Then leucocytes migrate to site of injury- chemotaxis** • Chemotaxis and activation is mediated thru various bacterial products, cytokines, chemical factors, Ag-Ab complexes products of necrosis **Then leucocyte activation to enable phagocytosis and enzyme release** Phagocytosis and release of various enzymes from leucocytes	Highlighted
2. Type III immune mediated hypersensitivity	1. What is the pathogenesis of type III hypersensitivity? Prompt: Immune mediated	**Antibodies bind antigens & then induce inflammation** directly or by activating complement. The recruited leukocytes produce tissue damage by release of lysosomal enzymes and generation of toxic free radicals 3 phases (systemic diseases) a) Formation of antigen antibody complexes in circulation b) Deposition of **immune complexes** in various tissues c**) inflammatory reaction** at the site of deposition	Highlighted
	2. What are the common sites for immune complex deposition	Renal glomeruli, joints, skin, heart, serosal surfaces, small blood vessels	3 to pass
	3. Give some examples of diseases caused by Type 3 hypersensitivity	SLE, polyarteritis nodosa, post strep GN, Acute GN, reactive arthritis, serum sickness, arthus reaction	3 to pass

TOPIC	QUESTION	KNOWLEDGE	PASS CRITERIA
3. Candidiasis	1. What is the clinical spectrum of candida infection?	(Benign commensal) **Superficial mucosal infn** – mouth, vagina, oesophagus **Superficial cutaneous infn** – intertrigo, nappy rash, balanitis, folliculitis, paronychia, onychomycosis Chronic mucocutaneous (T-cell defects, endocrinopathy) **Invasive (disseminated)** – myocardial/ abscess/endocarditis, cerebral abscess/meningitis, renal/hepatic abscess, endophthalmitis, pneumonia	Highlighted – something from each category
	2. What mechanisms enable candida to cause disease? Prompt: What are the virulence factors?	1) **Phenotypic switching** to adapt rapidly to changes in host environment 2)**Adhesion to host cells** - imp. determ. of virulence –via adhesins (several types) 3) **Production of enzymes** (aspartyl proteases and catalases) degrade extracellular matrix proteins and may aid intracellular survival 4) secretion of adenosine – blocks neutrophil degranulation	1/3 Highlighted
4. Pathogenesis of atherosclerosis	1. Outline the steps involved in the pathogenesis of atherosclerosis.	Response to injury hypothesis: **1. Endothelial injury and dysfunction** 2. Lipoprotein (mainly LDL) accumulation and oxidation in vessel wall **3. Monocyte adhesion and migration into intima and transformation into foam cells and macrophages** 4. Platelet adhesion **5. Smooth muscle cell migration from media into intima** 6. Subsequent smooth muscle cell proliferation in intima **7. Enhanced lipid accumulation within intimal cells (macrophages and smooth muscle cells)**	Must have highlighted
	2. List the potential causes of endothelial injury?	**1. Hyperlipidaemia,** **2. Hypertension,** **3. Smoking** **4. Haemodynamic factors (disturbed flow patterns)** 5. Homocysteine, 6. Toxins, 7. Viruses, 8. Immune reactions	3 of highlighted and 1 other to pass
5. Pituitary Adenomas:	1. How are pituitary adenomas classified? Prompt: Name two cell types involved.	Classification based on **hormone cell-type**: prolactin cell, growth hormone cell (densely or sparsely granulated), thyroid stimulating cell, ACTH cell, gonadotroph cell (including silent and oncocytic), mixed GH-prolactin cell, Other plurihormonal cell, hormone negative.	Highlighted & 2 cell types to pass. If describe "functional" or "silent" adenomas – move to prompt
	2. What clinical syndromes may they produce?	Prolactinoma: amenorrhea, galactorrhea, loss of libido, and infertility Somatotroph (GH): gigantism or acromegaly ACTH: Cushing's syndrome Gonadotroph: local effects (headaches, visual impairment, diplopia, pituitary apoplexy), hypogonadism (lethargy, loss of libido, amenorrhoea)	