Pathology Basics VIVAs (Pathology)

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2015.1.B.1

Question 2 Mediators of inflammation (pp 56-66) **Subject:** Path LOA: 1	What stimuli cause production of inflammatory mediators? What are the chemical mediators of acute inflammation and what are their actions?	Substances released from necrotic cells, microbial products, cell injury, mechanical irritation. **Histamine**: vasodilation, inc vasc perm, endoth activation **PG**: vasodilation, inc vasc perm **Leukotrienes**: inc vasc perm, chemotaxis, WC adhesion & activation **PAF**: vasodil, inc vasc perm, chemotaxis, WC adhesion, degran **Complement**: WC chemo and activation, vasodilat **Cytokines** (TNF, IL-1): endo activation (adhesion), fever, pain, hypotension, dec vasc resist **Chemokines**: chemotaxis, WC activation **Kinins**: inc vasc perm, vasodil, pain, sm m contraction	2 to pass. 4 to pass (including names and actions)

2015.1.D.1

Question 4 Cutaneous wound healing (pp102-108) **Subject:** Path LOA:1	1. **Describe the phases of cutaneous wound healing?**	**1.Inflammation, proliferation, and maturation**. Phases overlap, and separation arbitrary. The initial injury -> platelet adhesion and aggregation + formation of clot on wound surface -> ***Inflammation***. ***Proliferative*** phase -> formation of granulation tissue, proliferation and migration of connective tissue cells, and re-epithelialization of the wound surface. ***Maturation*** involves ECM deposition, tissue remodelling + wound contraction.	**2 of 3 phases in bold with correct descriptions to pass**
	2. **What factors influence cutaneous wound healing?**	***2.Systemic factors:*** **•Nutrition.** Protein deficiency and vitamin C deficiency, -> retard healing. **•Metabolic status** : Diabetes mellitus, -> delayed healing **•Circulatory status**: Inadequate blood supply or drainage (arteriosclerosis or varicose veins. **•Hormones** eg. glucocorticoids influence various components of inflammation, also inhibit collagen synthesis. ***Local factors:*** **•*Infection*** single most important cause of delay in healing, **•*Mechanical factors,*** (early motion of wounds). **•*Foreign bodies*** impede healing. **•*Size, location, and type of wound (mechanism of injury).***	**2 systemic and 2 local factors to pass**
	3. **What is wound contraction?**	***3.Wound contraction generally occurs in large surface wounds***. The contraction **helps to close the wound by** decreasing the gap between its dermal edges + **reducing the wound surface area**. Important feature in healing by secondary union. Initial steps of wound contraction involve formation, at the edge of the wound, of a **network of *myofibroblasts***.	**Bold to pass**

2013.2.B.2

Question 1 PATHOLOGY LOA: 1	*"A patient presents with chronic inflammatory arthritis."* 1. What are the characteristics of chronic inflammation? 2. Why does macrophage accumulation persist in chronic inflammation? 3. What are the causes of chronic inflammation? (prompt can you give an eg. of each)	• Inflammation for a **prolonged period** (week or more). • Characterised by **macrophages**, lymphocytes and plasma cells • With simultaneous-active inflammation/ **tissue destruction** and **attempts at repair** by connective tissue, fibrosis **Continued recruitment** of monocytes (continued expression of adhesion molecules and chemotactic factors) Local proliferation of macrophages Immobilisation of macrophages • **Persistent infection**- TB, syphilis • **Autoimmune**-RA, MS, IBD, SLE • **Prolonged exposure to an agent**: exogenous-silica->silicosis , FB, persistent trauma endogenous-lipid->atherosclerosis	¾ Bold to pass Bold 2/3 bold with examples

2014.2.B.2

Question 1 Acute inflammation – questions to focus on acute inflammation not prostatitis specifically (as this is an LOA 3 topic) (pp 48-56) **Subject:** Path LOA: 1	1. What are the three major components of acute inflammation?	1. **Dilation of small vessels** leading to increase blood flow. 2. **Increased permeability of the microvasculature** enabling plasma protein and leucocytes to leave the circulation. 3. **Emigration of leucocytes from the microcirculation to the site of injury**.	Bold to pass Neutrophils predominate in the early inflammatory (6 – 24 hours) infiltrate and are later replaced by monocytes and macrophages (24 – 48 hours).
	2. How are leucocytes delivered to the site of injury? PROMPT: What are the three processes that leucocytes undergo to move from the blood to the site of injury?	This is a multistep process mediated and controlled by adhesion molecules and chemokines. 1) **Margination:** Occurs when leucocytes adopt peripheral position along the epithelium. Rolling (transient adherence mediated by selectins), activation and firm attachment (mediated by integrins) to the endothelium. 2) **Transmigration** (diapedesis): across the endothelium. Migration through interendothelial spaces typically in post capillary venules. 3) **Chemotaxis**: Leucocytes move toward the site of injury along a chemical gradient of chemoattractants, which can be exogenous or endogenous.	Bold to pass Polymerisation of actin at the leading edge of the cell establishes a "front wheel " drive in the direction of the injury
	3. Name some of the chemoattractants responsible for chemotaxis?	Most common exogenous agent **Bacterial products**. Endogenous: IL-8, **C5a**, and Leukotriene B4. All bind to specific receptors and promote polymerisation of actin.	Bold + 1
	4. What chemical mediators are responsible for pain, fever and tissue damage?	**IL-1,** TNF, Prostaglandins, Bradykinin, Neutrophil and Macrophage Lysosomal enzymes, Oxygen metabolites, NO.	Bold + 1

2013.1.1

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

2013.1.3

Question 1: LOA: 1 Vascular changes of acute inflammation	1. In acute inflammation what changes occur in blood vessels? Prompt: What happens next?	1. Changes in blood flow: (transient constriction), **vasodilation** (NO mediated) lead to **increased flow** • **Increased permeability,** loss of protein-rich fluid • Fluid loss & dilation lead to **stasis/congestion** • Leukocytes accum at vasc endothelium, endothelium expresses adhesion molecs, leuks adhere & migrate out	3/4 Bold
	2. What are the mechanisms for the increased vascular permeability seen in acute inflammation?	2. Chem mediated **endothelial cell contraction** (caused by eg histamine, LKT, sub P) • Endothelial injury direct/microbes/leuks eg burns • Increased transcytosis of fluids/proteins via channels of connected vesicles/vacuoles (vesiculovacuolar organelles) stim by factors eg VEGF	2/3 must include bold

2012.2.1

Q1 Hyperplasia LOA: 1	1. What is hyperplasia? 2. What are the causes of hyperplasia? 3. Give some examples of hyperplasia *Prompt: can you give me a physiological/pathological example?*	Hyperplasia is an **increase in the number of cells** in an organ/tissue, usually get increased mass of organ/tissue a. Hormonal effects – reversible with withdrawal of hormonal stimulation b. Tissue damage or resection - compensatory hyperplasia c. Growth factors - pathological hyperplasia d. Increased workload (muscle) - as for hypertrophy Physiological: female breast at puberty and during pregnancy, partial hepatectomy, Pathological: endometrium – hyperplasia, dysfunctional uterine bleeding; BPH; Papilloma virus	Bold to pass 2/4 required to pass 1 physiological and 1 pathological cause to pass

2012.2.2

Q1 Metaplasia LOA 1	1. What is metaplasia? 2. Describe some examples 3. What are the possible outcomes of metaplasia? 4.	1. Replacement of one normal cell type with another normal cell type; can be adaptive or pathological. 2. Columnar to squamous (respiratory-chronic irritation eg smoking; excretory ducts due to stones eg salivary, bile). Squamous to columnar (Barrett oesophagus). Connective tissue (myositis ossificans). 3. Malignant transformation, reversibility/resolution, ongoing	Correct definition and 2 examples to pass 2 to pass

2012.2.2

Q2 Mechanisms of Cellular Injury LOA 1	1.? What happens inside cells when they are injured? *Prompt: mechanisms of cell injury* 2. What is a free radical? 3. What are the pathologic effects of free radicals? *Prompt: At a cellular level.*	1. ATP depletion, mitochondrial damage, calcium influx, accumulation of free radicals or ROS, membrane damage, DNA/protein damage 2. Chemical species that have a **single unpaired electron** in outer orbit eg reactive oxygen species: superoxide, hydrogen peroxide, hydroxyl, ONOO- peroxynitrite 3. Overall can cause **necrosis** or apoptosis or can stimulate production of degrading enzymes Directly can cause: **Lipid peroxidation** (plasma or organelle membrane damage) **Oxidation of proteins** (affect protein structure eg enzymes) **DNA lesions** (breaks in DNA or cross-linkages)	3/6 Principal & one example to pass Necrosis & 1/3 bolded effects

2012.2.1

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

2012.2.3

Q1 Morphologic patterns and outcomes of acute inflammation LOA: 1	1. What are the different types of acute inflammation? *Prompt: What are the morphological patterns of acute inflammation?*	**1.a. Serous inflammation:** thin fluid from plasma or mesothelial lining cells e.g. burns, effusions (pericardial, pleural) **b. Fibrinous inflammation:** more severe injuries and greater vascular permeability allows larger molecules such as fibrin e.g. characteristic of inflammation in body cavities (pericardial sac,meninges,pleura) **c. Suppurative / purulent inflammation:** large amounts of pus / purulent exudates – neutrophils,necrotic cells,oedema fluid e.g. organism type (staph) ; site (appendicitis) **d. Ulcers:** local defect in surface of an organ/tissue	2 with examples
	2. What are the outcomes of acute inflammation?	**2.a. Complete resolution +/- scarring** **b. Abscess formation** (suppurative inflammation) **c. Fibrosis** (fibrinous inflammation) **d. Chronic inflammation**	2 of 4

2012.2.4

Q1 Hypertrophy LOA: 1	1. What is hypertrophy? 2. What are the types of hypertrophy? 3. Describe examples of each type hypertrophy? *Prompt: Can you give examples of physiologic and pathologic hypertrophy?*	**Increased size of a tissue due to increased cell size);** Due to synthesis of structural components. May be **physiological or pathological** depending upon increased functional demand or specific hormonal stimulation. Cell hypertrophy can occur in dividing or non-dividing cells Physiological: skeletal muscles with exercise, uterus in pregnancy (hormonal), breasts in lactation. Pathological: prostate in BPH, heart in chronic hypertension.	Bold One example of each

2012.2.4

Q2 Mediators of acute inflammation LOA: 1	1. What are the chemical mediators of acute inflammation? 2. What do they do? -	Histamine	Vasodilation, increased vasc permeability, endothelial activation	4 to pass 4 general correct actions
		Serotonin	Vasodilation, increased vasc permeability	
		Prostaglandins	Vasodilation, pain, fever	
		Leukotrienes	Increased vasc permeability, chemotaxis, leukocyte adhesion and activation	
		Platelet-activating factor	Vasodilation, increased vasc permeability, leukocyte adhesion, chemotaxis, degranulation, oxidative burst	
		Reactive oxygen species	Killing of microbes, tissue damage	
		Nitric oxide	Vascular smooth muscle relaxation, killing of microbes	
		Cytokines (TNF, IL-1)	Local endothelial activation (expression of adhesion molecules), fever/pain/anorexia/hypotension, decr vascular resistance (shock)	
		Chemokines	Chemotaxis, leukocyte activation	
		Complement (C5a, C3a, C4a)	Leukocyte chemotaxis and activation, vasodilation (mast cell stim	
		Kinins	Incr vasc permeability, smth muscle contraction, vasodilation, pain	
		Proteases activated during coagulation	Endothelial activation, leukocyte recruitment	

2012.1.3

Question 2 Wound Healing LOA: 1	**Describe the process of healing of an incised skin wound?** (Prompt: include the timing of these processes.)	**a) Formation of a blood clot – immediate** **b) Neutrophil migration at wound margins – within 24 hours** **c) Formation of granulation tissue (fibroblasts and vascular endothelial tissue). Blood vessels are leaky and proteins and fluid pass into the extravascular space leading to oedema– 24-72 hours** d) Cell proliferation and Collagen deposition – neutrophils are replaced by macrophages between 48 and 96 hours e) Scar formation – leucocytic infiltrate, oedema and increased vascularity disappear; increased accumulation of collagen – second week f) Wound Contraction – formation of myofibroblasts at the wound edges that contract. g) Connective tissue remodelling h) Recovery of Tensile strength – 10% at 1 week to a peak of 70-80% at 3 months	**Bold 3 and 2 others = 5**
	What factors influence wound healing?	a) Local (infection / mechanical eg motion of wound / FB / size, location, type eg incised vs blunt trauma) b) Systemic (nutrition / metabolic status / circulatory status / hormones)	**To pass:** **2 local & 2 systemic**

2011.2.1

Question 1 LOA: 1	1.What leukocytes types are characteristic of acute inflammation? (Prompt for 2)	**1. Neutrophils first 6-24 hours** Monocytes 24-48 hours Neutrophils may last longer (4 days) in pseudomonas Lymphocytes in viral Eosinophils in hypersensitivity	**Bold + 1 other**
	2. How do leucocytes get to an area of acute inflammation?	2. **Margination** of WCC in vessels, rolling and **Adhesion** to endothelium (pavementing) (Selectins) **Migration and diapedesis** across endothelium (PECAM1, CD31, Integrins) **Migration towards chemotactic** stimulus in tissue (bacterial products, cytokines, IL8, C5A)	**3 bold**
	3. Why do neutrophils predominate in the inflammatory response in the first 6-24 hours?	3. More numerous in the blood Respond more rapidly to chemokines May attach more firmly to adhesion molecules Neutrophils are short lived - disappear after 24-48 hrs (monocytes live longer)	**1/4**

2011.2.2

Question 1 LOA: 1	1. What are the characteristics of chronic inflammation?	1.Inflammation for a **prolonged period** (week or more) Characterised by **macrophage** With simultaneous - active inflammation - **tissue destruction** - **attempts at repair**	**Bold**
	2. What are the causes of chronic inflammation? *Prompt: Can you give an example of each of these?*	2.**Persistent infection** TB, syphilis, PUD **Prolonged exposure toxic agents** exogenous = silica / FB endogenous = lipid - atherosclerosis **Autoimmune** RA; lupus	**2/3 Bold with one example**
	3. Why does macrophage accumulation persist in chronic inflammation?	**Continued recruitment** of monocytes (continued expression of adhesion molecules and chemotactic factors) Local proliferation of macrophages Immobilisation of macrophages	**Bold**

2011.2.3

Question 2 LOA: 1	**1.Describe the pathogenesis of Fibrosis?**	Fibrosis = excess deposition of collagen & ECM in chronic disease **Frustrated healing/chronic inflam >** **Persistent stimulus** (infections, autoimmune , trauma) Macrophage/Lcyte stimulation > **Growth factors** PDGF, FGF, TGF -> **prolif fibroblasts**, endothelial cells, spec fibrogenic cells	4/7 including macrophages highlighted features with > production v less bkdown mentioned (may be prompted)
	(Prompt, What cells are activated in fibrosis?)	**Macrophage -alternative pathway activation**, by IL-4, IL-13, cytokines from TH2 , Mast, eosinophils **TGF-β** almost always involved Actions: Monocyte attractant (L/Mac) Fibroblast activation/proliferation Increased collagen fibronectin synthesis/secretion Inhibition of metalloproteinases	**Macrophages** 2/4 actions
	2 Please provide some examples	Cirrhosis, chronic pancreatitis, pulm fibrosis Pneumoconiosis, constrictive pericarditis, Glomerulonephritis	3 to pass

2011.1.1

Question 1. **Ischaemic cell injury**	1.What are the **stages of ischaemic cell injury?**	• **Initial Reversible** • **Irreversible (prolonged ischaemia injury and necrosis)**	2/2
	2. Describe the **sequence of events that occurs in reversible ischaemic cellular injury**. PROMPTS What occurs in the cell? What happens to pH?	• Due to loss of oxidative phosphorylation → **decreased ATP →failure of sodium pump** → loss of K+; influx of Na+ and H2O → iso-osmotic cell swelling. • **Increase in Ca++** initially release from intracellular stores then influx of Ca++ across plasma membrane → failure of ATP generation, activation of enzymes, induction of apoptosis → membrane and nuclear damage • **Decreased cellular pH due to increased lactate (increased anaerobic metabolism)** • Loss of glycogen, decreased protein synthesis • Loss of microvilli, formation of cell surface blebs, myelin figures, mitochondria + ER swelling, ribosome detachment clumping of nuclear chromatin fatty change	Bold (3 items)
	3. Describe **the morphological changes of irreversible ischaemic** injury	• Severe swelling of mitochondria • Extensive damage to plasma membrane • Swelling of lysosomes • Cell death by necrosis/apoptosis	2/4

2011.1.2

Question 1. **Atrophy**	1. **What is atrophy?**	**Shrinkage in the size of an organ or tissue** due to decrease in cell size and number.	Must know
	2. **What are the causes of atrophy?**	• Disuse • Denervation • Diminished blood supply • Inadequate nutrition • Loss of endocrine stimulation • Pressure	At least 4
	3. Give **some examples of atrophy**	• Fracture disuse • damage to nerves causing muscle atrophy • breast/reproductive organs from oestrogen lack	At least 2

2011.1.3

Question 1. **Cell Death / Necrosis**	**1. Describe the cellular changes in necrosis** PROMPT Start with the cellular features.	• Usually irreversible injury • Often adjacent inflammation • **Swollen cells** • Increased eosinophilia • Myelin figures (whorls of cell membrane bits) • Nucleus fades (karyolysis), may shrink (pyknosis) and then fragments (karyorrhexis) • Organelle disruption → amorphous mass • **Cell membrane disrupted**, contents released	• Swelling • Disruption of cell integrity.
	2. What are the patterns of tissue necrosis? PROMPT What are the different macroscopic appearances of necrotic tissues?	• **Coagulative** (architecture preserved) • **Liquefactive** (digestion → liquid viscous mass) • Caseous (friable white) • *Gangrenous (usually applied to limb. Typically coagulative. Superimposed liquefaction from infection → 'wet gangrene') • *Fat necrosis (focal areas of fat destruction) • Fibrinoid (microscopic feature of Ag-Ab complexes in vessel walls from immune mediated)	• Coagulative • Liquefactive Prompt with names needs to describe difference *these terms clinical not true pathology terms

2011.1.3

Question 2.
 	
Cell derived mediators of inflammation
	1. Which mediators of inflammation are derived from cells?	• Preformed
		  o **Vasoactive amines**
		  ▪ **Histamines**
		  ▪ Serotonin
		• Newly synthesized
		  o **Arachidonic metabolites**
		  ▪ Prostaglandins
		  ▪ Leukotrienes
		  ▪ Lipoxins
		  o Reactive Oxygen Species
		  o Platelet activating factors
		  o Nitric Oxide
		  o Cytokines (TNF, IL1)& Chemokines
			Pass = bold + 1 other

	2. Which cells release histamine?	Widely distributed in tissues, richest sources: • **Mast cells** • **Basophils** • **Platelets**	**Pass =/> 2**
	3. What **are the effects of histamines in an inflammatory response?**	• **Dilation of the arterioles** • **Increased vascular permeability of the venules** • Can cause constriction of large arteries	**Pass = bold (2)**

2010.2.1

Question 1.1 Vascular Changes of Inflammation	1. Describe the vascular changes in acute inflammation 2. What are the mechanisms of increased vascular permeability?	1.1. **Vasodilatation:** opening of arterioles and capillary beds mediated by histamine and Nitric Oxide leading to increased blood flow 1.2. **Increased vascular permeability** 1.3. **Stasis:** due to PP permeability and increased viscosity 2. 2.1. Endothelial contraction / retraction: gaps in venules due to histamine and leukotrienes < 30mins, immediate transient response eg.ultraviolet radiation and kinins and leukotrienes 2-12hrs, delayed prolonged leakage eg. late appearing sunburn 2.2. Direct vascular endothelial injury eg. in severe burns, microbial toxin injury, amplified by neutrophil activation, rapid onset but may last days 2.3. Leukocyte mediated leakage, in venules and pulm capillaries, long lasting for hours 2.4. Trancytosis increased Tx of fluid and protein thru endothelial cell, VEGF	1. All 3 2. 2 out of 4

2010.2.2

Question 2.1 Hypertrophy	1. What is tissue hypertrophy? 2. What are examples of hypertrophy (Prompt: How is it classified??) 3. How is hyperplasia different form hypertrophy?	1.1. **Increase in cellular size not number** leading to overall organ/tissue size increase 1.2. Cell size increased by **more structural components and** increased synthesis of cellular proteins 1.3. Triggered by increased functional demand or stimulation by hormones or growth factors 1.4. Can be selective hypertrophy of specific sub-organelles 2. Examples 2.1. **Physiological** skeletal muscle enhancement through training or uterus under influence of hormones such as oestrogen 2.2. **Pathological** such as cardiomegaly in hypertension and CCF (has an **upper limit** after which regression occurs -> cell injury -> apoptosis/necrosis) 3. Hyperplasia involves an **increase in the number** of cells.	1. Bold 2. Bold (+ 1 example of each) 3. Bold

2010.2.3

Question 3.2 Angiogenesis	1. What is angiogenesis? 2. Please give some examples? 3. What steps are involved in angiogenesis from pre existing vessels?	1. **The process of blood vessel formation in the adult.** 2 methods 1.1. Branching and extension of existing vessels 1.2. Recruitment of endothelial progenitor cells (EPCs) 2. Wound healing, chronic inflammation, proliferating endometrium, tumours, etc 3. Steps in angiogenesis 3.1. Vasodilation 3.2. Proteolytic degradation of basement membrane 3.3. Endothelial cells migrate to angiogenic stimuli 3.4. Maturation 3.5. Capillary formation 3.6. Recruitment of periendothelial cells for support structure formation 4. Inhibitors such as endostatin are released by proteinases (This is a small fragment of collagen that inhibits endothelial proliferation and also angiogenesis)	1. **Bold** and one other 2. **Any 2** 3. **Any 3**

2010.2.4

Question 4.1 Cellular Events of Inflammation	1. How do leucocytes get to an area of acute inflammation? 2. What is the role of leukocytes in acute inflammation?	1.1 **Margination** of WCC in vessels, rolling and adhesion to endothelium (pavementing) (Selectins) 1.2 **Migration** and **diapedesis** across endothelium (PECAM1, CD31, Integrins) 1.3 **Migration towards chemotactic** stimulus in tissue (bacterial products, cytokines, IL8, C5A) 2 2.1 **Recognition and attachment** to materials (opsonins) mediated by receptors 2.2 Killing of microbes: **phagocytosis /engulfment /killing and degradation** (H2O2-MPO-Halide) 2.3 **Release of products –** Amplify the inflammatory reaction (lysosomal enzymes, reactive oxygen/nitrogen)	1. All Bold 2. 3/5 Bold

2010.1.1

			NOTES
Question 1: Reperfusion injury	(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

2010.1.1

Question 2: Apoptosis	a) What is apoptosis ?	**Programmed cell death** / " suicide programme"	
	Prompt *Describe features and purpose of apoptosis*	Remove degraded- un needed cells, Stop excess growth, Tightly controlled Activates degradation enzymes, Intact membrane packaging(es), Phagocytosis encouraged = end point **Non inflammatory.**	Physiological or pathological initiators/ Capsases/ Intrinsic/ extrinsic paths Mitochondrial v death receptor
	b) List some important stimuli for apoptosis ?	a) loss of growth/ stimulating hormones (e.g. GH, nerve growth, loss of sex hormones) b) excessive DNA damage (via p53 build up) c) unfolded protein build up d) developmental atrophy, (embryogenesis) e) proliferative tissues- homeostasis = non useful cells/ excess to function- loss of contact inhibition f) loss of useful cells after finished purpose (e.g. neutrophils/ lymph post inf) g) cells with harmful characteristics (e.g. autoimmune antigens /xs mutations) h) infections (viral leading to cell death) i) parenchymal damage after duct obstruction	3 concepts

2010.1.2

			NOTES
Question 1 Metaplasia	a) What is metaplasia and give some examples?	• **Reversible change** (Among differentiated cells such as epithelial or mesenchymal) • Where **one cell type is replaced by another** by reprogramming of precursor stem cells or undifferentiated mesenchymal cells Examples: • Respiratory tract: trachea and bronchi in respiratory tract – due to chronic irritation such as smoking; ciliated columnar to stratified squamous • GIT: oesophagus – due to chronic gastric acid reflux; squamous to intestinal-like columnar "Barrett's oesophagus"	a) Highlighted and 1/2 examples
	(b) How may metaplasia progress? (Prompt: What is the potential undesirable outcome of metaplasia?)	Cells lose normal protective function Persistence of influence that initiated the metaplasia **initiates malignant transformation** (e.g. squamous cell lung ca; adenocarcinoma oesophagus) Reverses	(b) Highlighted

2010.1.2

Question 2 Wound Healing	a) What systemic factors affect wound healing? (50%)	1)Nutrition- (protein/ Vit C/ zinc/debilitation) 2) Metabolic- partic diabetes/ hypermetabolic/ unwell/ sepsis 3) Hormonal (steroids? effect of other hormone deficiencies/ XS catechols) 4) Circulatory status (e.g shocked/ hypotensive PVD/ venous ob, lymphatic obstruction)/ 5) age 6) drugs	Need **3 factors + 3 examples**
	b) What local factors impede wound healing (50%)	a) **Infection** b) Type/ / size of wound/not opposed c) Position- eg vasc/mvt/ pressure d) foreign bodies e) Wound vascularity/ local pressure excess f) Movement- excess g) Genetic features h) Excessive granulation " proud wounds" i) Neuropathic wounds	**Bold plus** **At least 3 local factors**- some

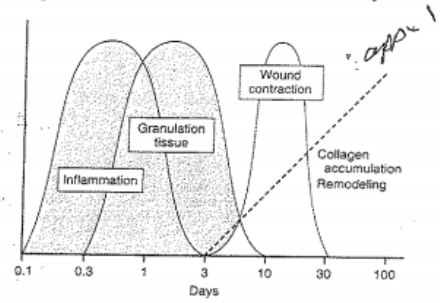
2010.1.3

			NOTES
Question 1: Hypertrophy	(a) What is hypertrophy?	**Increase in the size of cells** – due to the **synthesis of more structural components** – resulting in an increase in the size of the organ; caused by increased functional demand or by hormonal stimulation. – pathological or physiological.	a) Highlighted
	(b) Give examples of physiological and pathological hypertrophy	Physiological – Skeletal muscle (gym etc – workload); Uterus in pregnancy (hormonal) Pathological – Myocardium (due to hypertension, aortic stenosis – workload); BPH	b) One example of each

2009.2

Question 2: Chronic inflammation	(a) What cell types are present in chronic inflammation?	**Macrophages** Lymphocytes Plasma cells Eosinophils Mast cells Neutrophils	Bold plus 2 others to pass
	(b) What processes mediate the persistent accumulation of macrophages seen in chronic inflammation?	1. **Continued recruitment** of monocytes (continued expression of adhesion molecules and chemotactic factors) 2. Local proliferation of macrophages 3. Immobilisation of macrophages	Bold to pass
	(c) What products are released by activated macrophages in chronic inflammation?	**Products associated with tissue injury:** • Toxic O_2 metabolites; Proteases (elastases, collagenases); Neutrophil chemotactic factors; Coagulation factors; AA metabolites; Nitric oxide **Products associated with fibrosis:** • Growth factors (PDGF, FGF, TGF); Fibrogenic cytokines; Angiogenesis factors (FGF); "Remodelling" collagenases	Processes in bold and an example of each Simple list (of 5 or more) passes. Better pass if organised into groups

2009.2

Question 1	Describe the process of skin wound healing by first intention. Prompt: Describe the timeline of these steps.  **FIGURE 3-20** Phases of wound healing. (Modified from Clark RAF: Wound repair. In Clark RAF (ed): The molecular and cellular biology of wound repair, 2nd ed, New York, Plenum Press, 1996, p. 3.)	• 24 hours: Scab; Neutrophils; Clot • 3 to 7 days: Mitoses; Granulation tissue; Macrophage; Fibroblast; New capillary • Weeks: Fibrous union ***<24 hours***: neutrophils at the margins of the incision,. 24 to 48 hours: epithelial cells move from the wound edges and fuse in the midline beneath the surface scab, producing a continuous but thin epithelial layer that closes the wound. ***By day 3***, neutrophils replaced by macrophages. Granulation tissue progressively invades the incision space. Collagen fibres in the margins of incision. Epithelial cell proliferation thickens the epidermal layer. ***By day 5***, the incisional filled with granulation tissue. Neovascularization is maximal. Collagen bridges the incision. The epidermis recovers its normal thickness. ***During the second week***, continued accumulation of collagen and proliferation of fibroblasts. The leukocytic infiltrate, oedema, and increased vascularity have largely disappeared. ***By the end of the first month***, the scar is made up of a cellular connective tissue devoid of inflammatory infiltrate, covered now by intact epidermis.	Timeline + • Clot • Inflammation (neutrophils + macrophages) • Granulation • Remodelling

2009.2

Question 1: Reversible Cell Injury	What are the morphological and chemical changes associated with early cell injury.	1. Decreased generation of ATP 2. Loss of cell membrane integrity 3. Defects in protein synthesis 4. Cytoskeletal damage 5. DNA damage	3 out of 5 to pass
Question 2:	What are the phenomena that characterize irreversible cell injury	The first is the inability to reverse **mitochondrial dysfunction** (lack of oxidative phosphorylation and ATP generation) even after resolution of the original injury. The second is the development of profound **disturbances in membrane** function.	Bold to pass
Question 3:	Can you give an example of a protein that leaks across degraded cell membranes? Prompt – "specific organs"	1. Cardiac muscle – contains a specific isoform of the enzyme creatine kinase and of the contractile protein troponin. 2. Liver (and specifically bile duct epithelium) – contains a temperature-resistent isoform of the enzyme alkaline phosphatase. 3. Hepatocytes – contain transaminases.	1 example to pass

2009.2

Question 2: Host Defences	(a) What are the normal barriers to infection by ingested pathogens in the gastrointestinal tract?	• Acid gastric secretions; • viscous mucosal layer; • lytic pancreatic enzymes; • bile detergents; • secreted IgA antibodies; • competition for nutrients with commensal bacteria; • clearance by defaecation	3/7 to pass
	(b) Describe the barriers to infection that exist within the respiratory tract.	• **Mucociliary blanket** within upper airways for trapping large microbes • **Coughing** (clears microbes from trachea) • **Ciliary action** within trachea and large airways (moves them up to be swallowed) • **Alveolar macrophages** or neutrophils attack and destroy microbes	2/4 to pass
	(c) What processes can disrupt the normal protective mucociliary action?	• Smoking; • cystic fibrosis (viscous secretions); • aspiration of stomach contents; • trauma of intubation; • viral infection; • bacterial infection	3/6 to pass

2009.1

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

2009.1

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?

2009.1

Question 4: **Vitamin K**	**What is the function of Vitamin K?**	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	Need 3/4
	What are the causes of Vitamin K deficiency?	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)	Should know all the clotting factors and Protein C & S

2008.2

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

2008.2

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

2008.2

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.

2008.2

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

2008.1

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

2008.1

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

2008.1

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

2008.1

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.	

2008.1

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.