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TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	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
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 infl) 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
Question 3: Emphysema	1. What is the pathological definition of emphysema?	"Emphysema is a condition of the lung characterised by abnormal permanent **enlargement of the airspaces** distal to the terminal bronchiole, accompanied by **destruction of their walls**, & without obvious fibrosis"	**Bold to pass** Permanent Enlargement + destruction
	2. Describe the pathogenesis of emphysema	**Protease – antiprotease theory** ***Alveolar wall destruction results from an imbalance between proteases (mainly elastase) and antiproteases*** **Elastases** from **Neutrophils**, also Macrophages, Mast cells, pancreas, bacteria **Anti-elastases**: **α_1AT**, secretory leukoprotease inhibitor, serum α_1 macroglobulin **α_1AT** inhibits neutrophil proteases. PiZZ variant predisposes to emphysema Neutrophils normally sequestered in lung (L > U) and a few gain access to the alveolar space. - Any stimulus that ↑ number of leukocytes (neutrophils / macrophages) in lung or release of their elastase containing granules ↑ elastocytic activity. - Stimulated neutrophils also release **oxygen free radicals** which inhibit α1-AT activity meaning process of elastic tissue destruction is unchecked	Know that key is imbalance between proteases (mainly elastase) and antiproteases
	3. What is the role of cigarette smoke?	• Smokers have ↑ **neutrophils & macrophages in alveoli**, - smoking stimulates neutrophil chemotactic factor (e.g. IL-8), nicotine chemotactic, smoke activates alternative complement pathway • **Smoking stimulates release of neutrophil elastase,** proteinase 3, Catepsin G • Smoking ↑ elastase activity in macrophages (not inhib by α1-AT) • Reactive oxygen species in cigarette smoke deplete glutathione and superoxide dismutase Note centri-acinar distribution due to impaction of smoke particles in small bronchi / bronchioles with neutrophil influx. Differs to pan-acinar emphysema associated with α1-AT deficiency and chronic low level proteolysis from neutrophils in transit through the lung circulation.	2 effects

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Question 4: Aortic dissection	a) Describe the pathogenesis of an aortic dissection.	a)Medial weakness (commonly from **hypertension**), medial hypertrophy vasa vasorum, **intimal tear**, blood flow dissects the media -> medial haematoma. Cystic medial degeneration Risk factors - HT, CT disease eg Marfan's, Ehlers-Danlos, iatrogenic, pregnancy,	**Bold to pass**
	b) How are aortic dissections classified?	**By site of involvement, proximal (A) and distal (B),** DeBakey I, II, III I – ascending and descending II – ascending only III – descending only (better prognosis)	**bold**
	c) What are the potential consequences of the disease?	Rupture back into intima or out through adventitia Most common cause of death is rupture into pericardial, pleural or peritoneal cavities Other outcomes include cardiac tamponade, aortic insufficiency, MI, extension into any of the branches of the aorta causing obstruction +/- ischaemia, transverse myelitis	At least 3
Question 5: Meningitis	a) Classify meningitis with examples of important causes.	- Acute pyogenic: bacterial - Aseptic: viral, chemical - Chronic: infection: TB, infiltration: carcinomatous	Must have bacterial and viral and at least one other
	b) What are the likely organisms causing acute bacterial meningitis in different age groups?	◦ E coli/Group B strep: neonates ◦ Pneumococci: infants/older(all ages beyond neonates really) ◦ Meningococci: All ages beyond neonates esp. young adults ◦ Haemophilus: Children but decreased incidence with Immunisation ◦ Listeria. extremes of age ◦ Unusual orgs e.g staph aureus post N/surg. Immuno compromised eg gram negatives.	3 of 6
	c) What are the typical CSF findings in acute bacterial meningitis?	◦ Raised pressure ◦ Turbid ◦ Raised protein ◦ Lower glucose ◦ *Raised neutrophils ◦ *+ve bacteria on gram stain or culture	* and one other

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TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	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
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
Question 3: Coagulation Cascade	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**

Question 4: Portal Hypertension	1. Classify portal hypertension giving examples for each. Prompt for most important hepatic cause.	**Increased resistance to portal blood flow classified as:** - **Pre hepatic**: portal vein thrombosis or narrowing - ***Hepatic: cirrhosis,** granulomatous disease, massive fatty change, schisto, nodular regenerative hyperplasia - **Post hepatic**, R heart failure, constrictive pericarditis, hepatic vein occlusion	3 groups including hepatic. Cirrhosis and one other cause
	2. What are the major clinical consequences of portal hypertension due to cirrhosis?	- Ascites: with potential for infection - Porto systemic venous shunts: varices > upper GI bleed. Other sites e.g caput, h'roids, retroperit. - Splenomegaly: thrombocytopenia - Hepatic encephalopathy > coma	At least 3 consequences
	3. What mechanism are involved in the formation of ascites?	- **Starlings forces**: increased pressure, decreased albumin - Increased formation of hepatic lymph overwhelms thoracic duct drainage > percolation into peritoneum - Intestinal fluid leak: ^pressure in intestinal capillaries and osmotic effect of protein rich ascitic fluid - Renal retention of Na and H2O due to 2ndary ^aldosterone.	Starlings forces and one other
Question 5: Influenza	i) Describe the structure and classification of influenza viruses	**ssRNA, bound by nucleoprotein that determines type (A, B or C) and a lipid bilayer that contains both haemagglutinin and neuraminidase** (determining subtype eg H1N1)	Need RNA and major types
	ii) What is the difference between antigenic drift and shift?	Only in influenza type A **Drift – mutation** of the haemaglutinin and neuraminidase antigens allowing escape from most host antibodies (epidemic) **Shift – antigens replaced via recombination of RNA** segments with those of animal viruses (pandemic) Types B and C do not show drift or shift, mostly infect children, who develop antibodies preventing re-infection	Bold
	iii) How does the human body clear a primary influenza virus infection?	**2 mechanisms – cytotoxic T cells and macrophages** cytotoxic T cells kill virus infected cells, an intracellular antiinfluenza protein (Mx1)is induced in macrophages by cytokines IFN-a and IFN-b. Future infection is prevented (haemagglutinin Ab) and ameliorated (neuraminidase Ab)	Bold to pass

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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
Question 2: Oedema	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
Question 3: Type 2 Hypersensitivity – Antibody mediated	1. What is type 2 hypersensitivity?	"Type 2 hypersensitivity is **mediated by antibodies** directed toward antigens present on the surface of cells or other tissue components"	Antibody mediated One of cell surface & extracellular matrix
	2. Describe the different types of type 2 hypersensitivity reactions and give examples of each.	**Three types** **(A) Opsonisation, Complement & Fc Receptor Mediated Phagocytosis** • Ig G,M activate complement, C3b & C4b recognised by phagocytes • activates complement system & membrane attack complex causing lysis of cells • Ig G recognised by phagocytes • Ab dependent cellular cytotoxicity (ADCC) Mono, Macro, Neut, Eosin, NK - transfusion reactions - erythroblastosis foetalis - auto immune haemolytic anaemia; agranulocytosis; thrombocytopaenia - certain drug reactions **(B) Complement and Fc receptor Mediated Inflammation** *C5A (+C4A & C3A) stimulate Neutrophil and Monocyte attack via Fc receptors releasing enzymes and Oxygen free radicals* *e.g: glomerulonephritis* *Vascular Organ graft rejection* *Goodpastures* **(C) Antibody Mediated Cellular Dysfunction** *Antireceptor antibodies disturb the normal function of receptors without causing cell injury.* e.g. myasthenia gravis (ACh receptor antibodies) Graves Disease - pemphigus vulgaris	2 of 3 types with one example Able to describe complement dependant reaction plus one other with examples

Question 4: Hepatitis D	i) Describe how the Hepatitis D virus infects the human body	RNA virus **Must always be in conjunction with Hep B** 1) **acute infection** – indistinguishable from classical acute Hep B.) Exposure to serum containing both Hep B and D. HBV must establish first to provide HBsAg necessary for development of complete HDV viridons 2) **superinfection.** -chronic HBV carrier exposed to new inoculum of HDV. Disease develops 30-40 days later 3) helper-independent latent infection- in liver transplantation patients	Bold to pass
	ii) Prompt: *Superinfection is one of the ways that Hepatitis D can infect the human host.* How does superinfection with HDV manifest?	1) severe acute hepatitis in previously unrecognised HBV carrier 2) exacerbation of preexisting mild chronic hepatitis B 3) 80-90% chronic progressive disease and cirrhosis	Need one
	iii) How is Hepatitis D infection diagnosed?	**IgM anti-HDV** – most reliable marker of recent HDV exposure but late and short lived HBV an HDV coinfection – best with IgM against both HDAg and HBcAg *2 phases –* *acute phase – active HDV replication, suppression of HBV, high ALT levels* *chronic phase – HDV replication decreases, HBV replication increases, ALT levels fluctuate, progression to cirrhosis and hepatocellular cancer* *HDV RNA detectable in blood and liver just prior and in early days of acute symptomatic disease* *In chronic delta hepatitis, HBsAg is present and IgM and IgG anti-HDV antibodies persist for months*	At least one
Question 5: Haemolytic anaemia	1. Classify haemolytic anaemias	- Intravascular/extravascular Or - extrinsic/intrinsic to the RBC. Or - hereditary/acquired	One classification,
	2. Describe the common features of haemolytic anaemias.	Features: - *Decreased RBC life span(< 120/7) due to premature destruction - ^ erythropoietin and erythropoiesis - Accumulation of products of Hb catabolism - reticulocytosis	• premature RBC destruction and one other feature
	3. Give some important causes of intravascular haemolysis. Prompt for examples	Intravascular - Mechanical injury: cardiac valves, microangiopathic. repetitive physical trauma - Complement fixation: ABO incompatible blood transfusion - Intracellular parasites: malaria - Exogenous toxins: clostridia	• 2 of 4
	If required **4. Apart from anaemia what are the results/manifestations of intravascular haemolysis?**	**- *Haemoglobinaemia** **- Haemoglobinuria** **- *Unconjugated hyperbilirubinaemia(jaundice) from catabolism of haem groups in mononuclear phagocyte system** **- Haemosiderinuria and renal haemosiderosis** **- Decreased serum haptoglobin due binding with free Hb and then cleared by monophag system.** **- Free Hb oxidized to metHb** **- Reticulocytosis**	* **Hbaemia and hyperbilirubinaemia to pass and one other** **OR 3 of 7**