Immunology VIVAs (Pathology)

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2014.2.D.1

Question 4 Type 4 hypersensitivity reaction (pp 205-208; 1356) **Subject:** Path LOA: 1	1. Describe the sequence of events that lead to this reaction. Prompt: what cells are involved?	Injury **Initiated by antigen** sensitised CD4+ or CD8+ **T cells** Retinal antigens may be transported in the lymphatics of the damaged eye Reaction may occur in both eyes causing a Pan Uveitis. CD4+ predominate in autoimmune disease CD8+ in post infectious (esp viral) reactions **Can be cytokine** (CD4+ Th1 or TH17 cells involved) **or direct cellular** (Cyotoxic lymphocyte) **mediated** tissue injury (either satisfactory).	Requires antigen and either cytokine or direct cellular mechanisms to pass
	2. What tissue changes would occur	Perivascular cellular infiltrates, tissue oedema, granuloma formation, cell destruction.	**(2/4 to pass)**
	3. Name other examples of Type IV hypersensitivity reactions.	Type I diabetes Multiple sclerosis Rh arthritis Inflammatory bowel disease Guillain Barre Contact sensitivity dermatitis Tuberculin reaction Granulomatous diseases Viral hepatitis	**(2 examples to pass)**

2014.1.B.3

Question 1 Type 1 hypersensitivity reaction **Subject:** Path LOA: 1	1.What type of hypersensitivity reaction is involved? 2.What are the sequence of events involved in type I hypersensitivity reactions following re exposure to an allergen?	**Type 1** **Mast cells** armed with pre formed **IgE antibodies** > on re exposure to **specific antigen** > **release of mediators** from mast cells: **1. preformed mediators – e.g histamine**/ proteases/ chemotactic factors, 2. lipid mediators e.g leukotrienes C4 and D4/ PG D2/ PAF and 3. Cytokines e.g TNF and chemokines > **Immediate and late phase reactions**	**Bold**
	3.What changes occur at the tissue level?	1.Vasodilatation 2.increased vascular permeability 3. smooth muscle spasm/ bronchospasm 4. cellular infiltration 5. epithelial damage	**3 of 5 to pass**

2013.2.C.1

Question 4 **PATHOLOGY** **Type 3 Hypersensitivity** LOA: 1 (Robbins pp 204-205)	1. What is the pathogenesis of serum sickness? Prompt (if required): How is the tissue damage caused?	**1. Type 3 hypersensitivity** Phase 1: **Formation** of **Immune complexes.** Protein Ag, 1/52 -> Ab -> blood -> Ag-Ab complexes Phase 2: **Deposition** of immune complexes. Medium size, Ag excess most pathogenic High pressure filtration , glomeruli, joints Phase 3: **Tissue injury** caused by immune complexes **Acute inflam reaction** ~ day 10 IgG & IgM (C' fixing Ab) bind to leukocyte Fc receptors. Leuk recruitment and activation - release proteases/lysozymal enzymes ->damage. Deposition, activation and Consumption of C' and decreased C3 levels -> inflam reaction and tissue damage	Bold 3 Phases
	2. What are some clinical features?	2. Fever, urticaria, arthralgia, LN enlargement, proteinuria	3 of 5
	3. What are some other examples of Type III hypersensitivity?	3. Acute: post strep G-N, reactive arthritis, Arthus reaction Chronic: SLE, PAN, other vasculitides, possibly membranous G-N,	3 examples

2013.1.1

Question 2 Type 2 Hypersensitivity Reaction LOA: 1	1. What is Type 2 hypersensitivity? 2. Describe the mechanisms involved giving examples for each mechanism.	**1 Hypersensitivity caused by antibodies that react with antigens present on cell surfaces or in the extracellular matrix** Antigens can be intrinsic to the membrane or matrix or extrinsic eg. Drug metabolite **2 a) Opsonisation & phagocytosis: IgG antibodies opsonise cells plus complement activation** generates C3b & C4b recognized by phagocyte Fc & protein receptors resulting in **phagocytosis & destruction of opsonised cells** ADCC- cells coated with Abs killed by monos, neutros, eosinos and NK cells **Examples:** transfusion reaction, erythroblastosis fetalis, autoimmune haemolytic anaemia, agranulocytosis,, thrombocytopaenia, drug reactions when a drug acts as a hapten **b) Complement and Fc receptor mediated inflammation: antibodies bind to fixed tissue** such as basement membranes, extracellular matrix ... **activates complement** ... generate by-products particularly chemotactic agent C5a ... direct PMN migration and C3a and C5a = **increase vascular permeability. PMNs activated** by C3a and Fc receptors... release of pro-inflammatory substances like prostaglandins, production of lysosomal enzymes, reactive O2 species **Examples:** glomerulonephritis, vascular rejection in organ grafts, vasculitis caused by ANCA, Goodpastures c) **Antibody mediated cellular dysfunction:** antibodies directed against cell surface **receptors impair or dysregulate function without causing cell injury or inflammation** **Examples:** myasthenia gravis, Graves's disease, insulin resistant diabetes, pemphigus vulgaris, pernicious anaemia	Bold (concept)_ Bold 2/3 With 1 example in each

2013.1.3

Question 2 LOA: 2 The normal immune response	1. What are the major classes of lymphocytes? 2. What is the role of each class of lymphocytes in the normal immune system? Prompt- What is the role of B-cells? What is the role of T-Cells?	1. B lymphocytes CD4+ helper T- Lymphocytes CD8+ Cytotoxic T Lymphocytes Natural Killer (NK) Cells 2. Adaptive immunity – circulate widely & rec-circulate esp Ts - respond to foreign substances/Ag. Can become effector or memory cells B cells: recognise Ag via memb IgM/IgD –plasma cell -secretes Ig/Ab = humoral immunity. (B cells also have compl R, FcR, CD40) T cells: Ag specific T cell R - binds to Ag on cells (on MHC molecules on APCs) – activates cell depending on type = cell-mediated immunity CD4/T helper recog class II MHC bound Ag: cytokine release – leads to macrophage activation, inflam, B cell stimulation CD8/ T cytotoxic recog class I MHC bound Ag: infected cell destruction NK Cells- kill inf&tumor cells. No prior exp needed. Healthy cell Class I MHC=>inhibits NK. Can secrete cytokines=>inflame	B&T B-Humoral plus concept T-Cell mediated plus concept

2012.2.3

Q2 Type 1 Hypersensitivity Reaction LOA: 1	1. What is a type I hypersensitivity reaction? 2. What is the immune mechanism that causes it? 3. What pathological effects do the substances released from mast cells have?	1. A **rapid** immunologic reaction due to **antigen and antibody(IgE)** combining. 2. **Previous Ag exposure** results in activation of T_h2 cells results in **IgE Ab production** by B cells. IgE binds to mast cells. **Repeat Ag exposure**, Ag-Ab bind and results in **mast cell degranulation. Vasoactive amines** (Histamine), and lipid mediators (Leukotrienes, PG) released. May have **late phase reaction** (Cytokines) 3. Vascular dilation/ oedema, SM contraction, mucus production	Bold required 3/6 bold with concept 2 to pass

2011.2.1

Question 2 LOA: 1	What diseases are caused by Type 4 hypersensitivity?	Type 1 Diabetes Insulin, Glutamic acid decarboxylase Rheumatoid arthritis Joint synovium Multiple sclerosis Myelin basic protein, proteolipid protein, Crohn's disease ? commensal bacteria Periph neropathy (?GBS) protein Ag of periph nerve myelin Contact dermatitis environmental, e.g. poison ivy	**3** examples to pass
	Describe the tuberculin reaction (Prompt for cellular response and timecourse?)	Responses of differentiated effector T cells TH1 -> cytokines, IFNγ, stim and **activate macrophages** _> inflamm TH17 ->Chemokines, cytokines, IL-17, 22, **recruit neutophils & mono, CD4 cells** **Tuberculin reaction** start **8-12 hr**, peak **21-72** hr **Perivasc cuffing**, endothelial hypertrophy, **epithelioid** cells, **granuloma**	Bold, 3/6 (time delayed as in hours)

2010.2.1

Question 1.2 Antibody Mediated Hypersensitivity	1. What is antibody - mediated hypersensitivity? 2. Describe the mechanisms which mediate the hypersensitivity response 3. List an example or examples for each mechanism	1. **Caused by antibodies that react with antigens present on cell surfaces or in the extracellular matrix** Antigens can be intrinsic to the membrane or matrix or extrinsic eg. Drug metabolite 2. Mechanism of hypersensitivity response 2.1. **Opsonisation and phagocytosis: IgG antibodies opsonise cells plus complement activation** generates C3b and C4b recognized by phagocyte Fc and protein receptors resulting in **phagocytosis and destruction of opsonised cells** **Examples:** transfusion reaction, erythroblastosis fetalis, autoimmune haemolytic anaemia, agranulocytosis, thrombocytopaenia, drug reactions when a drug acts as a hapten 2.2. **Complement and Fc receptor mediated inflammation: antibodies bind to fixed tissue** such as basement membranes, extracellular matrix ... **activates complement** ... generate by-products particularly chemotactic agent C5a ... direct PMN migration and C3a and C5a = **increase vascular permeability. PMNs activated** by C3a and Fc receptors... release of pro- inflammatory substances like prostaglandins, production of lysosomal enzymes, reactive O2 species **Examples:** glomerulonephritis, vascular rejection in organ grafts, vasculitis caused by ANCA, Goodpastures 2.3. **Antibody mediated cellular dysfunction:** antibodies directed against cell surface **receptors impair or dysregulate function without causing cell injury or inflammation** **Examples:** myasthenia gravis, Graves's disease, insulin resistant diabetes, pemphigus vulgaris **2.4. Antibody dependant cellular cytotoxicity** **Examples:** IgG coats cells, effector cells such as monocytes, neutrophils, eosinophils and NK cells then bind and lyse cells without phagocytosis, role in specific diseases uncertain.	1. Bold 2. Bold 2/4 3. 2/4

2010.2.3

Question 3.1 Type 1 (Immediate) Hypersensitivity	1. What are the features of Type 1 hypersensitivity? 2. What are the actions of mast cell mediators in Type I Hyeprsensitivity (and give examples) 3. What is the late phase reaction	**1.1. Immediate reaction, , previously sensitised individuals, IgE mediated** 1.2. **Mast cell** and or basophils involved 1.3. **Mediators** involved include Histamine, other amines, enzymes proteases, proteoglycans, heparin, leukotrienes, C4, PAF, Prostaglandins, Cytokines **2.1 Cellular infiltration –** leukotrienes, chemotaxis, PAF, Cytokines 2.2 **Vasoactive effects –** Hist, PAF, Leukotrienes, PG D4 **2.3 Smooth muscle spasm –** leukotrienes, histamine, PG, PAF **3 Ongoing inflammatory reaction without additional exposure to triggering ag**	1. 3/5 bold 2. Histamine + 2 others + reasonable actions 3. Ongoing

2010.1.3

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

2009.2

Question 1: Type I Hypersensitivity	What is a Type I hypersensitivity reaction?	**Rapid immunologic reaction (minutes)** **Antigen – antibody** **IgE** Mast cells Previously sensitised individual	Bold to pass
Question 2:	What are the Primary mediators within the mast cell granules and their actions.	1. **Biogenic amines/histamine**. The most important vasoactive amine is histamine. **Histamine** causes intense smooth muscle contraction, increased vascular permeability, and increased secretion by nasal, bronchial, and gastric glands. 2. **Enzymes. (named)** These are contained in the granule matrix and include neutral proteases (chymase, tryptase) and several acid hydrolases. The enzymes cause tissue damage and lead to the generation of kinins and activated components of complement (e.g. C3a) by acting on their precursor proteins. 3. **Proteoglycans**. These include heparin, a well-known anticoagulant, and chondroitin sulfate. The proteoglycans serve to package and store the other mediators in the granules.	Pass – 2 out of 3 groups must include biogenic amines and example of each
Question 3: **(if time)** Second, Late-phase Reaction	What characterizes the second, late-phase reaction?	The late phase reaction is characterized by infiltration of the tissues with eosinophils, neutrophils, basophils, monocytes, and CD4+ T cells as well as tissue destruction, typically in the form of mucosal epithelial cell damage. Time course 2-24 hours later without additional exposure – may last for days.	

2009.1

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 $T_H1$cells 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, **perivascular 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 $T_H1$cells after recognising antigen presented on APCs in association with class II MHC molecules. **$T_H1$cells** can enter the circulation and remain in the **memory** pool of T cells for long periods (years)	2/4 bold

2008.2

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

2008.2

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