The Royal College of Pathologists
Pathology: the science behind the cure

Part 1 examination

Immunology: First paper

This paper is for both medically qualified and clinical scientist candidates

Tuesday 23 September 2014

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

Each part of a question is awarded equal marks unless otherwise stated in the question.

Question 1
Answer both parts of this question.

a) Briefly outline five non-immune, non-specific defenses against infection. For each give a single example of the clinical consequence(s) when this is impaired. *(25% of marks for this question)*

b) Describe the major elements of the innate immune system that provide defence against pyogenic infection. Illustrate your answer with five diverse examples of defects in the elements described and their clinical consequences. *(75% of marks for this question)*

Question 2
Answer all three parts of this question.

a) Describe the usual pathway by which bradykinin is generated and causes angioedema. *(20% of marks for this question)*

b) List the known types of bradykinin-mediated angioedema. *(20% of marks for this question)*

c) Describe the mechanisms by which genetic, environmental and therapeutic factors may affect bradykinin-mediated angioedemas. *(60% of marks for this question)*

Question 3
Answer all three parts of this question.

a) Define the terms “traceability” and “uncertainty of measurement”. *(25% of marks for this question)*

b) Compare and contrast the traceability of a measurement of serum total IgG and the measurement of serum IgG antibodies to glomerular basement membrane. *(25% of marks for this question)*

c) Describe the sources of uncertainties from end-to-end (request to report) associated with a test, giving examples where appropriate. *(50% of marks for this question)*

Question 4
For each of the following molecules outine their (i) production, (ii) function, and (iii) clinical effects of genetic variation:

a) Complement factor H.

b) Phagosomal NADPH oxidase.

c) STAT 3.

Question 5
Answer both parts of this question.

a) Describe the clinical utility of laboratory-based component-resolved diagnostic testing in allergy. Illustrate your answer using hazelnut, latex and soya as examples.

b) What is mastocytosis? Describe the symptoms which occur and the classification of mastocytosis. What are the key investigations required to diagnose mastocytosis?

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Tuesday 25 March 2014
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Each part of a question is awarded equal marks unless otherwise stated in the question.

Question 1
Answer both parts of this question:

a) Write short notes on the mechanisms of basophil activation.

b) Describe the characteristics of a granuloma and the key immunological events that lead to its formation.

Question 2
Answer both parts of this question:

a) Briefly describe the cells and receptors involved in allergen capture and the co-stimulatory proteins and cytokines involved in the synthesis of specific IgE.

b) Write short notes on the molecular mechanisms and clinical significance of primary immune deficiencies that specifically predispose to mycobacterial infection.

Question 3
Outline the function, cellular distribution and clinical significance associated with defects in gene expression of the following proteins:

a) IL-2RG (common gamma chain).
b) STAT-3.
c) FOXP3.

Question 4
Write short notes on each of the following:

a) Proteins and organelles involved in the formation of MHC class II-peptide complexes.

b) Immunological mechanisms of antibody-mediated solid organ rejection.

c) The clinical utility of flow cytometric determination of peripheral blood memory B cell subsets.

Question 5

Answer both parts of this question:

a) Outline the most important molecular events and phenotypic changes that take place during antigen-independent B cell maturation. Where known, give examples of genetic defects that can cause disease in humans.

b) Describe the contribution of the HLA-DQ2 (DQA1*05:01, DQB1*02:01; also known as DQ2.5) allele to the pathogenesis of coeliac disease.

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Tuesday 24 September 2013

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

Each part of a question is awarded equal marks unless otherwise stated in the question.

1. Answer both parts to this question:

a) Outline the development of Th17 T cells. Discuss both their physiological role and human diseases associated with Th17 pathway abnormalities. *(Two thirds of marks for this question)*
b) Outline the principles of both (i) population screening of newborns for severe combined immunodeficiency, and (ii) the current methodology used for this purpose. *(One third of marks for this question)*

2. Answer both parts to this question:

a) Write short notes on immunoglobulin class switching, illustrating your answer with examples of the failure of these processes in man.
b) Describe the processes involved in the generation of immunoglobulin antigen diversity. You may use annotated diagrams in your answer if you wish.

3. Answer both parts to this question:

a) Outline mechanisms of immune defence that protect man from pneumococcal infection, illustrating your answer with genetic disorders that lead to increased susceptibility to pneumococcal sepsis. *(Two thirds of marks for this question)*

b) Briefly describe (i) the clinical features, (ii) the diagnosis, and (iii) the principles of treatment of mevalonate kinase deficiency. *(One third of marks for this question)*

4. Answer both parts to this question:

a) Define immunological tolerance and briefly describe the mechanisms of T cell tolerance, giving examples of single gene defects leading to failure of these processes in man.
b) Briefly describe the mechanisms of allergen specific immunotherapy.

5. Answer all three parts to this question:

a) Compare and contrast the key features of recognition receptors in the innate and adaptive immune systems. *(One quarter of marks for this question)*
b) Discuss the ligands and molecular signaling pathways relevant to Toll-like receptors (TLR). You may use annotated diagrams in your answer if you wish. *(Half of marks for this question)*

List defects in TLR pathways that are known to result in human disease. *(One quarter of marks for this question)*

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Part 1 examination

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Tuesday 25 September 2012

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

Each part of a question is awarded equal marks unless otherwise stated in the question.

1. Describe the transcription factors and cytokines critical for determining the differentiation of post-thymic naïve CD4 T cells. Describe the resulting phenotypes and functions of each T helper cell subset. Using examples from human disease, briefly discuss the clinical consequences of deficiency of two named transcription factors.

2. Answer both parts of this question:

   a) Describe the steps in activation and control of the alternate complement pathway. You may use a diagram to illustrate your answer if you wish.

   b) Describe the role of complement in the humoral immune response. How do inborn complement defects affect antibody production and function?

Please turn over for questions 3, 4 and 5

3. Write short notes on each of the following topics:

    a) IgE-independent mechanisms of mast cell degranulation.

    b) How defects in apoptosis predispose to lymphoid malignancy.

    c) How acetyl choline receptor antibodies cause disease.

4. Write short notes describing the mechanisms of action and widely recognized clinical applications for each of the following drugs:

    a) Icatibant.

    b) Mycophenolate mofetil.

    c) Rituximab.

    d) Omalizumab.

5. Write short notes describing the cellular distribution, function, and biological significance of each of the following receptors:

    a) Toll-like receptor 3.

    b) CD23 (Fc**ε**RII).

    c) CXCR4.

End of paper

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Part 1 examination

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Tuesday 20th March 2012

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

Each part of a question is awarded equal marks unless otherwise stated in the question.

1 Write short notes on the molecular mechanisms and clinical significance of each of the following:

a) Receptor-ligand interactions between the human immunodeficiency virus (HIV) and cells of the immune system.

b) Mendelian susceptibility to mycobacterial infection.

c) T-dependent and T-independent antibody responses.

2 Using short note format, describe the functions and normal expression of each of the following proteins, and the clinical features associated with defects in their genes:

a) Recombinase-activating genes (RAG)

b) Fas (CD95)

c) Autoimmune regulator (AIRE).

Please turn over for questions 3, 4 and 5

3 Answer both parts of this question:

a) Outline the immunological mechanisms involved in rejection of renal allografts.

b) Describe the strategies for the prevention and treatment of renal transplant rejection, giving examples where relevant.

4 Using short note format, answer all three parts of this question:

a) Describe the regulation of natural killer cell activation.

b) Describe the mechanisms by which cytomegalovirus evades immune recognition.

c) Briefly outline the features of human primary immunodeficiency disorders where herpes virus susceptibility is the predominant feature. Describe the mechanisms of this susceptibility where known.

5 Write short notes on the importance of each of the following in the synthesis of IgE. Use examples from immunodeficiency disorders or the treatment of allergic disease to illustrate your answer.

a) Co-stimulatory molecules.

b) Cytokines.

c) Enzymes and transcription factors involved in immunoglobulin class switching.

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Part 1 examination

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Tuesday 20th September 2011

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

Each part of a question is awarded equal marks unless otherwise stated in the question.

1 Write short notes on each of the following, including details of the molecular mechanisms in your answer.

a) T lymphocyte trafficking, with particular relevance to mesenteric lymph nodes and the intestine.

b) Transepithelial transport of immunoglobulins.

c) Killing of a virally infected cell by CD8 cytotoxic T cells.

2 Answer both parts of this question.

a) Compare and contrast the structure, expression and functions of MHC class I and class II molecules.

b) Briefly describe the organisation of the MHC class II locus. Using relevant examples discuss the mechanisms by which this locus may be associated with autoimmune disease.

Please turn over for Questions 3, 4 & 5

3 Briefly describe the molecular mechanisms of each of the following, and discuss how these determine the principles of treatment of the condition.

a) Hereditary angioedema type 1.

b) IgE-mediated anaphylactic reactions.

c) TNF-receptor-associated periodic syndrome.

4 Write short notes on each of the following:

a) Mechanisms of bacterial killing by neutrophils.

b) The role of cytokines and co-stimulatory molecules in regulating the synthesis of IgE.

c) Human Toll-like receptors and their role in protection from viral infection.

5 Answer all three parts of this question.

a) Briefly outline the development of B lymphocytes in peripheral lymphoid organs. Include reference to lymphomas associated with each stage of development.

b) Describe the principles of identification of clonality in the diagnosis of T and B cell lymphomas.

c) Briefly describe the principles of *in vitro* monoclonal antibody production, and comment on the different structural types of therapeutic monoclonal antibodies available. (A list of individual therapeutic monoclonal antibodies is not required).

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Part 1 examination

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Tuesday 22nd March 2011

Candidates must answer FOUR questions ONLY

Time allowed: Three hours

Each part of a question is awarded equal marks unless otherwise stated in the question.

1 Answer both parts of this question:

a) The first postulate of the clonal selection hypothesis states that: "*Each lymphocyte bears a single type of receptor with a unique specificity*". Briefly describe the molecular mechanisms that generate T lymphocytes with unique specificities, illustrating your answer with inherited diseases caused by defects in this process.

b) The second postulate known as clonal expansion states that: "*On binding antigen the lymphocyte is activated to divide and to produce many identical progeny*". Briefly describe the mechanisms that regulate and restore the lymphocyte pool after clonal expansion has occurred, illustrating your answer with the inherited diseases associated with defects in this process.

Please turn over for Questions 2, 3, 4 & 5

2 Write short notes on each of the following:

a) The mechanisms of human immunity to fungal infections.

b) The molecular basis of genetic disorders associated with predisposition to fungal infection in humans.

c) The mechanisms and clinical consequences of hypersensitivity reactions to *Aspergillus*.

3 Write short notes on each of the following molecules. You should refer to the cellular distribution, ligands, known functions, and any associated diagnostic or clinical significance.

a) CD40 ligand (CD154).

b) B cell activating factor receptor (BAFF-R).

c) CD20.

4 Answer all parts of this question:

a) Briefly describe the development, cellular characteristics and functions of eosinophils.

b) Give a brief account of the regulation of B cell isotype switching to IgE production with emphasis on the cellular and molecular processes involved.

c) Some antigens are more likely than others to elicit an IgE antibody response. Giving relevant examples, describe the factors that are thought to affect the allergenicity of an antigen.

5 Write short notes on each of the following T cell subsets, with reference to their development, phenotype and mechanisms of action.

a) Th17 cells.

b) Natural regulatory T cells (T-regs).

Invariant natural killer cells (iNKTs).

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Tuesday 21st September 2010

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

Each part of a question is awarded equal marks unless otherwise stated in the question.

1 Answer both parts of this question:

a) Compare and contrast the immune responses needed to protect against infection with the measles virus and against the effects of tetanus toxin. *(20% of marks)*

b) Describe the cellular mechanisms by which the currently used vaccines against measles virus and tetanus toxoid induce protective immune responses in man. *(80% of marks)*

2 For each of the following molecules, using short notes, describe their cellular expression, how they interact with both their ligand and their receptor, and their function:

a) HLA-A.
b) HLA-DR.
c) HLA-DM.
d) HLA-E.
e) CD1.

Please turn over for Questions 3, 4 & 5

3 Write short notes on the biology, clinical features, and molecular basis of each of the following:

a) Oral allergy syndrome (illustrate your answer with examples).
b) Wiskott-Aldrich syndrome.
c) Pemphigus.

4 Answer both parts of this question:

a) Explain the principles underlying gene therapy for primary immunodeficiency disorders. Give one example of how it has been used to treat a named primary immunodeficiency disorder. Outline the advantages and disadvantages of gene therapy compared to allogenic bone marrow transplantation.

b) Discuss the principles and use of recombinant allergens in both the diagnosis and treatment of allergic conditions.

5 Answer both parts of this question.

a) Briefly describe the activation and control of the complement pathways. Your answer may be presented as an annotated diagram(s) if you so wish. *(40% of marks)*

b) Describe the pathogenic mechanisms underlying each of the following conditions:
   i. Type II membranoproliferative glomerulonephritis. *(20% of marks)*
   ii. Hypocomplementaemic urticarial vasculitis syndrome. *(20% of marks)*
   iii. Paroxysmal nocturnal haemoglobinuria. *(20% of marks)*

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Tuesday 23rd March 2010

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

Each part of a question is awarded equal marks unless otherwise stated in the question.

1 Write short notes on each of the following:

a) Compare T-dependent and T-independent antibody responses.

b) Describe the strategies used by the immune system to resist infection by encapsulated organisms. Illustrate your answer with examples of human immune deficiency predisposing to infections with such organisms.

c) Briefly describe the contribution of Toll-like receptor signalling to the protection of the human host from viral infection.

2 Write short notes on each of the following:

a) Explain the role of tumour necrosis factor in the acute phase response to sepsis. *(25% of marks for this part)*

b) What do you understand by the term "inflammasome"? Briefly describe the role of the inflammasome and its modulators in inflammation, illustrating your response with known defects found in auto-inflammatory disease. *(50%)*

c) Describe how cytokines can be targeted in the treatment of the auto-inflammatory diseases. *(25%)*

Please turn over for Questions 3, 4 & 5

3 Write short notes on each of the following:

a) Describe the mechanisms underlying the generation of central and peripheral tolerance in T and B lymphocytes.
b) Describe the genetic abnormalities in monogenic disorders (excluding SCID variants) that are associated with failure of immune tolerance, and outline the mechanisms by which these cause disease. In your answer briefly describe any relevant animal models.
c) Describe the classification and mechanisms of renal allograft rejection.

4 Write short notes on each of the following:

a) Mechanisms of bacterial killing by neutrophils.
b) Defects of interferon gamma receptors.
c) The source, functions and disease associations of B-cell activating factor (BAFF).

5 Answer both parts of this question.

a) Describe the classification of human mast cells and list their mediators. Describe the four most important mechanisms by which drugs can cause mast cell activation, using specific examples to illustrate each mechanism you describe.
b) Outline the classification, causes and pathophysiology of urticaria.