THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 14 March 2006

IMMUNOLOGY

Second Paper *(For Non-Medical Candidates)*

Candidates must answer FOUR questions ONLY and must answer all parts of multi-part questions

Time allowed - THREE HOURS

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1. Your Immunology laboratory is reviewing its repertoire of tests. Comment on the advantages and disadvantages of each of the changes suggested, and in each case how you would implement quality assurance if the changes were adopted:

   a) Replacement of testing for rheumatoid factor by testing for antibodies to cyclical citrullinated peptide

   b) The introduction of serum free light chain quantitation in place of urine free light chain electrophoresis

   c) Change in method for anti-nuclear antibody detection from indirect immunofluorescence to ELISA

   d) The introduction of flow cytometric detection of CD40-ligand

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

2. Please answer all parts of this question:

   a) Outline the key features of the immunopathology and clinical disease associations of infection with Human T Lymphotropic Virus type 1 (HTLV-1).

   b) Outline the immunological features of thymoma with immunodeficiency (Good's syndrome).

   c) Provide a critical commentary on the diagnostic tests available for the investigation of patients with suspected allergy to apples.

3. Define the 'anti phospholipid syndrome'. Critically evaluate laboratory investigations that are needed to establish this diagnosis with reference to the quality control and predictive value of these tests. Discuss other disease states where these tests maybe positive.

4. Please answer all parts of this question using the short notes format:

   a) **Briefly**, discuss the genetic defects that lead to MHC class I and MHC class II deficiency syndromes and the differences in their clinical presentation

   b) Write short notes on molecular defects leading to common variable immunodeficiency

   c) Write short notes on the immunopathology, epidemiology and diagnosis of Latex Allergy

5. Your hospital postgraduate tutor has asked you to write a brief guidance document for hospital doctors on primary immunodeficiency including the methods of presentation, the most useful initial screening tests and criteria for referral to an immunologist. What information would you include in such a document?

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 20 September 2005

IMMUNOLOGY

Second Paper *(For Non-Medical Candidates)*

Candidates must answer FOUR questions ONLY and must answer all parts of multi-part questions

Time allowed - THREE HOURS

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1. Answer both parts of this question:

   a) Critically discuss the clinical utility of measuring serum levels of specific IgE for the diagnosis of food allergy.

   b) What laboratory tests are useful in the investigation of an adult patient with a history of recurrent angio-oedema? Briefly indicate the clinical utility of each test.

2. Write short notes on each of the following:

   a) The autoantibodies associated with Paraneoplastic syndromes.

   b) Anti-glomerular basement membrane antibodies.

   c) The clinical utility of detecting neutrophil cytoplasmic antibodies (ANCA).

Please turn over for Questions 3, 4 and 5

3. Answer all parts of this question:

   a) What are the "biological" agents, which have been, used to block the activity of TNF? Summarise the evidence that supports their clinical use.

   b) Critically discuss the clinical utility of detecting autoantibodies associated with Type 1 diabetes.

4. Answer all parts of this question:

   a) A man of 30 is referred to you because of suspected immunodeficiency. Recently he had been admitted to hospital where a diagnosis of Cryptococcal meningitis had been made. Because of visual disturbance in his left eye he had been referred to the ophthalmologists where a diagnosis of CMV retinitis had been established. His lymphocyte count was 0.6 X 10^9/L. His serum IgG level was reduced (1.5 g/L), with normal IgA and IgM levels. HIV antibody test was negative. **Briefly** outline your differential diagnosis. Indicate the further investigations you would undertake to confirm or refute your diagnosis, giving a **brief**, critical commentary on the potential diagnostic value of each.

   b) A five-year old Caucasian child born to non-consanguinous parents has a history of recurrent episodes of high fever accompanied by a skin rash, arthralgia and myalgia. The febrile episodes recur at 3-4 monthly intervals, are accompanied by a raised ESR, and leucocytosis and last from one to three weeks. Infection screen including blood cultures and viral serology has been repeatedly negative. **Briefly** outline your differential diagnosis. Indicate the further laboratory investigations you would undertake to confirm or refute your diagnosis, giving a **brief**, critical commentary on the potential diagnostic value of each.

5. What is anaphylaxis? **Briefly** outline the causes of anaphylaxis. Discuss in detail the immunological mechanisms underlying anaphylaxis.

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 15 March 2005

IMMUNOLOGY

Second Paper *(For Non-Medical Candidates)*

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

1. **Please answer all parts of this question:**

   Discuss how the use of Flow-Cytometry for phenotypic analysis and functional assessment of cells of the immune system, can aid in the diagnosis of primary immunodeficiency diseases affecting:

   (a) lymphocytes
   (b) neutrophils

   You should illustrate your answer by referring to specific examples of primary immunodeficiency.

Please turn over for questions 2, 3, 4 and 5

2. **Please answer all parts of this question:**

   (a) Define the term cryoglobulin. How are cryoglobulins classified?

   (b) What types of immunopathology may be caused by cryoglobulins?

   (c) Briefly outline the laboratory investigations that you would carry out to detect and characterise a cryoglobulin.

   (d) What are the possible underlying causes of a cryoglobulinaemia?

   (e) What additional immunological tests may help in the assessment of a patient with a cryoglobulinaemia?

3. Briefly summarise the main indications for investigating the complement system in routine clinical practice. Outline how you would investigate a patient with suspected inherited complement deficiency so that you can arrive at a diagnosis. Your investigations should be set out in a logical sequence starting with screening tests and proceeding to specific tests to detect defects in specific parts of the complement cascade.

4. **Please answer all parts of this question:**

   (a) In the context of renal allografting, explain the terms “hyperacute”, “acute” and “chronic” rejection.

   (b) Summarise the key pathological mechanisms which contribute to each of these types of renal allograft rejection.

   (c) What is the evidence that supports the importance of tissue matching of unrelated cadaveric transplant donor-recipient pairs?

   (d) Briefly outline the HLA laboratory investigations used to minimise the risk of immunologically-mediated rejection of renal allografts.

Please turn over for question 5

5. Your local rheumatologist informs you that the Elisa based assay for autoantibodies to dsDNA appears to be generating results which do not fit with the clinical status of patients seen in his clinic.

   (a) Outline the clinical utility of tests to detect autoantibodies to dsDNA.

   (b) Briefly discuss the advantages and disadvantages of different assay methods used to detect and quantify autoantibodies to dsDNA .

   (c) Outline how you would establish the *sensitivity and specificity* of different tests for detecting antibodies to dsDNA.

   (d) What are the main requirements for achieving satisfactory quality assurance of tests used for the detection of autoantibodies to dsDNA?

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 21 September 2004

IMMUNOLOGY

Second Paper *(For Non-Medical Candidates)*

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

1. Your laboratory is faced with an escalating workload for antinuclear antibodies (ANA), including antibodies to double stranded DNA (anti-dsDNA) and antibodies to extractable nuclear antigens (anti-ENA). Much of the requesting appears to be indiscriminate. How would you formulate evidence-based guidelines to help manage the laboratory workload for these assays and ensure appropriate test requesting? What influence does the methods used for detecting these antibodies have on the guidelines you recommend?

2. Write brief answers to **all** sections of the following question:

   (a) What auto-antibodies are known to be associated with paraneoplastic syndromes affecting the nervous system? How do they produce pathogenic effects? What are the theories that explain why they are generated? What methods are available to detect them?

Please turn over for Questions 2b and c, 3, 4 and 5

(b) Define “hyperacute organ graft rejection”. What are the pathogenic mechanisms underlying this process? How can this complication be prevented?

(c) How may deficiency of Mannan Binding Lectin arise? What are the clinical consequences of a low serum Mannan Binding Lectin Level? What methods are available to identify individuals with Mannan Binding Lectin deficiency?

3. Please answer **both** parts of this question:

(a) Outline the possible causes of i) Exercise induced anaphylaxis and ii) The oral allergy syndrome. In each case discuss the clinical utility of investigations that you would use to confirm the diagnosis.

(b) Compare and contrast the clinical utility of tests that you would use to diagnose IgE mediated hypersensitivity to foods that commonly cause acute allergic reactions. Discuss the sensitivity, specificity, positive predictive value and negative predictive value, of any investigations that you cite.

4. A four-month old girl born to consanguineous Asian parents presents with persistent diarrhoea associated with a rotavirus infection. She also had generalised erythoderma, hepato-splenomegaly and eosinophilia. Briefly outline your differential diagnosis with reasons. How would you investigate her immune system to support your conclusions? Explain the reasons for your choice of investigations. What are the principles underlying the further management of this patient?

Please turn over for Question 5

5. Write brief answers to **all** sections of the following question:

(a) What do you understand by the term idiopathic CD4 T cell lymphocytopaenia? What disorders should be considered in the differential diagnosis? Briefly outline the principles of management of idiopathic CD4 T lymphopaenia.

(b) What is C3 inactivator (Nephritic Factor)? How is it detected? What are the clinical associations of a positive C3 Inactivator (Nephritic Factor)?

(c) What is the evidence that pemphigus vulgaris is an autoimmune disease? How does this evidence influence management of the condition?

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Part 1 Examination

Tuesday 16 March 2004

IMMUNOLOGY

Second Paper *(For Non-Medical Candidates)*

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

1. Compare and contrast each of the following pairs of patients with respect to their susceptibility to opportunistic infection. Discuss the investigations, which might be useful when making decisions regarding prophylaxis to prevent opportunistic infection and treatment of the underlying condition.

   (a) A 19 year old male with HIV infection and a CD4 count of 490 $x10^9$ / L [normal range 455 - 1320 $x10^9$/l] and a 19 year old male with hyper IgM syndrome and a CD4 count of 490 $x10^9$/ L

   (b) A 42 year old male with HIV infection and a CD4 count of 200 $x10^9$/ L [Normal range 455 - 1320 $x10^9$/l] and a 42 year old male with common variable immunodeficiency (CVID), with systemic granuloma formation and a CD4 count of 200 $x10^9$/ L.

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

2. Please answer **all** parts of this question.

Three clinical vignettes are given below. In each case **briefly** outline:

(a) Your differential diagnoses in priority order, with reasons,

(b) Additional features in the history which may help you discriminate between these possibilities,

(c) The further investigations that would help you to arrive at a definitive diagnosis; give your reasons for this selection.

A: A 33 year-old woman developed itching in her mouth and swelling of her lips and tongue immediately after eating a fresh peach. She did not develop difficulty in breathing or swallowing, and her symptoms subsided spontaneously over two hours. She can eat tinned peaches without any problem.

B: A 27 year-old female had recurrent boils for 7 years. There were 20 episodes in total with 3 requiring surgical drainage.

C: A 63 year-old man gives a history of local non-itching swelling precipitated by trauma and recurrent abdominal pain, of 18 months duration that was so severe that he had been admitted to hospital on 14 occasions. In each case the pain had resolved spontaneously after a few days. He had been treated for irritable bowel syndrome without success. He is awaiting exploratory laparotomy.

Please turn over for Questions 3, 4 and 5

3. Describe in detail how you would investigate a patient with suspected complement deficiency so that you can arrive at a diagnosis. Your investigations should be set out in a logical sequence starting with screening tests and proceeding to specific tests to detect defects in specific parts of the complement cascade. Your answer should address inherited and acquired complement deficiencies.

4. Write short notes on each of the following:

   (a) Anti-tissue transglutaminase antibodies

   (b) Criteria for the diagnosis of primary anti-phospholipid syndrome

   (c) Statistical tests that can be used to determine if the observed difference between two sets of measured data from different patient groups (eg. Serum IgG levels in g/l) are due to chance.

5. Please answer all parts of this question.

   (a) What are anti-cyclic citrullinated peptide antibodies?

   (b) Describe their value in the diagnosis and monitoring of autoimmune disease.

   (c) Briefly outline their possible relationship to the pathogenesis of Rheumatoid Arthritis.