The Royal College of Pathologists

Part 1 examination

Immunology: Second paper (For Medical Candidates)

Tuesday 25 September 2007

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

1 Write short notes on each of the following:

a. Laboratory methods of identification of HLA alloantibodies and indications for their use.
b. The mechanism of action of anti-IgE antibodies in treatment of allergic disease.
c. The principles underlying haemolytic assays of complement function and their clinical utility.

2 Please answer both parts of this question:

a. Discuss the clinical utility of monoclonal antibody therapy for autoimmune diseases, giving examples.
b. What are the potential complications of monoclonal antibody therapy and what strategies can be employed to minimize these?

Please turn over for Questions 3, 4 and 5

3 You are contacted by the anaesthetic team in your hospital concerning a patient who has had a suspected anaphylactic reaction in theatre. The patient has been appropriately resuscitated.

a. What immediate investigations would you recommend to confirm anaphylaxis and how would you interpret the results?
b. What classes of agents can cause anaphylaxis during anaesthesia?
c. How would you investigate this patient to identify the underlying cause of anaphylaxis?

Support your answer by referring to published evidence or guidelines.

4 Write short notes on each of the following:

a. Vaccination against human papillomavirus
b. Laboratory assessment of antibody responses to pneumococcal polysaccharide
c. Audit in laboratory quality assurance

Please turn over for Question 5

5 Please answer BOTH parts of this question:

5a A 55yr old woman gives a one year history of recurrent angioedema without urticaria.

- Give your differential diagnosis with reasons.
- What additional features in the history may help you distinguish between these possibilities?
- Outline the further investigations you would carry out to help you arrive at a definitive diagnosis, giving reasons for your selection of tests

5b A woman aged 40 years presented with abdominal pain and diarrhoea, and colonic biopsy demonstrated CMV nuclear inclusions in the affected mucosa. She had a 5-year history of recurrent otitis media and maxillary sinusitis. Over the last 3 years she has had cryotherapy for extensive viral warts on her hands and feet, which have recurred after treatment. Investigation at this stage revealed serum IgG, IgA and IgM levels of 3.6 g/l, 0.1 g/l and 0.1 g/l, respectively. Her lymphocyte profile is as follows: total lymphocyte count, 0.8 x10^9/l (Normal 1.0-3.0), CD3 0.58 x10^9/l, (Normal 0.7-2.1), CD4 0.36 x10^9/l (Normal 0.4-1.4), CD8 0.21 x10^9/l (Normal 0.2-0.9), CD19 0.01 x10^9/l (Normal 0.1-0.5), CD3-CD56+ 0.2 x10^9/l (Normal 0.12-0.88).

- Discuss your differential diagnosis of this patient, with reasons.
- What further investigations would you perform to confirm or refute the diagnostic possibilities you have outlined. Indicate what abnormalities you would look for in each investigation.

The Royal College of Pathologists

Part 1 examination

Immunology: Second paper (For Medical Candidates)

Tuesday 27 March 2007

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

1. Write short notes on each of the following:

    a) aspirin sensitivity. Include in your answer clinical symptoms, methods of diagnosis and principles of treatment

    b) sublingual immunotherapy. Include in your answer indications, mechanisms of action and adverse effects

    c) in-vitro diagnostic tests for tuberculosis (based on assessing immune responses to this organism). Include in your answer comment on clinical utility, underlying scientific principles and pitfalls.

2. You are asked to see a 2 year old boy who has been admitted with his second episode of bacteriologically proven pneumococcal meningitis. His parents inform you that his identical twin brother has also had two episodes of pneumococcal pneumonia. There is no other infective history in either child and both are thriving.

    a) Outline your differential diagnosis, with reasons

    b) For each potential diagnosis, outline the laboratory investigation, clinical management and prognosis. You may use a tabulated format for this answer.

Please turn over for Questions 3, 4 and 5

3. Write short notes on the methodology and diagnostic utility of the immunological laboratory investigations for:

    a) autoimmune liver diseases

    b) pulmonary-renal syndromes

    c) anaphylaxis.

4. Write short notes on:

    a) immunological diseases associated with a thymoma

    b) methods available for the detection of free light chains

    c) the anti-phospholipid syndrome.

5. Outline the clinical utility of tests to detect antibodies to extractable nuclear antigens (ENA). Describe the available techniques for the detection of antibodies to extractable nuclear antigens. Discuss the benefits and drawbacks of each method and how this influences their use in the diagnostic immunology laboratory.

The Royal College of Pathologists

Part 1 examination

Immunology - second paper *(For Medical Candidates)*

Tuesday 19 September 2006

Candidates must answer FOUR of the following questions ONLY
and must answer ALL parts of multi-part questions

Time allowed: 3 hours

1. Discuss the evidence base for the use of intravenous immunoglobulin in the treatment of neurological diseases. Illustrate your answer with examples of licensed and non-licensed uses.

2. Discuss the immunological mechanisms responsible for the immediate diffuse urticaria, laryngeal oedema and collapse that occurred in a 60 year old male who was stung by a bee. Discuss the scientific basis for the various treatments that would be administered to this patient in the first 12 hours. At a subsequent attendance in the allergy clinic what investigations and therapeutic options would you consider? Give reasons for your choice.

Please turn over for Questions 3, 4 and 5

3. Answer **both parts** of this question:
   a. A 55 year old male with a below knee amputation, presents with a purpuric rash on his remaining foot with small gangrenous lesions on his toes. You are reluctant to

undertake a skin biopsy because of poor tissue viability and there was no histological examination of the amputated limb removed 5 years previously for gangrene. What is your differential diagnosis and what tests would help you refine this list?

b. A 52 year old female presents with claudication of her upper arms and has been shown to have bilateral axillary arterial stenoses and an ESR measuring 62mm/hr. What is your differential diagnosis and what tests would help you refine this list?

4. Discuss the clinical utility and quality assurance of **all** of the following:
   a. Serological tests for the diagnosis and monitoring of coeliac disease
   b. Mast cell tryptase measurements
   c. Tests for the detection of Rheumatoid factor
   d. Anti-Cyclic Citrullinated Peptide antibodies.

5. Answer **all parts** of this question:
   a. Briefly outline the principles underlying the use of flow cytometry for the diagnosis of disorders of the immune system
   b. Detail the immunophenotypic (flow-cytometric) analyses that you would employ to investigate each of the following:
      i. Leucocyte adhesion deficiency
      ii. Common variable immunodeficiency
      iii. Hyper-IgM syndromes
      iv. Immune dysfunction, polyendocrinopathy, enteropathy, X-linked (IPEX).
   c. In each case give reasons for your choice of immunophenotypic panels.

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 14 March 2006

IMMUNOLOGY

Second Paper *(For Medical Candidates)*

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

Time allowed - THREE HOURS

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 Critically review the clinical importance of lung damage as a complication of primary antibody deficiency. What are the other disease co-factors, which may contribute to the progress of lung damage in these patients? Briefly, outline how you would identify and manage the principal pulmonary complications of primary antibody deficiency.

3 Briefly outline the key features of the current consensus on the diagnosis and management of C1 Inhibitor deficiency.

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 adverse effects of Immunosuppression post-Renal-transplantation.

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 Medical Candidates)*

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

Time allowed - THREE HOURS

1. A 21 year old veterinary student presents with a three-year history of rhinorrhoea, sneezing and itchy eyes. Outline the aspects of the history that you would need to obtain to manage this patient and indicate why. Explain the treatment options that are available and when you would use each of them. **Briefly** outline the advantages, disadvantages and complications, of each therapeutic option.

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) Outline the adverse effects of Intravenous Immunoglobulin therapy and how these can be minimised.

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. Answer **both** parts of this question:

a) When and why would you prescribe an adrenaline auto-injector?

b) **Briefly** outline your plan of investigation of a patient who developed anaphylaxis during surgery under general anaesthesia.

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 15 March 2005

IMMUNOLOGY

Second Paper *(For 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. **Please answer all parts of this question:**

(a) Which occupational and patient groups have an increased risk of latex allergy?

(b) Outline the different types of latex allergy (hypersensitivity) that are recognised and their clinical presentations.

(c) Briefly describe the diagnostic tests available for confirming or refuting a diagnosis of latex allergy giving a critical commentary on the potential diagnostic value of each.

(d) Summarise the important points that a patient information leaflet concerning latex allergy must cover.

4. 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.

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 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 how you would support your clinical suspicion by further investigations.

(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.

~~(d)~~

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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.

(a) 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?

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 16 March 2004

IMMUNOLOGY

Second Paper *(For Medical Candidates)*

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

2. Compare and contrast each of the following pairs of patients with respect to their susceptibility to opportunistic infection. What prophylaxis would you advise in each case? Discuss the investigations, which might be useful when making decisions regarding prophylaxis and treatment.

   (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 clinical features 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. An Asian male child presents with pneumonia at the age of 2 years. His parents give a history of recurrent upper and lower respiratory tract infections in the last 18 months. His weight is in the third centile for age. The referring letter says that the immunoglobulins were previously found to be low. Outline:

   (a) Your differential diagnosis

   (b) The immunological investigations that you would initiate to differentiate between the above possibilities

   (c) The supplementary investigations that might be indicated to identify possible complications of the underlying diagnosis

   (d) The principles of management of a 2 year-old child with primary antibody deficiency.

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. Write short notes on each of the following:

   (a) Selection of individuals for Hymenoptera venom desensitisation immunotherapy

   (b) The classification and immunopathology of immunologically-mediated renal disease

   (c) Adverse effects of immunosuppression used after renal-transplantation.