



The Royal College of **Pathologists**

Pathology: the science behind the cure

Part 1 examination

Immunology: Second paper

This paper is for medically qualified candidates only

Tuesday 22 September 2009

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

- 1 Using short notes answer each of the following with respect to antiphospholipid syndrome:
 - a) Outline the criteria necessary for a diagnosis of antiphospholipid syndrome
 - b) Describe the diagnostic tests used to support this diagnosis
 - c) Critically appraise the value of the tests described

- 2 Write short notes on the clinical features, immunological investigation, and management of each of the following conditions:
 - a) Exercise-induced anaphylaxis
 - b) Allergic eosinophilic oesophagitis
 - c) Allergic bronchopulmonary aspergillosis

Please turn over for Questions 3, 4 & 5

- 3 Answer both parts of this question.
- a) You have been asked to write your Immunology laboratory's plan in the event of the Pathology integrated computer system (including both order communications and results reporting functions) "crashing" on a Monday morning with recovery predicted to take between three and five days. Write your response in the form of a laboratory controlled-document, including consideration of both your user and laboratory needs, and what tests you would prioritise along with the clinical rationale behind your decisions.
 - b) Your hospital's Ear Nose and Throat team have asked you to write a guideline for the investigation of a patient with sicca for use by both their surgical trainees and local general practitioners. Your response should be written in an appropriate format, including clinical features, reasons behind the selection of immunological tests recommended, other diagnostic tests which may be helpful, and why it is important not to miss a diagnosis of primary Sjogren's syndrome.
- 4 You are telephoned in the Immunology laboratory with a request for advice concerning the following clinical scenarios. What further information would you wish to know, what immunological investigations would you recommend (and why), and what advice would you give with respect to immunological treatment (and why)?
- a) A pest control officer with a history of a severely swollen arm following multiple wasp stings
 - b) A young adult with sickle cell anaemia and Howell-Jolly bodies on blood film with a recent episode of pneumococcal septicaemia.
 - c) A 60-year-old male with rheumatoid arthritis, recurrent chest infections and an IgG level of 2.0 g/L
- 5 Using short notes, describe the clinical features, underlying genetic defects, immunological evaluation, and principles of treatment of primary disorders of granulocyte function.



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

Part 1 examination

Immunology: Second paper

This paper is for both medically qualified and clinical scientist candidates.

Tuesday 24 March 2009

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

1. Answer all three parts of this question:
 - a) Describe the classification of cryoglobulinaemia, including the principal disease associations of each category.
 - b) Write a standard operating procedure (SOP) for the collection of samples for cryoglobulin determination by a phlebotomy centre in a recently opened independent treatment centre (ITC) for which your laboratory provides an analytical service. The ITC is situated adjacent to your hospital campus, 0.5 miles from your laboratory. It does not wish to use the hospital phlebotomy service. Bear in mind your response to part a) of this question.
 - c) How might you facilitate and monitor the introduction of this SOP?

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

2. Using short notes answer both parts of this question:

- a) Briefly outline the main clinical features of C1 inhibitor deficiency, explain the mechanism resulting in these manifestations, and comment on the scientific basis of current and proposed therapies.
- b) List the important “immunological” differential diagnoses for a 60 year old patient with a 5 year history of recurrent chest infections who has been found to have low total immunoglobulin levels and a mediastinal mass. Which immunology tests would you recommend to help achieve a diagnosis? Comment on the reasons for your choices with reference to the likely findings for each diagnosis.

3. Answer both parts of the question:

- a) A renal physician telephones you for advice about further investigation of a 20 year-old female who presented acutely with significant proteinuria and renal impairment. Renal biopsy has shown a diffuse proliferative glomerulonephritis, highly suggestive of lupus nephritis, but ANA performed in your laboratory was reported as negative last week. Advice is requested concerning (i) the result; and (ii) whether further immunological tests should be performed. What is your response?
- b) The Clinical Director of the Ear Nose and Throat (ENT) service is compiling a training manual for ENT trainees. You are asked to write a brief piece for the manual on Wegener’s granulomatosis with reference to (i) clinical features of ENT involvement; (ii) how the diagnosis is made in the ENT setting; and (iii) who to test for ANCA in the ENT clinic. Please write your answer in an appropriate format.

Please turn over for Questions 4 & 5

4. Describe the principles of flow cytometric analysis. How may this technique be applied to the study of non-clonal disorders in the three following situations?
- a) Defects of B cells.
 - b) Defects of phagocytes.
 - c) Defects of NK cells.
5. For each of the following three hypersensitivity disorders, briefly describe (i) the clinical features; (ii) the immunological testing strategy; and (iii) the problems which may be associated with interpretation of the results:
- a) Bakers' asthma.
 - b) Wheat-dependent exercise-induced anaphylaxis.
 - c) Birch pollen-associated oral allergy syndrome.



The Royal College of Pathologists

Pathology: the science behind the cure

Part 1 examination

Immunology: Second paper

for medically qualified candidates only

Tuesday 23 September 2008

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

1. Discuss the utility of flow cytometry in the investigation and management of patients with primary immunodeficiencies. Illustrate your answer with appropriate examples.

2. Write short notes on each of the following conditions associated with neutrophil dysfunction covering clinical features, pathogenesis, and laboratory testing in your answers:
 - a) Warts, Hypogammaglobulinaemia, Infection, Myelokathexis (WHIM) syndrome.
 - b) Leucocyte adhesion deficiency (LAD).
 - c) Shwachman-Bodian-Diamond syndrome.

Please turn over for Questions 3, 4 & 5

3. Answer both parts of the question. *Part (a) is awarded two thirds of the marks and part (b) one third of the marks for this question.*
- a) Explain how (i) internal quality control, and (ii) external quality assessment procedures should be used to quality assure allergen specific IgE measurements.
 - b) How would you use the audit process for clinical governance within the Immunology laboratory?
4. Discuss the indications, likely mechanisms of action, and potential adverse effects of each of the following therapeutic modalities:
- a) Mycophenolate mofetil.
 - b) Rituximab.
 - c) Intravenous immunoglobulin in autoimmune disease.
5. Outline the “immunological” differential diagnosis of each of the following scenarios. Suggest which immunology laboratory tests should be requested, giving reasons for your choices, and comment on the interpretation of their results:
- a) A 60 year old male who had presented to the Emergency Department with three episodes of angioedema in the past 12 months.
 - b) A 40 year old female presenting to the acute medical service with shortness of breath, haemoptysis and renal failure (pulmonary renal syndrome).
 - c) A 50 year old male presenting to the Immunology clinic with a history of recurrent chest infections with an IgG level of 5.0g/L in the absence of an obvious paraprotein band on serum protein electrophoresis.



The Royal College of Pathologists

Part 1 examination

Immunology: Second paper

Tuesday 18 March 2008

Candidates must answer FOUR questions ONLY

Time allowed: 3 hours

- 1 Write short notes on all of the following:
 - a Idiopathic CD4 T lymphopenia
 - c Food and exercise induced anaphylaxis
 - d Anti-synthetase syndrome

- 2 Describe the clinical utility, advantages and disadvantages of the different methods currently available for the investigation serum paraproteins in the diagnostic immunology laboratory.

Please turn over for Questions 3, 4 and 5

3 Answer both parts of this question:

3a Deficiencies of single complement components, or of complement regulatory factors, are associated with predictable disease states. For each of the following, write short notes, indicating the likely clinical consequences of deficiency.

Factor H

Decay accelerating factor

C4

Properdin

C6

3b A 63 year old retired teacher, presented with a six month history of relapsing / remitting urticaria, weight loss, fatigue and malaise. His general practitioner (GP) initially prescribed anti-histamines, but these were ineffective, even at double the normal dose. The rash and symptoms improved on oral prednisolone at a dose of 30 mg daily. The patient wondered about wheat and dairy allergy, and had tried exclusion diets, with no benefit. The GP referred the patient following blood test investigations which showed low levels of serum complement, C3 (0.24g/l : nr > 0.6g/l), and C4 (0.02g/l : nr > 0.15g/l).

- i. Outline your differential diagnosis, with reasons.
- ii What investigations are indicated to confirm or refute these possible diagnoses?

Please turn over for Questions 4 and 5

4 Answer both parts of this question.

4a A 9 month old Asian baby boy, born at full term was given BCG at birth. At 3 months of age he developed an enlarged axillary lymph node 2cm in diameter which showed granulomatous inflammation with numerous macrophages containing acid-fast bacilli. *M.bovis* BCG was grown from the lymph node biopsy. The child was treated with standard anti-mycobacterial chemotherapy. Six months later (at age of 9 months), his body weight had fallen from the 25th to the 5th centile and he was noted to have hepatomegaly.. He was anaemic (haemoglobin was 8.0 g/l) and his CRP was 90mg/l.

i Outline your differential diagnosis, with reasons.

ii What investigations are indicated to confirm or refute these possible diagnoses?

4b Discuss the value of test immunisation in the context of investigating suspected antibody deficiency. In your answer indicate specific immunisations that could be safely used to test-immunise children and adults, and also outline the advantages and limitations of currently available laboratory tests.

5 Your laboratory wishes to introduce a new ELISA assay to detect antibodies to Tissue Transglutaminase, for routine use. In this context, write short notes on the following.

a How would you establish the reference range?

b How would you determine the sensitivity, specificity, positive predictive value and negative predictive value of the assay for you local population?

c How would you evaluate reproducibility of the assay?

d How would you audit clinical utility following routine use of this assay in your centre?



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, $0.8 \times 10^9/l$ (Normal 1.0-3.0), CD3 $0.58 \times 10^9/l$, (Normal 0.7-2.1), CD4 $0.36 \times 10^9/l$ (Normal 0.4-1.4), CD8 $0.21 \times 10^9/l$ (Normal 0.2-0.9), CD19 $0.01 \times 10^9/l$ (Normal 0.1-0.5), CD3-CD56+ $0.2 \times 10^9/l$ (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.