The Royal College of Pathologists

Part 1 examination

Histocompatibility & Immunogenetics: First paper

Tuesday 27 March 2007

*Candidates must answer **ALL** questions in **Section A***
*Candidates must answer **TWO** questions from **Section B***
*Candidates must answer **FOUR** questions ONLY*
Questions may be attempted in any order

Time allowed: 3 hours

Section A

1 In relation to minor (mH) histocompatibility antigens:

a)What are the most clinically relevant genetic systems currently known?
b)What are the immunological mechanisms involved in their recognition?
c)How can the mH be used in the development of immunotherapy protocols?

2 In relation to clinical allogeneic haematopoietic stem cell transplantation:

a) Which sources of haematopoietic stem cells (HSC) are currently used clinically?
b) What are the main features of each of the various sources of HSC?
c) How does each of the different sources of HSC influence graft rejection or the development of graft versus host disease (GVHD)?

Please turn over for Section B (Questions 3, 4 and 5)

Section B

3 Describe the mechanisms which may contribute to the development of chronic allograft nephropathy.

4 Discuss the impact of matching at the broad and allelic level for all HLA loci in solid organ and stem cell transplantation.

5 Discuss laboratory and clinical strategies for managing sensitised patients.

The Royal College of Pathologists

Part 1 examination

Histocompatibility & Immunogenetics: Second paper

Tuesday 27 March 2007

*Candidates must answer **ALL** questions in **Section A***
*Candidates must answer **ONE** question from **Section B***
*Candidates must answer **FOUR** questions ONLY*
Questions may be attempted in any order

Time allowed: 3 hours

Section A

1 Write short notes on the relevance of the Human Tissue Act to H&I laboratories in **THREE** of the following categories:

a) Obtaining and documenting consent
b) Design and performance of laboratory research projects
c) Clinical transplantation
d) Training, clinical audit and quality control

2 Write short notes describing the influence of HLA typing in the clinical management of **THREE** of the following conditions:

a) HIV infection
b) narcolepsy
c) ankylosing spondylitis
d) actinic prurigo

Please turn over for Section A Question 3 and Section B (Questions 4 and 5)

3 In relation to immunological reactions to blood transfusions:

a) Describe TWO immunological reactions induced by white cells or platelets and indicate the main antigenic systems and antibodies involved
b) What tests are available to aid their diagnosis?
c) How can these immunological reactions be prevented?

Section B

4 Describe the key features of a quality management system and the contribution they make to the provision of an H&I laboratory service

5 Briefly outline the processes involved in attaining laboratory accreditation in Histocompatibility and Immunogenetics. Discuss similarities and differences in accreditation requirements between Clinical Pathology Accreditation and the European Federation for Immunogenetics.

The Royal College of Pathologists

Part 1 examination

Histocompatibility and immunogenetics: First paper

Tuesday 19 September 2006

Candidates must answer FOUR of the following questions ONLY

Time allowed: 3 hours

1. Describe the structure and function of MHC Class I Like Antigens and discuss their role in transplantation.

2 Discuss approaches to HLA and non-HLA mismatching in allogeneic haematopoietic stem cell transplantation:
a) in order to increase opportunities for transplantation where fully HLA matched donors are not available
b) as a strategy to generate a positive therapeutic benefit.

3 ABO compatibility has long been regarded as a pre-requisite for solid organ transplantation. Discuss whether this is still the case in the current era and ways in which ABO incompatibility barriers can be overcome.

Please turn over for Questions 4 and 5

4 The extended HLA A*01, B*08, DRB1*03, DQB1*02 haplotype is the most common in Western European populations despite a strong association with a range

of autoimmune diseases. Give examples of component/s within this haplotype associated with specific diseases. Speculate on reasons why this haplotype is still so common despite these disadvantages.

5 Write short notes on **all** of the following:

a) The structure of MHC class I and II molecules
b) Antigen processing and presentation
c) The molecular interactions between T cells and antigen presenting cells required to initiate an immune response.

The Royal College of Pathologists

Part 1 examination

Histocompatibility and immunogenetics: Second paper

Tuesday 19 September 2006

Candidates must answer FOUR of the following questions ONLY

Time allowed: 3 hours

1 Discuss the impact of the Human Tissue Act 2004 on clinical transplantation and H&I laboratory practice.

2 Describe the methods available to determine donor specific sensitisation in solid organ transplantation. When should the outcome of such tests be a veto to transplantation?

3 Discuss issues affecting equity of access to renal transplantation and how these have been addressed by the new UK Transplant allocation scheme.

4 Outline the key components of horizontal, vertical and clinical audit. Discuss how such audits contribute to laboratory management, accreditation and service development.

5 Discuss laboratory approaches to post-transplant monitoring and the clinical significance of the results in:
   a) solid organ transplantation
   b) haematopoietic stem cell transplantation.

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 20 September 2005

Histocompatibility and Immunogenetics

First Paper

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

1 Discuss the role of non-HLA genes encoded within the MHC in the rejection of renal allografts.

2 The HLA genes are the most polymorphic in the human genome. Discuss the theories for the generation of this polymorphism and how it contributes to immune function.

3 Describe, with examples, how a detailed knowledge of HLA and disease associations can be useful in elucidating molecular mechanisms of disease pathogenesis.

4 What methods may be used to monitor chimerism? Outline how the information obtained may be used clinically.

5 Discuss the role of genetic factors in haematopoietic stem cell transplant outcome.

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 20 September 2005

Histocompatibility and Immunogenetics

Second Paper

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

1 Discuss the immune causes of refractoriness to random platelet transfusion and the role of the H&I laboratory in the management of these patients.

2 In renal transplantation, the advantages of HLA matching are outweighed by prolonged cold ischaemia time. Discuss clinical observations which support or refute this statement and describe how this issue is addressed by current organ allocation policies.

3 Describe how the terms of the Human Tissue Act 2004 will impact upon the field of Transplantation.

4 Discuss the role of antibody removal in renal transplantation and the application of antibody detection methods in facilitating this process.

5 What are the critical components of a quality system and what advantages do they bring to the laboratory?

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 21 September 2004

Histocompatibility and Immunogenetics

First Paper

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

1. Antigen presenting cells can present a diverse array of antigenic peptides to T cells. With reference to the cell surface and intracellular molecules and processes involved, explain how this is achieved.

2. Discuss the role of genetic polymorphisms in regulating pathways of innate immunity.

3. With examples, critically evaluate the diagnostic utility of HLA and disease testing.

4. Describe the mechanisms leading to chronic allograft nephropathy, and suggest genetic factors which may contribute to this condition.

5. Discuss clinical and genetic factors affecting outcome after haemopoietic stem cell transplantation. How would these factors influence the selection of an appropriate donor?

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 21 September 2004

Histocompatibility and Immunogenetics

Second Paper

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

1. Discuss the detection and clinical relevance of antibodies in solid organ transplantation with reference to relevant guidelines/standards.

2. Discuss the role of the Histocompatibility & Immunogenetics laboratory in post-transplant monitoring.

3. Outline current and prospective UK and EU legislation and directives that impact upon working practices in Histocompatibility & Immunogenetics laboratories.

4. Outline current and potential future strategies to address the shortage of cadaver organs for solid organ transplantation.

5. Briefly describe the current WHO HLA nomenclature system. Critically discuss (with examples) the proposition that an HLA allelic designation is a guide to molecular function.

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 23 September 2003

HISTOCOMPATIBILITY AND IMMUNOGENETICS

First Paper

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

1. Discuss the evidence for a pathological role for HLA specific antibodies in acute and chronic transplant rejection. Outline the laboratory tests required for the accurate diagnosis of acute humoral rejection.

2. Describe the molecular mechanisms involved in antigen processing and presentation in the context of direct as compared with indirect allorecognition.

3. Discuss and describe the role of non-HLA polymorphic gene products in the outcome of solid organ and haemopoietic stem cell transplantation.

4. Describe the immunological barriers to xenotransplantation and discuss the progress that has been made in overcoming them.

5. Describe the different sources of haemopoietic stem cells for transplantation and discuss their relative advantages and disadvantages.

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 23 September 2003

HISTOCOMPATIBILITY AND IMMUNOGENETICS

Second Paper

Candidates MUST answer FOUR questions only

Time allowed - THREE HOURS

1. Describe and discuss the immunological reactions associated with the transfusion of HLA incompatible blood or blood products.

2. Outline the external quality assurance schemes for Histocompatibility and Immunogenetics that are currently available from UK NEQAS. With reference to each of the schemes, discuss the advantages and disadvantages of scoring by consensus as compared with scoring against a gold standard.

3. Describe the strategy you would adopt to select an unrelated donor for a potential haemopoietic stem cell transplant recipient. Discuss the selection criteria and the laboratory testing that might be required.

4. Describe the different approaches adopted nationally and internationally to facilitate renal transplantation for highly sensitised patients. Which approach would you recommend for a 15 year old highly sensitised patient who was stable on dialysis and had been waiting 6 months for a transplant? Explain the reasons for your recommendation.

5. Discuss how genetic polymorphisms might influence a patient's response to immunosuppressive therapy. Speculate on how a Histocompatibility and Immunogenetics laboratory might develop a pharmacogenomics service that would contribute to patient management following transplantation.

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 24 September 2002

HISTOCOMPATIBILITY AND IMMUNOGENETICS

First Paper

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

1. Discuss the role of genetic factors in the outcome of haemopoietic stem cell transplantation using related and unrelated donors.

2. Discuss the importance of HLA epitopes in the development of alloantibodies and the utility of methods for detecting and predicting the full range of antibody reactivity.

3. Discuss the genetics, function and clinical relevance of NK cell receptors.

4. Discuss the potential use of dendritic cells in immunotherapy.

5. HLA matching and complete equity of access to renal transplants are mutually exclusive. Outline the reasoning behind this statement and discuss whether HLA matching should continue to be the primary factor in organ allocation in the UK.

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

Tuesday 24 September 2002

HISTOCOMPATIBILITY AND IMMUNOGENETICS

Second Paper

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

1. The removal of antibody combined with use of IvIG has been advocated for use in the transplantation of the highly sensitised patient. Discuss this approach including the role of the H&I laboratory in this process.

2. Describe the contribution of quality control and quality assessment to the running of laboratory services. Outline the measures you would put in place to ensure appropriate quality monitoring in an H & I laboratory.

3. Beyond HLA, discuss the proposition that H&I laboratories have an important role in elucidating the contribution of other genetic factors that influence immune responses.

4. Discuss the role of the H&I laboratory in the management of patients with HLA related reactions following the transfusion of blood and blood products.

5. EFI Standard D2.100 states that 'determination of haplotypes and genotypes can only be done by family studies'. Explain this standard and discuss its relevance to related stem cell and solid organ transplantation.

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

September 2000

HISTOCOMPATIBILITY & IMMUNOGENETICS

First Paper

Candidates must answer FOUR questions ONLY
Time allowed - THREE HOURS

1. Describe the molecular events involved in transplant rejection. How may these mechanisms be influenced by immunosuppressive drugs?

2. What diseases are effectively treated with stem cell transplantation? How successful is this treatment and how are stem cells for transplantation procured?

3. Outline the principles of flow cytometry. Compare the different flow cytometry techniques available for the detection and definition of HLA specific antibodies and discuss their relative advantages and disadvantages.

4. "Crossmatching must be performed prospectively" is a currently accepted EFI standard for histocompatibility testing in renal transplantation. Discuss whether this standard should always apply.

5. Is HLA typing relevant for the diagnosis of HLA associated diseases?

THE ROYAL COLLEGE OF PATHOLOGISTS

Part 1 Examination

September 2000

HISTOCOMPATIBILITY & IMMUNOGENETICS

Second Paper

Candidates must answer FOUR questions ONLY

Time allowed - THREE HOURS

1. Outline the current rules for allocation of cadaver donor kidneys for transplantation in the UK. What role does HLA matching play? How have these rules been agreed?

2. Describe how HLA polymorphisms are defined in the laboratory. Discuss the likely origins of the polymorphism.

3. How might a histocompatibility laboratory contribute to the management of patients with blood transfusion reactions?

4. Review the schemes currently available from UK NEQAS for Histocompatibility and Immunogenetics. What additional schemes might you consider to be relevant?

5. What is meant by clinical audit and why is this relevant to a Histocompatibility and Immunogenetics laboratory?