Q.1 The immune system protects us from infectious agents and the damage they cause by a variety of effector cells and molecules. Innate immune system works in close cooperation with the adaptive immune system. However, the adaptive immune system is capable of eliminating infections more efficiently because of certain complex attributes.

a) What are the functional components common to both the systems?
b) Give four important distinguishing features that set apart the two systems.

Q.2 Development of human B lymphocytes in the bone marrow is a beautifully coordinated, differentiation sequence with important clinical implications. Five of the pivotal events are:

1. Cytoplasmic μ chains present in the B cell
2. Immunoglobulin heavy chain rearrangement
3. Immunoglobulin light chain rearrangement
4. Surface IgD and IgM present on the B cell
5. Surface IgM present on the B cell

a) Arrange the above mentioned events in the order of occurrence (first event...last event).
b) Give a brief account of each event (1-2 sentences).

Q.3 T-lymphocytes are considered to be principal mediators of the most effective adaptive immune response against tumors, but most tumors are weakly immunogenic and immune response often fails to prevent tumor growth. On the other hand some tumors do induce an effective immune response that prevents their growth.

a) Why are most tumors weakly immunogenic?
b) What two types of tumors illicit a strong specific immune response and why?
c) What is the likely mechanism involved in the induction of immune response and killing of tumor cells by T-lymphocytes?
Q.4 Complement system is activated by three different pathways. Multiple regulatory proteins inhibit complement activation to prevent damage to self cells.

a) What are the complement regulatory proteins that inhibit complement activation on self cells?
b) How does the acquired deficiency of alternate pathway regulatory proteins cause increased consumption of complement proteins?
c) How will you investigate defects in complement activation by alternate pathway?

Q.5 A male patient resident of Islamabad, 32 years of age with a diagnosis of bronchial asthma for 4 years, presented with complaints of severe exacerbation of his symptoms with frequent ER visits during spring season from March to May. On investigation, his skin prick test was positive to several allergens including paper mulberry, rag weed pollen, dandelion, grass and bottle brush pollen. Allergen specific IgE was positive for these allergens as well. He was labeled as having allergic asthma. He was advised medication and allergen avoidance measures.

a) What is allergen specific immunotherapy? What are its common indications and routes of administration?
b) What is the mechanism by which it reduces sensitivity to specific allergens?
c) Will you suggest specific immunotherapy in this patient?

Q.6 a) What are the recommendations for administration of Influenza vaccine to immunocompetent children and adults who live in a household with immunocompromised individuals?
b) Should the live Rotavirus vaccine be given to the immunocompetent children living in a household with an immunocompromised individual? If yes, what should be the precaution for that immunisation?
c) If an HIV patient is travelling to a yellow fever endemic area, what is the rationale of administration of live yellow fever vaccine to that patient?
Q.7 A baby boy, 10 months of age presented with 5 months history of recurrent skin infections with multiple abscesses in axilla, groins and neck. USG revealed a 2x2 cm hepatic abscess in right hepatic lobe. One of his male sibling died of similar complaints at 1 year of age.

a) What is the most likely immune deficiency and briefly describe its mechanism?
b) Which immunological test will you perform to reach the diagnosis? Outline the principle of the technique.
c) What will be the test results of patient's mother as a carrier?

Q.8 You were consulted by a colleague trying to establish C4d staining on renal biopsies by immunofluorescence.

a) What would be your advice regarding establishment of infrastructure and quality assurance.
b) Enumerate associated laboratory investigations which are required to formulate an opinion about transplant rejection.

Q.9 As a consultant Immunologist, you have been asked to prepare guidelines for IVIG administration in patients with primary immunodeficiencies.

a) What are the factors you will consider in laying down the guidelines?
b) What will you suggest regarding IVIG administration in a 45 year old male patient with a creatinine clearance of 60 ml/min (Ref. range: 100-130 ml/min)?
c) What are the other approved indications for IVIG administration?

Q.10 You are planning to setup flow cytometry based lab test service in your department.

a) What factors would you consider in the process?
b) How would you manage the quality assurance of the service?
Q.11 A male child, 7 years of age presented with intermittent fever and frequent chest infections since 3 months of age. His parents are first cousins and one of his younger sibling died at 5th postnatal day due to sepsis. He has history of repeated hospital admissions. His mother reports that he has a bad squint and abnormal gait. His immune deficiency work up reveals normal IgA, IgG and IgM levels. Lymphocyte subset analysis reveals a little decrease in absolute numbers of CD4, CD8 and CD19 cells. DHR and CH50 were also in normal reference limits.

a) What are the important points that you will look for in examination of this child to reach a diagnosis?

b) Enlist the differential diagnosis.

c) What further immunological investigations you will carry out?

Q.12 A male child, 10 months of age presented with recurrent chest infections and failure to thrive. His immunoglobulin levels at 9 months of age were:

<table>
<thead>
<tr>
<th></th>
<th>9 months old</th>
<th>Reference range</th>
</tr>
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<tbody>
<tr>
<td>IgG</td>
<td>1.57</td>
<td>2.17-9.04 g/l</td>
</tr>
<tr>
<td>IgA</td>
<td>0.10</td>
<td>0.11-0.90 g/l</td>
</tr>
<tr>
<td>IgM</td>
<td>1.32</td>
<td>0.34-1.26 g/l</td>
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a) What further information would you request?

b) Give the differential diagnoses with a brief justification for each diagnosis. Which investigations would you suggest to establish the diagnosis?

c) Outline the principles of initial management of this patient.

Q.13 A 40 years old known patient of chronic liver disease, consequent upon hepatitis C virus infections, presented with non-pruritic rash on both legs after one week. He also complained of easy fatiguability joint pains and facial puffiness. Labs showed raised WBC count, Tests for ANA, ANCA and anti-GMB were negative. Serum urea and creatinine were markedly raised. The consultant physician requested your help for lab workup.

a) Give the most probable diagnosis.

b) How would you proceed to investigate this patient in the immunology lab?
Q.14 A 45-year-old female presented with pain in hip and shoulder joints with early osteoporosis. Additional presenting features included Raynaud’s phenomenon and irritable bowel syndrome associated constipation, chronic urinary tract and upper respiratory infections. She was taking Fosamax plus D (alendronate with vitamin D3 - because of low bone density), There were no nodules, rash, heart burns or vasculitic lesions. On investigation, she was found to have a raised C-reactive protein (CRP) level (27mg/l) with a normal haemoglobin and white-cell count. A latex test for rheumatoid factor was positive.

a) What is the most likely diagnosis?
b) Keeping Raynaud’s phenomenon in mind, List the three most important differential diagnoses you wish to pursue.
c) State the three most useful immunology laboratory tests. Include reference to the differential diagnosis as the basis for your investigative strategy. Critically appraise the clinical utility and limitations of each test you describe in this case.

Q.15 A 22-year-old male jackhammer operator who was recently diagnosed with rheumatoid arthritis presents with difficulty in holding his drill and other tools. He also notes an occasional “electric shock” sensation in his right index and middle fingers along with bluish discoloration of nails. Physical examination reveals bilateral (right greater than left) wrist synovitis. His CRP was 48mg/l, with Rheumatoid factor (RF) and anti cyclic citrullinated antibodies (CCP) positive.

a) What are the risk factors for developing Raynaud’s disease?
b) Briefly state target antigen and diagnostic value of RF.
c) What advice would you offer regarding Raynaud’s disease?
Q.16 A 70 years old male presented with two months history of progressive weakness, backache and breathlessness on mild exertion. Lab workup revealed anaemia with presence of serum and urinary para proteins, lytic lesions were detected in the skull. He was treated for multiple myeloma. Give an outline of assessment of response to the treatment in this case.

Q.17 A 30 years old male patient with end stage renal disease (ESRD) of unknown cause on maintenance haemodialysis received kidney transplant from his brother, 27 years old, with one haplotype three antigen match. Pre transplant complement dependent microlymphocytotoxicity and flowcytometric crossmatch were negative. Antibody screening for HLA class I and class II were also negative. Maintenance immunosuppression was cyclosporine, azathioprine and Deltacortil. Six months post transplant there is rise in serum creatinine from 0.89mg/dl to 3.20mg/dl. Renal graft biopsy was performed which showed acute vascular rejection (type 3).

   a) Give diagnostic criteria of acute antibody mediated rejection (AMR).
   b) What immunological tests will be required to confirm antibody mediated components?
   c) Outline the treatment options for this patient.

Q.18 A female, 20 years of age presented to medical OPD with 3 months history of persistent flu like symptoms of watery eyes, runny nose with occasional episodes of chest tightness and difficulty in breathing for which she had to land in ER twice. She told that she had moved in a new house 3 months back. She had no previous history of childhood asthma or atopy. Her mother told that she suffered from acute breathlessness once when she stayed with her grandmother for 2 days, 2 years ago. Her pulmonary function tests showed an FEV1/FVC ratio below 80% of the expected value and it was reversible with bronchodilators.

   a) What further points will you ask from the patient to reach the diagnosis?
   b) Enumerate the appropriate immunological tests that you will perform to reach the diagnosis?
   c) What are the relative sensitivity, specificity, positive and negative predictive value and over all clinical efficiency of skin prick test and in vitro tests like allergen specific IgE to inhalation allergens?
Q. 19 You are entrusted with the establishment of immunology services for a renal transplant program.

   a) Enumerate the laboratory tests that you would like to establish for the detection of donor specific antibodies.
   b) Give in brief the steps you would like to make your reports for donor specific antibodies comprehensive and interpretative.

Q. 20 a) Give in brief the molecular techniques as they evolved to NGS (Next Generation Sequencing)
   b) Prepare a list of possible clinical applications of NGS.

The End