Introduction to the Patient-Oriented Problem-Solving (POPS) System

The purpose of this exercise is twofold. One is to help you learn how to apply your basic knowledge of immunology to clinical problems. The other is to help you learn how to work with other people (i.e., how to learn from them and solve problems together). Good health professionals must first be able to learn from their patients and then be able to teach them. With this in mind, the data necessary for the solution of the patient-oriented immunological problem have been divided into four parts so that everyone in your group must share data to arrive at a diagnosis.

This activity consists of four phases. First, you will review the attached set of objectives, do background reading on the topics to be covered, and complete the pretest on your own. In the second phase, you will join three other students and review the pretest answers in an "open-book" discussion. In the third phase, the group will solve patient-oriented problems. Finally, you will take a posttest, individually, which will enable you to assess your progress.

Please do your best to teach each other; seek additional information from your textbooks and share it with each other and, as a group, arrive at the correct diagnosis in a logical way. At the end of the exercise, everyone in the group should agree on the diagnosis and be able to identify the data that were (1) consistent with the diagnosis, (2) irrelevant to making the correct diagnosis, or (3) inconsistent with the diagnosis. You also should understand the principles behind each observation and laboratory assay.
Immunodeficiency Disease

Introduction

It has been known for centuries that there is great inter-individual variation in susceptibility to various infectious diseases. However, with the advent of antibiotics in the past half century, a unique group of children has been recognized. Formerly, these children died of infections before they were one year of age. Now that they can be saved with antibiotics, it has become clear that these children do not develop immunity and, hence, repeatedly get the same life-threatening infections, such as pneumonia. This results from incomplete development of their immune systems. The primary problem of these persons is therefore an immune deficiency disease that renders them highly susceptible to certain types of infections.

When your group has completed this activity you should be able to

1) describe the functions of cell-mediated immunity (CMI) and the consequences of a deficiency in CMI.

2) describe the functions of antibody-mediated (humoral) immunity and the consequences of this type of deficiency.

3) discuss the approach to the differentiation between deficiencies of humoral immunity, CMI, phagocyte cell function, and complement.

4) list the different types of antibody-mediated immune deficiencies.

5) describe the consequences of combined immune deficiency.

6) describe the use of surface markers and mitogens for identification of T- and B-lymphocytes and state the postulated roles of these cells in the immune response.

7) describe the histologic distribution of T-cells and B-cells in the lymphoid tissues.

8) interpret results from the following lab tests:
   - Measurement of serum immunoglobulins
   - Measurement of antibody titers, i.e., enzymoimmunoassay, complement fixation, and 50% viral plaque reduction assay
   - Measurement of "natural" blood group antibody (isoagglutinins)
   - Measurement of hemolytic complement activity (CH50)
   - Skin testing with mumps antigen, purified-protein derivative (PPD) of tuberculin, histoplasmin, Candida antigens, and tetanus toxoid
   - Phytohemagglutinin (PHA) stimulation of peripheral blood lymphocytes
   - Measurement of antibodies to pneumococcal polysaccharides
   - Enumeration of lymphocyte subsets by flow cytometry

The goals of this activity are both to help you learn immunology and to increase your interpersonal skills. The fundamental aspect of all health professional activities is helping others. Like all behavior, this helping behavior becomes more effective and natural with practice. This POPS activity will enable you to practice by helping your fellow students learn basic science. Your skills in helping your fellow students should relate to your ability to help your patients in the future.

When you have become familiar with the objectives, complete the pretest on the next page.
Pretest

Instructions.- Please mark your answers to the following questions on this exam to facilitate later discussion and review. If your instructor has provided a separate answer form, please be sure to fill in the identification section; then answer the questions both on the form and on this exam.

Choose the one correct or most appropriate answer. If you do not know an answer, leave it blank. Do not guess. Health professionals who think they know something, but don't, can do real harm. Those who know they don't know something can get help.

Don't be upset if you don't know all the answers. The purpose of the pretest is to alert you to certain important concepts. The posttest will be similar to the pretest.

1. Detectable serum antibody against a T-independent pathogen is a good indication that:
   (A) a functional B-cell system exists.
   (B) a functional T-cell system exists.
   (C) both functional T-cell and B-cell systems must exist.
   (D) a cellular immune response to the pathogen has been mounted.
   (E) the patient has an immune deficiency.

2. Positive skin tests showing delayed-type hypersensitivity, such as for mumps or tuberculosis, indicate that:
   (A) a humoral immune response has occurred.
   (B) a cell-mediated immune response has occurred.
   (C) both the T-cell and B-cell systems are functional.
   (D) only the B-cell system is functional.
   (E) the patient has an immune deficiency.

3. A T-cell deficiency associated with thymic hypoplasia leads to infections predominantly of the following type(s):
   (A) intracellular bacterial (e.g., Mycobacterium) and extracellular bacterial (e.g., Staphylococcus)
   (B) extracellular bacterial (e.g., Staphylococcus) and viral
   (C) viral and intracellular bacterial
   (D) fungal and extracellular bacterial
   (E) none of the above

4. Infantile, X-linked agammaglobulinemia is associated with excessive infections of the following type(s):
   (A) intracellular bacterial (e.g., Mycobacterium)
   (B) extracellular bacterial (e.g., Staphylococcus)
   (C) viral
   (D) fungal
   (E) none of the above
5. Reaction to poison ivy is
(A) an antibody-mediated response referred to as allergic contact dermatitis.
(B) a cell-mediated response referred to as allergic contact dermatitis.
(C) a purely chemical response to caustic irritants.
(D) an IgE-mediated response referred to as allergic contact dermatitis.
(E) none of the above.

6. A lack of germinal centers and primary follicles in the lymph nodes, appendix, and spleen may indicate
(A) a deficient B-cell system.
(B) an acute dietary deficiency.
(C) a deficient cell-mediated immune system.
(D) an elderly patient.
(E) a deficient T-cell system.

7. A normal primary immune response in a human requires approximately how much time to produce detectable antibody levels in the blood?
(A) 5 to 10 hours
(B) 1 to 2 days
(C) 1 week
(D) 1 month
(E) 5 to 15 minutes

8. The complement system can be called
(A) a specific enhancer of nonspecific immunity.
(B) a specific enhancer of specific immunity.
(C) a nonspecific enhancer of nonspecific immunity.
(D) a nonspecific enhancer of specific immunity.
(E) none of the above.
Pretest (continued)

Questions 9 through 11 refer to the following data:
The sera (X and Y) and bronchial secretions (Z) were heated at 56°C for 30 minutes to destroy any complement present. Serum or secretions were then mixed with an antigen (Ag) in the presence of complement and incubated to allow fixation of complement if antibody (Ab) were present. To determine if complement remained in an active or "unfixed" state, indicator red blood cells (RBCs with antibody on their surfaces) were added after the incubation. Any unfixed complement then lysed the indicator RBCs.

Each of the 12 rows represents a reaction in a separate tube
+ means reagent added; - means reagent not added

<table>
<thead>
<tr>
<th>Tube</th>
<th>Antigen</th>
<th>Complement</th>
<th>Lysis of RBCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum X</td>
<td>Antigen 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>+</td>
<td>+</td>
<td>no</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>+</td>
<td>yes</td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>-</td>
<td>yes</td>
</tr>
<tr>
<td>4</td>
<td>+</td>
<td>+</td>
<td>no</td>
</tr>
<tr>
<td>Serum Y</td>
<td>Antigen 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>+</td>
<td>no</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
<td>+</td>
<td>no</td>
</tr>
<tr>
<td>7</td>
<td>+</td>
<td>-</td>
<td>yes</td>
</tr>
<tr>
<td>8</td>
<td>+</td>
<td>+</td>
<td>no</td>
</tr>
<tr>
<td>Secretions Z</td>
<td>Antigen 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>+</td>
<td>+</td>
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<td>10</td>
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<td>11</td>
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<td>yes</td>
</tr>
<tr>
<td>12</td>
<td>+</td>
<td>+</td>
<td>no</td>
</tr>
</tbody>
</table>

9. Is there antibody to antigen 1 in serum X?
   A. yes
   B. no
   C. can't tell, because Ag fixes complement without Ab present (anticomplementary Ag)
   D. can't tell, because antiserum fixes complement without homologous Ag present (anticomplementary antiserum)
   E. can't tell, because antiserum and homologous Ag lyse cells without complement

10. Is there antibody to antigen 2 in serum Y?
    A. yes
    B. no
    C. can't tell, because Ag fixes complement without Ab present (anticomplementary Ag)
    D. can't tell, because antiserum fixes complement without homologous Ag present (anticomplementary antiserum)
    E. can't tell, because antiserum and homologous Ag lyse cells without complement

11. Is there antibody to antigen 3 in bronchial secretions Z?
    A. yes
    B. no
    C. can't tell, because Ag fixes complement without Ab present
    D. can't tell, because bronchial secretions fix complement without homologous Ag present
    E. can't tell, because Ab such as IgA (which does not fix complement) could be present
Pretest (continued)

Questions 12 and 13 refer to the following data:

Explanation of Virus Neutralization Assay

This solid circle on the left represents a monolayer (a layer one cell thick) of monkey kidney fibroblasts in tissue culture.

![Image of untreated monolayer and poliovirus added monolayer.](untreated_monolayer.png)

Three days after a solution containing approximately ten infectious poliovirus particles was added, the monolayer of cells looked like the image on the right. (Each hole represents one “plaque”, i.e., an area where the cells were killed by the poliovirus.)

To determine the amount of antibody to poliovirus present, a standard amount of virus was added to increasing dilutions of the antiserum being tested. The serum-virus mixture was then spread over the surface of the tissue culture monolayer. The number of plaques obtained at each dilution was compared with the number of plaques obtained by plating the standard virus preparation without antiserum, thereby allowing a determination of the 50% plaque reduction titer.

This type of assay was done for poliovirus type 1 on serum from a patient, and the following results were obtained:

<table>
<thead>
<tr>
<th>Serum Dilution</th>
<th>1:2</th>
<th>1:10</th>
<th>1:50</th>
<th>1:250</th>
<th>1:1250</th>
<th>No Serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of plaques</td>
<td>0</td>
<td>2</td>
<td>40</td>
<td>60</td>
<td>101</td>
<td>120</td>
</tr>
</tbody>
</table>

12. A valid conclusion would be:
(A) the patient is not currently infected with type 1 poliovirus.
(B) the patient has Ab against type 1 poliovirus.
(C) the patient currently has an infection with type 1 poliovirus.
(D) the patient has a bacterial infection.
(E) the patient has no antibody against type 1 poliovirus.

13. The 50% plaque reduction titer deduced from the above data is:
(A) between 10 and 50.
(B) 250.
(C) about 60.
(D) between 250 and 1250.
(E) between 50 and 250.

When you have completed the pretest, consult your study materials. Try to identify the correct answers and understand the concepts that make them correct. The list of objectives may be used as a guideline for your studies. When your group meets, you will have the responsibility of explaining some of the correct pretest answers to the others.

*Please bring your textbook and pretest to the group meeting.*