Booklet B
Pretest Correct Answers

Please discuss the answers to each question with the members of your group. Be sure that no one has any questions about them. If any one does, try to explain the rationale for the right answer. In explaining something to another person, most people gain a better understanding of it and often transmit a better understanding. The pretest discussion and patient-oriented problem-solving parts of this activity are "open book." Be sure to refer to textbooks, notes, and other written resources whenever questions arise.

2. A functional cellular immune system is necessary for delayed-type hypersensitivity. B is therefore correct. Humoral immunity (B-cell system) is not needed for this response.

6. Primary follicles are the major site of localization of B-cells in lymphoid tissue, and germinal centers are a site of T-cell-dependent proliferation of B-cells. A deficiency in humoral immunity (Ab or B-lymphocytes) is often associated with a deficiency in follicles. A is therefore correct. A deficient T-cell system is often associated with deficiency in the thymus and in germinal center development, but does not affect the appearance of primary follicles. C and E are therefore incorrect. B is incorrect since an acute dietary deficiency does not lead to an immune deficiency. In fact, antibody synthesis seems to be among the last protein synthetic functions to disappear during severe starvation. D is incorrect since age is not associated with loss of germinal centers.

13. The titer is 250, the reciprocal of the dilution giving a 50% reduction in number of plaques per culture (i.e., half of the "no serum" control is 60). B is therefore the correct answer. What if the 1:250 dilution had given 55 plaques per culture? Ask your colleagues how they would determine the titer. (Answer: Draw a graph of plaques vs. dilution and extrapolate the dilution factor from the 50% reduction.)

After discussing all the pretest answers, please instruct your group to proceed to the "Introduction to the Clinical Problem."
Introduction to the Clinical Problem

The goal 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.

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. At the end of this problem, you will look at the correct answers to the problem and compare them with the answers you and your group wrote.

Begin the problem by presenting the patient's history on the following page to your colleagues.
Immunodeficiency Disease

Data Sheet B

Physical Exam

Temperature = 39.7ºC  Respirations = 30/min.
Pulse = 98/min.  Blood pressure = 105/70 mmHg

Positive findings:

Patient appears somewhat small for his age and undernourished.

Tonsillar tissue is scanty.

Right posterior inferior chest has mild dullness to percussion, tubular breath sounds, and crackling rales.

Skin has approximately 20 scars from old boils, and both ankles have poison ivy rash.

Previous Immunizations:

Hepatitis B given at birth
DPT (diphtheria, acellular pertussis, tetanus) and Haemophilus influenza B series was given starting at 3 months of age.
Salk poliovirus vaccine was administered subcutaneously at age 3 months and again at 1 year.
Sabin poliovirus vaccine was administered orally in two doses about one month apart at age 5.

Skin Test (intradermal):

Mumps - 15 mm induration at 48 hours
Tuberculin - no erythema or induration at 48 hours with intermediate-strength purified protein (PPD)
Tetanus toxoid - 12 mm induration at 48 hours

PHA stimulation (PHA is a "nonspecific" mitogen that stimulates DNA synthesis in human T lymphocytes):

<table>
<thead>
<tr>
<th></th>
<th>PHA</th>
<th>No PHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATIENT</td>
<td>80</td>
<td>28</td>
</tr>
<tr>
<td>CONTROL</td>
<td>24,900</td>
<td>500</td>
</tr>
</tbody>
</table>

These numbers are counts of radioactivity from $^3$H-thymidine incorporated into DNA by $10^8$ lymphocytes stimulated by PHA for 72 hours and exposed to $^3$H-thymidine for the final 12 hours.
Nitroblue Tetrazolium (NBT) test

Neutrophils were separated from the patient and an age-matched normal control, adjusted to the same concentration, and incubated with IgG-opsonized particles (Immunobeads) in the presence or absence of NBT, a colorless substance which turns deep blue if reduced as a consequence of the neutrophil respiratory burst. The samples were arranged in the following way, each point run in quadruplicate (rows A-D):

- **Column 1**: Buffer blank
- **Column 2**: NBT blank (control for spontaneous NBT reduction)
- **Column 3**: NBT + patient's neutrophils (control for NBT reduction by non-stimulated cells)
- **Column 4**: Patient's neutrophils + immunobeads (control for neutrophil aggregation)
- **Column 5**: Immunobeads + NBT (control for NBT reduction by immunobeads)
- **Column 6**: NBT + patient's neutrophils + immunobeads (test for reduction caused by ingestion of opsonized beads)
- **Column 7**: NBT + control neutrophils (control for reduction by non-stimulated cells)
- **Column 8**: NBT blank (control for spontaneous reduction)
- **Column 9**: Immunobeads + NBT (control for NBT reduction by immunobeads)
- **Column 10**: NBT + control's neutrophils + immunobeads (test for reduction caused by ingestion of opsonized beads)

The results of the test are shown below.

The next step is to review additional laboratory data given on Data Sheet C.