

Immunodeficiency Disease

Developed by

Parker A. Small, Jr, MD
Department of Immunology and
Medical Microbiology
College of Medicine
University of Florida
Gainesville, Florida

Susan M. Johnson, PhD
College of Pharmacy
University of Florida
Gainesville, Florida

Updated by

G. Virella, MD, PhD
Medical University of South Carolina
Charleston, South Carolina

Note to Students: The fundamental purpose of all activities in the health-care professions is to help other people. Like all behaviors, helping behavior becomes more effective and natural with practice. This workbook enables you to practice by helping your fellow students to learn basic science. Your skill at helping your fellow students should relate to your ability to help your patients in the future. This is a *Patient-Oriented Problem-Solving ("POPS")* workbook designed for four students. Before beginning this session, you should have (a) studied the objectives designed to prepare you for it, (b) taken the pretest, and (c) reviewed the topics listed at the end of the pretest. Now, each of you should take one of the four color-coded booklets and follow the directions in it. If your group has only three students, one of you should take two booklets. Leave the remainder of the workbook intact until you are given further instructions.

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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.

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Introduction

It has been known for centuries that there is great Interindividual 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:
 - (A). Measurement of serum immunoglobulins
 - (B). Measurement of antibody titers, ie, enzymeimmunoassay, complement fixation, and 50% viral plaque reduction assay
 - (C). Measurement of "natural" blood group antibody (isoagglutinins)
 - (D). Measurement of hemolytic complement activity (CH50)
 - (E). Skin testing with mumps antigen, purified-protein derivative (PPD) of tuberculin, histoplasmin, Candida antigens, and tetanus toxoid
 - (F). Phytohemagglutinin (PHA) stimulation of peripheral blood lymphocytes
 - (G). Measurement of antibodies to pneumococcal polysaccharides
 - (H). 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.

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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.

3. As a general rule, antibody is important in protection against extracellular organisms. Cellular immunity is more important for protection against intracellular organisms, since antibody cannot penetrate living cells. A T-cell deficiency will therefore predispose the patient to intracellular bacterial, viral, and fungal infections. Therefore, the correct answer is C.
8. Complement consists of a group of serum factors capable of reacting with antibody-antigen complexes when the antibody is IgM, IgG1, IgG2, or IgG3, regardless of the antigenic specificity of that antibody (*nonspecific enhancement*). Once a humoral immune response produces antibody to a specific antigen (*specific immunity*), the complement system is often capable of nonspecifically enhancing that immunity by amplifying the reaction through various enzymatic reactions that lead to lysis of cells, increased phagocytosis, opsonization, and other effects. D is therefore the correct answer.
10. The complement fixation test on serum Y is inconclusive as to the presence of Ab to homologous Ag. Since indicator RBCs were not lysed when the antigen alone was exposed to the complement (tube 6), the antigen itself fixed complement without Ab present (ie, the antigen is anticomplementary). It is therefore impossible to tell whether antibody plus Ag also fixes complement. C is therefore correct.

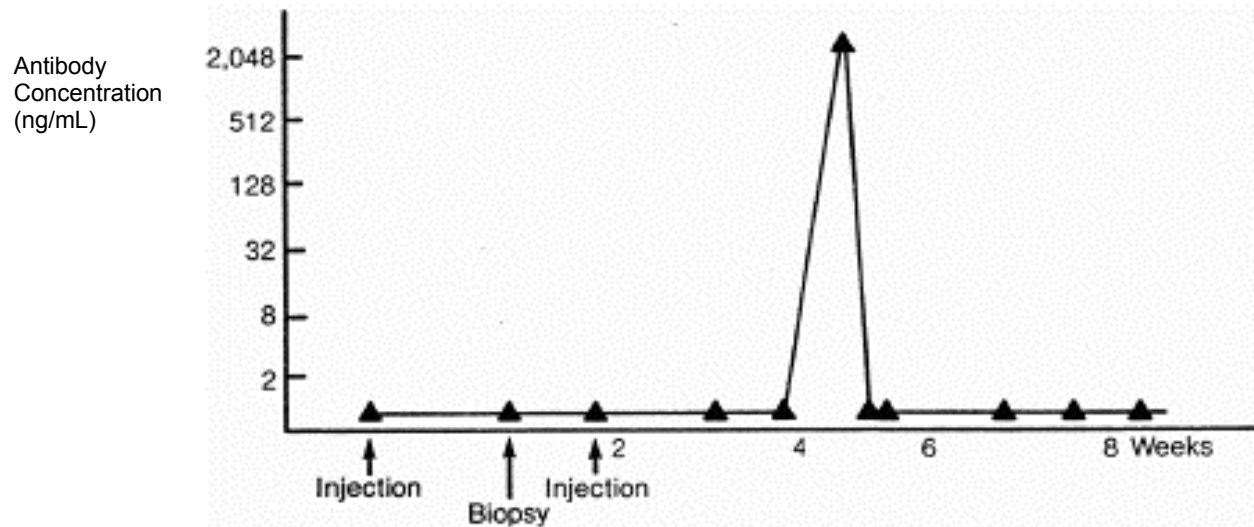
After discussing all the pretest answers, please instruct your group to proceed to the "Introduction to the Clinical Problem."

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Data sheet D

Other tests

The patient received the old *Haemophilus influenzae* polysaccharide vaccine subcutaneously in the left anterior thigh. Serum specimens drawn at 10 subsequent time points were tested for antibody to PRP and the results were plotted in the graph shown below (PRP, or polyribophosphate is the capsular polysaccharide of *Haemophilus influenzae* type b, against which protective immunity is directed). A small left inguinal lymph node was biopsied 10 days after the vaccine administration.



Peripheral blood lymphocyte subpopulations

- (A) Number of CD3+ lymphocytes (total T lymphocytes)
- (B) Number of CD4+ lymphocytes (helper T lymphocytes)
- (C) Number of CD8+ lymphocytes (cytotoxic/suppressor T cells)
- (D) Number of CD19+ lymphocytes (total B lymphocytes)

Patient	Normal range
2280/ μ L	700-2500/ μ L
1254/ μ L	430-600/ μ L
798/ μ L	280-1100/ μ L
12/ μ L	96-241/ μ L

When your group has completed its discussion, remove the group answer sheet and fill it out. Then compare your group answers with the correct answer sheet.

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Group Answer Sheet

Reminder - One of you should complete this sheet after the group has arrived at its answers.

1. *Diagnosis:* (Check one.)

_____ Normal immune system

_____ Granulocyte deficiency

_____ Complement deficiency

_____ Deficient cell-mediated immunity

_____ Humoral immune deficiency

_____ Combined immunodeficiency

2. *Data consistent with the diagnosis.* (Underline that data which you feel was of crucial importance.)

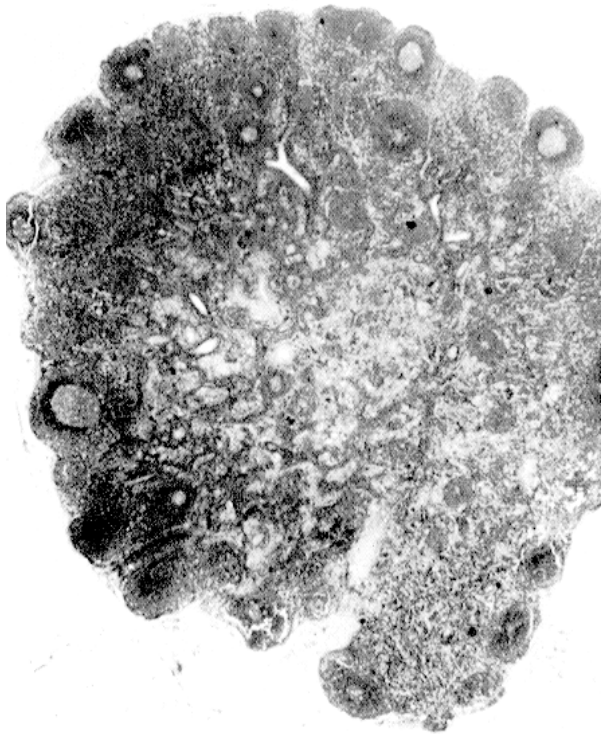
3. *Data irrelevant for making diagnosis:*

4. *Data inconsistent with the diagnosis.*

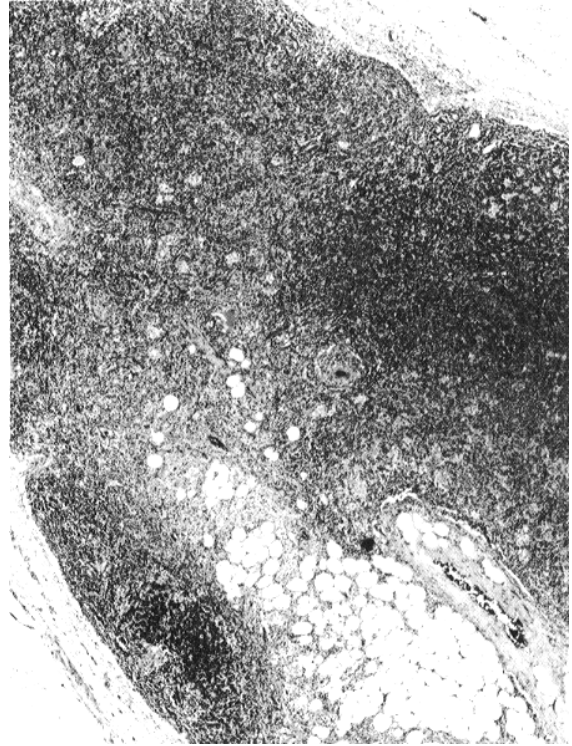
5. *Brief description of expected lymph node histology.*

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The following photographs illustrate normal lymph node architecture (A) and the abnormalities expected in this patient (B). Identify the abnormal lymph node and enumerate the abnormalities that you can see on it.



A



B

Figures reproduced from Stansfeld, A.G. and d'Ardenne, A.J. Lymph Node Biopsy Interpretation (2nd Ed.), Churchill Livingstone, Edinburgh, 1992.