

Influenza: Serologic Diagnosis and Epidemiology

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The reason the POPS system works so well is that they have been revised many times based on feedback from students and faculty.

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Note to Instructors

This workbook is divided into five sections:

1. Introduction to the POPS System, introduction to and objectives of the clinical simulation, and a pretest
2. Four booklets with pretest answers and the clinical problem(s)
3. Group question and answer sheets
4. Posttest
5. Posttest answers

Each student should receive a copy of section 1 to study and answer questions before the group problem-solving session. If you wish, section 2 also may be distributed for the students to review prior to the group session.

A Patient-Oriented Problem-Solving (POPS) System

System supported by the American Medical Association Education and Research Foundation

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

This is a Patient-Oriented Problem-Solving activity. The purposes are:

1. To help you learn how to apply your basic science knowledge to the solution of clinical problems
2. To help you learn how to better use sources (ie, textbooks and peers) that will be available to you throughout your career
3. To help you work with your fellow students and thus
 - a. increase your ability to evaluate your colleagues' opinions, thought processes, and diagnoses
 - b. increase communications skills
 - c. get to know your classmates better

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. Information exchange and group interaction are keys to the success of this phase. This process will allow you to teach your fellow students and, at the same time, learn from them. Finally, you will take a posttest, individually, which will enable you to assess your progress.

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Introduction

Influenza is an epidemic disease that occurs yearly and causes much suffering and loss of life. Moreover, at less frequent intervals (eg 1918, 1957, 1968 and 1977), influenza causes world pandemics; the one in 1918 caused 20 million deaths. This Patient-Oriented Problem-Solving activity deals with the laboratory procedure used to diagnose the disease. The basic concepts are also applicable to the diagnosis of many other diseases.

Influenza virus and certain other viruses are able to agglutinate red blood cells (RBCs). This is called hemagglutination (HA). However, in the presence of specific antibody to the virus, HA is blocked. This phenomenon provides the basis for an assay used to detect and quantitate specific antiviral antibodies in serum. This test is known as the hemagglutination inhibition (HI) assay.

In this activity, you will be asked to analyze HI data from several patients. Upon completion of the group session, you should be able to

- 1) determine, based upon HI data, whether a patient was
 - a) infected with the pathogen during the period of acute illness or
 - b) infected or immunized prior to that time with an antigenically identical or similar pathogen.

In order to accomplish these objectives, you must be able to

- 2) schematically draw the in vitro interactions of virus, RBCs, and antibody in HA and HI assays.
- 3) interpret an HI assay, determine the HI **titer**, and defend or dispute the validity of the data based on the controls.
- 4) compare **acute** and **convalescent serum titers** to determine whether there has been a significant increase in antibody.

In addition to learning these facts and concepts, it is important that you get to know your classmates better and become more skilled at teaching and learning from each other. Much of your learning during your clinical training and throughout your professional career will result from interactions with peers, house staff, and practicing physicians. Improving your ability to be patient with, considerate of, and helpful to your colleagues is easier now (when the “pressure” comes from a simulated clinical problem) than it will be when the well-being of an actual patient is at stake. Good habits that you develop now hopefully will continue in the future.

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

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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.

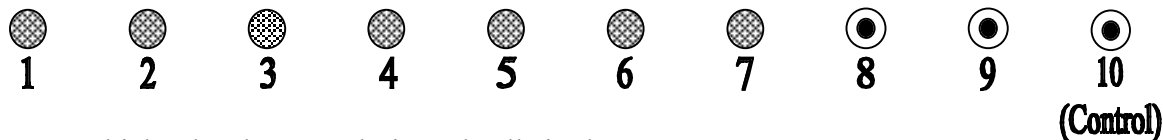
Choose the *one* correct or most appropriate answer. If you do not know an answer, leave it blank. Do not guess. Health professionals who think they know something, but don't, can do real harm. Those who *know* they don't know something can get help.

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

1. What is the minimal number of red blood cell (RBC) binding sites required on a virus for the virus to agglutinate RBCs?
(A) 0
(B) 1
(C) 2
(D) 10
(E) >10

Questions 2 through 4 relate to the following hemagglutination (HA) assay:

A 1.0 ml sample of influenza virus suspension was added to test tube #1, and 0.5 ml of saline was added to tubes #2 through #9. A 0.5 ml sample of the virus suspension was removed from tube #1 and added to tube #2. After mixing, 0.5 ml was removed from tube #2 and added to tube #3. This proceeded until all the dilutions were made and 0.5 ml from tube #9 was discarded. Tube #10 contained only 0.5 ml of saline. Chicken RBCs were then added to all the tubes, and the following pattern was observed. (Each circle represents one test tube viewed from above.)













2. Which tubes have agglutinated cells in them?
(A) 1 through 7
(B) 8 through 10
(C) 8 and 9
(D) 10
(E) None of the above
3. What is the dilution of virus suspension in tube #5 (ignoring the volume of RBCs added)?
(A) Undiluted
(B) 1:8
(C) 1:16
(D) 1:32
(E) None of the above

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4. What is the HA titer of the virus suspension?
- (A) 32
 - (B) 1:64
 - (C) 64
 - (D) 128
 - (E) 1:258
5. *In vitro* HA can be caused by
- (A) antibody to RBC and all viruses.
 - (B) antibody to RBC only.
 - (C) viruses only.
 - (D) some viruses and antibody to RBC.
 - (E) neither virus nor antibody.
6. Like most infectious diseases, the diagnosis of influenza is suspected on clinical grounds, and can be confirmed by all the following except:
- (A) Isolation of the pathogen
 - (B) Antigen detection
 - (C) IgM titers
 - (D) Rise in IgG titers (acute and convalescent)
 - (E) Elevated complement levels
7. In October, Mr. Smith, a 66-year old man, comes to your office for his annual physical examination. He received an influenza vaccine last fall and wants to know if he needs another one this year. You recommend influenza vaccination (an inactivated virus vaccine) to him for all of the following reasons except:
- (A) He is over age 65-years, and older persons suffer excessively from influenza.
 - (B) Influenza vaccine is an inactivated vaccine; antibody induced by inactivated vaccines tend not to last as long as that induced by live virus infection
 - (C) The influenza virus undergoes periodic antigenic changes; serum antibody is very specific, so a new vaccination is needed to induce specific antibody to the current circulating strain.
 - (D) Multiple influenza vaccinations induce anti-influenza cellular immunity, which is deficient in older persons.

The following hemagglutination inhibition (HI) assay pattern relates to questions 8 through 11.

Circles 1 through 7 represent test tubes to which have been added increasing dilutions of a serum containing antibody to influenza virus, followed by constant amounts of influenza virus, and finally RBCs. The controls contain RBCs plus saline (8), RBCs plus serum (9), or RBCs plus virus (10).

Dilution of Serum							Cell	Serum	Virus
1:10	1:20	1:40	1:80	1:160	1:320	1:640	Control	Control	Control
									
1	2	3	4	5	6	7	8	9	10

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8. Which of the test tubes demonstrate HI?

- (A) 1,2,3,4,8,9
- (B) 5,6,7,10
- (C) 8,9
- (D) 5,6,7
- (E) 1,2,3,4

9. Which of the drawings (A to E below) schematically represents the cellular and molecular events taking place in tube #2?



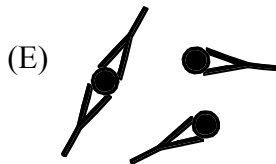
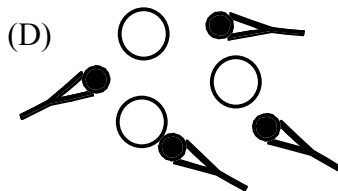
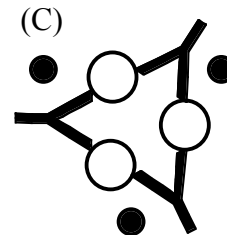
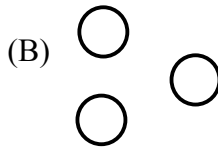
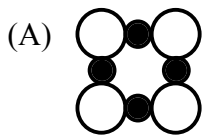
RBC



Antibody to virus



Virus



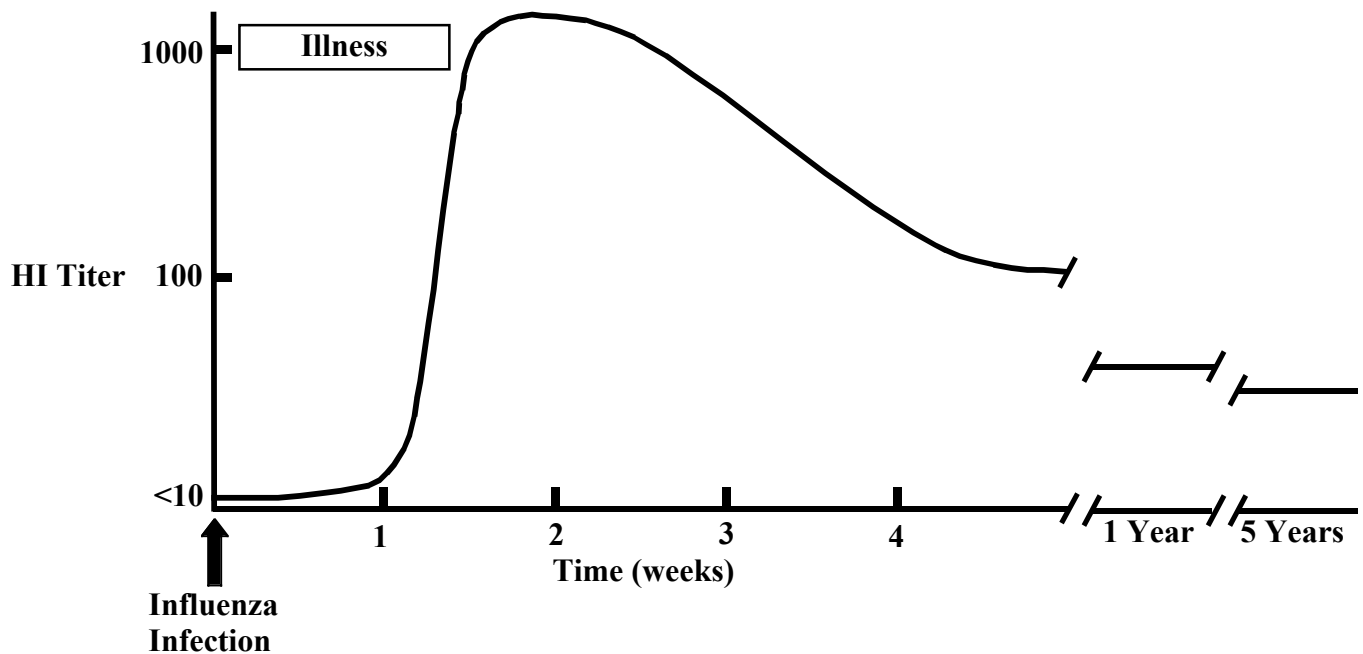
10. Which of the drawings (A through E in question 9) represents the virus control?

11. What is the titer of the serum assayed in the HI test?

- (A) Less than 10 (<10)
- (B) 80
- (C) 160
- (D) Greater than or equal to 640 (≥ 640)
- (E) Cannot be determined from the data

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Questions 12 and 13 pertain to the following graph:



12. Determine from the graph how long it takes to obtain an antibody increase after the onset of an influenza infection. (The ILLNESS box represents the duration of clinical disease.)
- (A) 1 to 2 days
 - (B) 3 to 6 days
 - (C) 1 to 2 weeks
 - (D) 3 to 4 weeks
 - (E) >1 month
13. Determine from the graph how long detectable antibody lasts.
- (A) Less than 1 month
 - (B) 1 to 11 months
 - (C) 1 year
 - (D) 5 years
 - (E) Greater than 5 years
14. What will produce a serum antibody rise to a specific influenza virus isolate in a 50-year-old patient?
- (A) An immunization with that influenza virus
 - (B) An infection with that influenza virus
 - (C) Both A and B
 - (D) Neither A nor B

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In answering questions 15 through 18, refer to the HI test below.











Answer *true* by selecting a.

Answer *false* by selecting b.

Answer by selecting c if it is impossible to determine whether the statement is true or false from the data given.

Leave the answer blank if you aren't sure.

Joe Brown had the following HI test results for influenza B antibody. (Joe has never had "flu shots" or other influenza immunizations.)

Dilution of Serum							Cell	Serum	Influenza Type B Virus
1:10	1:20	1:40	1:80	1:160	1:320	1:640	Control	Control	Control
									
1	2	3	4	5	6	7	8	9	10

15. Joe had an acute influenza B infection at the time of the test. a b c
16. Joe never had an infection with influenza B. a b c
17. Joe had antibody to influenza B in his serum. a b c
18. Joe had an influenza B infection during the past year. a b c

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