

Tetanus Immunity

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BOOK D

Note to Students The fundamental purpose of all activities in the health-care professions is to help other people. Like all behavior, 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.

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 (i.e., textbooks and peers) that will be available to you throughout your career

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

This clinical Simulation deals with tetanus, a life-threatening infection. Tetanus is caused by an exotoxin synthesized by the bacterium *Clostridium tetani*. The toxin is released after a wound is infected by this bacterium. This toxin causes muscle spasm, which may lead to death if not treated correctly. Spasms of the masseter muscles have led to the name lockjaw. Every time a patient with a wound is examined, the physician must determine the appropriate immunization for the prevention of tetanus. This simulation will help you understand the different approaches to the prevention of tetanus as well as the indications for each approach. The immunologic concepts addressed in this problem are fundamental to the understanding of many other diseases.

When you have completed this activity you should be able to

- 1) define and give several examples of immunity.
- 2) compare and contrast the terms antigen and antibody.
- 3) differentiate between active and passive immunization and be able to give examples of each.
- 4) compare and contrast the primary and secondary (anamnestic) immune responses in terms of their time course and magnitude.state
- 5) differences between acquired and innate immunity, as well as between specific and nonspecific immunity.
- 6) state which cell types are involved with cell-mediated and antibody-mediated immunity.
- 7) compare tetanus toxin and tetanus toxoid relative to toxicity and immunogenicity.
- 8) select the appropriate immunization for a patient with a wound, given his past medical history.

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

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Pretest Correct Answers

You have the answers to the ten pretest questions. First, study the answers in your booklet and then EXPLAIN them to your group. Please don't just read them to your classmates, and don't let your classmates read their answers to you. 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. The correct answer is E. Toxoid will stimulate the production of antitoxin, which will be protective. Heterologous antiserum will stimulate the production of antibody to the foreign protein; this response can lead to serum sickness. Toxin is lethal at doses below those required to stimulate antibody formation, so it will not produce an immune response but obviously will produce a very harmful nonimmune response (i.e., toxin will kill the first time a person is exposed to it).

There is a very important implication to the fact that it takes more toxin to stimulate the antibody production than to kill a person; unlike most diseases, someone recovering from tetanus (a very rare event if untreated) will not have developed immunity.

Homologous antiserum may, on some occasions, elicit antibody responses in certain situations (different allotypes or idiotypes). but these are neither beneficial nor dangerous.

7. The correct answer is B. Immunity means insusceptibility to a disease. Immunity can be innate or acquired, as shown in the diagram below. Innate immunity is present from birth and is independent of the life experiences of the person, whereas acquired immunity arises only after an infection or immunization and hence is acquired during life. Acquired immunity is specific for the infecting organism or immunizing antigen. Thus, a chickenpox infection protects specifically against reinfection by chickenpox virus but does not protect against measles virus infection. Innate immunity is usually nonspecific. For example, stomach acid destroys many different bacteria and viruses in food and thereby protects us from infection nonspecifically. Lysozyme in tears digest the cell wall of many bacteria and in so doing nonspecifically prevent conjunctivitis.

Specific acquired immunity is further subdivided into "antibody-mediated" or "cell-mediated," depending on whether antibody alone provides the protection or whether T-lymphocytes alone provide the protection. Do not be confused by the fact that antibody is synthesized in cells (B-lymphocytes); the origin of the molecules is not relevant to how protection is provided.

Antibody-mediated immunity is *active* when the person synthesizes his own antibody; it is *passive* when another person or animal synthesizes the antibody and it is subsequently injected into the person receiving the passive immunization. Cell-mediated immunity is *active* when the person's own T-cells are stimulated or *adoptive* when the source of stimulated T-cells is another person. Adoptive immunization is rarely used with humans because the recipient will reject the cells unless they are histocompatible (e.g. from an identical twin).

Since people are susceptible to tetanus until they are immunized, the immunity is acquired, not innate. Tetanus immunization protects against tetanus but no other disease, so the immunity is specific, not nonspecific. Since passive immunization with antiserum provides protection, that protection is antibody-mediated, not cell-mediated.

9. One injection of a heterologous serum, such as horse serum, may stimulate production of antibody to the foreign proteins. The foreign proteins may persist in the body long enough (seven to 14 days) to react with the newly formed antibody. Antibody-antigen complexes form in the blood and are deposited in various tissues, producing pathologic changes in those tissues. More specifically, deposition of immune complexes in the renal glomeruli leads to glomerulonephritis, and deposition in synovial membranes leads to arthritis. This process produces the disease called serum sickness. C is therefore correct.

When your group has finished discussing the pretest, you should read the "Instructions for the Clinical Problem" on the next page of your booklet.

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Instructions for the Clinical Problem

The purpose of this exercise is to allow you to apply your knowledge of active Vs passive immunization and primary Vs secondary (or anamnestic) immune response to a common medical problem.

Each of the four group members has a different case history. First, deal with your own patient. After reading your patient's case history, decide the therapy you would use, the reasons for the choice, and the consequences of alternative therapy. Next, fill out your answer sheet concerning your patient. After everybody has finished his/her problem, the group member with the first patient should present that case history to the other three group members and allow them time to individually decide therapy, the reasons for their choice, and the consequences of alternative therapy. They should then fill out their answer sheets for that patient (i.e., commit themselves to therapy before the group discussion). The group member who has the first patient should then present his/her choice of therapy to the group and defend it. Members who disagree with this choice, the reasons for it, or consequences of it should present their ideas and defend them. After discussion of the first patient is completed, compare your answers with those on the correct answer sheet for each patient.

This process will then be repeated for the other three cases. Patients should be presented in numerical order. At first glance, the patients' cases seem repetitious, but there are subtle and important differences!

Remember, this is an "open-book" activity, and you should consult your textbooks about any point you don't understand.

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Fourth Patient: Alice Wipple

A 35-year-old migrant worker arrives at your office with a three-inch jagged wound on her head. She was hit with a brick. Ten years ago she fell off a tractor while tilling a field and received a six-inch laceration of her left thigh. At that time, she was given tetanus antitoxin (equine) because she had never been immunized against tetanus. She and her fellow migrant workers left town before her physician could immunize her with tetanus toxoid. What do you do to prevent tetanus? Indicate your therapy on the Tetanus Immunity Clinical Problem Answer Sheet (instructions on the next page and treatment options for Alice on the bottom of the following page).

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Clinical Problem Answer Sheet

Check the box(es) that indicate(s) the preferred therapy for each patient. Then briefly write the reasons for your choice in the space provided. Finally, describe the consequences of each of the other therapies in the space provided under each therapy. Commit yourself in writing before the discussion begins. The answer sheet will not be collected.

Joe Alsop (First Patient)

- 1. Give tetanus toxin.
- 2. Give tetanus toxoid.
- 3. Give tetanus antitoxin (equine).
- 4. Give tetanus immune globulin (human).

Lester Williams (Second Patient)

- 1. Give tetanus toxin.
- 2. Give tetanus toxoid.
- 3. Give tetanus antitoxin (equine).
- 4. Give tetanus immune globulin (human).

Tommy Criton (Third Patient)

- 1. Give tetanus toxin.
- 2. Give tetanus toxoid.
- 3. Give tetanus antitoxin (equine).
- 4. Give tetanus immune globulin (human).

Alice Wipple (Fourth Patient)

- 1. Give tetanus toxin.
- 2. Give tetanus toxoid.
- 3. Give tetanus antitoxin (equine).
- 4. Give tetanus immune globulin (human).

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Correct Answers for Alice Wipple (Patient #4)

Tetanus Toxin

The patient dies!

Tetanus Toxoid

If the wound was infected by *Clostridium tetani*, the patient would die of tetanus one to two weeks after her injury. Alice had never been immunized against tetanus, and the primary immune response produced by tetanus toxoid is not rapid enough to provide adequate antibody before lethal amounts of toxin are produced. However, active immunization with tetanus toxoid should be used in conjunction with passive immunization so the patient will have immunity in the future.

Tetanus Antitoxin (Equine)

The patient died from an anaphylactic response. Alice was sensitized to the foreign protein (horse gamma globulin or other horse serum proteins) ten years earlier, i.e., the prior immunization led to prolonged production of anti-horse protein antibody. Upon injection of the horse protein this time, that antibody rapidly combined with the horse antigen and produced anaphylaxis.

Tetanus Immune Globulin (Human)

This is part of the optimal treatment for Alice. Passive immunization is the fastest and only foolproof way of getting toxin-neutralizing antibody to her in time to prevent tetanus. By the use of human antibody, you virtually eliminated the potential adverse effects that would probably occur with tetanus antitoxin (equine). Passive immunization does not confer prolonged protection, so she also needs to be actively immunized with tetanus toxoid at the same time in a separate injection site.

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Summary of Major Concepts of Tetanus Immunity and Boosters

Primary Immunization should be given to everybody to prevent tetanus. The precise ages at which diphtheria, pertussis, and tetanus (DPT) shots are given are listed in any pediatrics textbook and are best learned when you are studying pediatrics. In general, however, children receive three doses in the first six months of life and boosters at ages 1 and 5. These injections stimulate lymphocytes to produce antibody. These IgG antibody molecules have a half-life of three weeks, just like passively administered human IgG, but the "antibody factories" continue to turn out more antibody so it persists in high enough concentrations to provide protection for five to ten years (see Table 1). The injections also produce memory lymphocytes that, unlike the antibody, persist throughout life and are ready to rapidly produce antibody the next time the antigen, tetanus toxoid, is administered.

Booster immunization with tetanus toxoid can lead to the production of adequate amounts of protective antibody within three to five days (even when there is little or no circulating antibody) if there are memory lymphocytes primed by a previous tetanus toxoid injection. Remember: Previous disease will not stimulate the immune system in patients with tetanus, but it does in patients with most other infectious diseases.

Passive immunization with tetanus immune globulin (human) will provide instantaneous immunity, but antibodies disappear with a half-life of three weeks and memory lymphocytes are not produced to help the next time. It should never be the sole therapy in normal patients. Consult Table 1 for the appropriate treatment. Tetanus antitoxin (equine) should be used only when human antiserum is not available and passive immunization is imperative. When tetanus immune globulin (human) or tetanus antitoxin (equine) and tetanus toxoid are given at the same time, each should always be injected at different sites.

TABLE 1. Guide to tetanus prophylaxis in wound management
(Modified from Morbidity and Mortality Weekly Report 30:392-396, 401-407, 1981.)

Td = tetanus toxoid TIG = tetanus immune globulin (human)

History of tetanus immunization (doses)	Clean, minor wounds		All other wounds	
	Td	TIG	Td	TIG
Uncertain	Yes	No	Yes	Yes
0-1	Yes	No	Yes	Yes
2	Yes	No	Yes	No*
3 or more	No†	No	No‡	No

* Unless wound more than 24 hours old

† Unless more than 10 years since last dose

‡ Unless more than 5 years since last dose