

Basic Immunological Procedures



12

Molecular Diagnostic Techniques

Lela Buckingham, PhD, MB(ASCP), DLM (ASCP)

LEARNING OUTCOMES

After finishing this chapter, you should be able to:

1. Outline the mechanisms of central and peripheral tolerance that are essential in preventing the development of autoimmunity.
2. Describe genetic and environmental factors that are thought to contribute to the development of autoimmunity.
3. Discuss the relationship between microbial infections and the development of autoimmune disease.
4. Distinguish between organ-specific and systemic autoimmune diseases, giving examples of each.
5. Discuss the proposed etiology, immunopathology, and clinical manifestations of each of the following diseases: Systemic lupus erythematosus (SLE), Rheumatoid arthritis (RA), Granulomatosis with Polyangiitis (Wegener's Granulomatosis), Graves' disease, Hashimoto's thyroiditis, Celiac disease, Type I diabetes mellitus, Celiac disease, Autoimmune hepatitis, Primary biliary cirrhosis, Multiple sclerosis (MS), Myasthenia gravis (MG), Goodpasture's syndrome.
6. Associate each of the diseases listed above with their corresponding autoantibodies and laboratory findings.
7. List laboratory methods used to screen for and confirm the presence of antinuclear antibodies (ANA).
8. Describe common immunofluorescence patterns seen in the indirect immunofluorescence test for ANAs and their clinical significance.
9. Describe the c-ANCA and p-ANCA patterns seen in the indirect immunofluorescence test for ANCA and their clinical significance.
10. Discuss the clinical significance of rheumatoid factor (RF) and anti-CCP.
11. Differentiate between autoinflammatory diseases (AIDs) and autoimmune diseases, and provide examples of AIDs.

CHAPTER OUTLINE

INTRODUCTION TO CYTOKINES

CYTOKINES IN THE INNATE IMMUNE RESPONSE

Interleukin-1

Tumor Necrosis Factor- α

Interleukin-6

Chemokines

Transforming Growth Factor- β

Interferon- α and Interferon- β

CYTOKINES IN THE ADAPTIVE IMMUNE RESPONSE

T-helper 1 Cytokines

T-helper 2 Cytokines

Cytokines Associated with T Regulatory Cells

CYTOKINE AND ANTICYTOKINE THERAPIES

CLINICAL ASSAYS FOR CYTOKINES

SUMMARY

CASE STUDY

REVIEW QUESTIONS

REFERENCES



You can go to DavisPlus at davisplus.fadavis.com keyword stevens for the laboratory exercises that accompany this text.

KEY TERMS

Anergy	Autoimmune disease	Epitope spreading
Antinuclear antibody (ANA)	Autoimmune liver disease	Extractable nuclear antigen (ENA)
Anti-centromere antibodies	Autoimmune thyroid disease (AITD)	Fluorescent antinuclear antibody (FANA) testing
Anti-cyclic citrullinated peptide (anti-CCP)	Autoinflammatory disease	Goodpasture's syndrome
Anti-histone antibodies	Celiac disease	Granulomatosis with Polyangiitis (Wegener's Granulomatosis)
Anti-neutrophil cytoplasmic antibody (ANCA)	Central tolerance	
Anti-RNP antibody	CREST syndrome	
Auto-antibody	Double-stranded DNA (ds-DNA) antibodies	
	Epigenetics	

Molecular diagnostic assays are powerful tools used to gain information to aid in diagnosis and monitoring of disease and now play a central role in medicine. These techniques are based on the detection of specific nucleic acid sequences in microorganisms or particular cells. Such techniques may be an advantage in clinical diagnosis, as detection of nucleic acids can be accomplished long before antibody detection is possible. Immunodeficiency and autoimmune diseases that have a genetic basis can also be identified more quickly. Molecular diagnostics also contribute to therapeutic decisions, transplant selection, drug efficacy, forensics, and disease prognosis.¹ Molecular techniques used in the clinical laboratory to identify unique nucleic acid sequences include enzymatic cleavage of nucleic acids, gel electrophoresis, enzymatic amplification of target sequences, and hybridization with nucleic acid probes.

Characteristics Of Deoxyribonucleic Acid And Ribonucleic Acid

The two main types of nucleic acids are **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA)**. DNA carries the primary genetic information within chromosomes found in each cell. RNA, on the other hand, is an intermediate nucleic acid structure that helps convert the genetic information en-

coded within DNA into proteins that are the primary cellular component. Both DNA and RNA are macromolecules of nucleotides. A **nucleotide** is a unit composed of a phosphorylated ribose sugar and a nitrogen base. DNA and RNA have the same two purine bases, adenine and guanine, but the pyrimidine bases differ. DNA uses cytosine and thymine, while in RNA, cytosine is present, but uracil replaces thymine (**Fig. 12-1**).

The Ebola virus causes one of the most serious and fatal diseases known to humans. This single-stranded RNA virus begins its attack on the body within two to twenty-one days after exposure. Early symptoms include severe headache, fever, muscle pain, fatigue, diarrhea, vomiting, abdominal pain, and unexplained bruising or hemorrhaging. It is extremely infectious and can spread quickly through a population.

As the immune system tries to halt the spread of the virus, a profuse release of pro-inflammatory cytokines occurs, often called a cytokine storm. It is actually the overabundance of cytokines that is responsible for the devastating effects on the body. TNF-, in particular, causes the blood vessels to become

6-1 Clinical Correlations

The Role of Cytokine Storm in Ebola Virus Infection

The Ebola virus causes one of the most serious and fatal diseases known to humans. This single-stranded RNA virus begins its attack on the body within two to twenty-one days after exposure. Early symptoms include severe headache, fever, muscle pain, fatigue, diarrhea, vomiting, abdominal pain, and unexplained bruising or hemorrhaging. It is extremely infectious and can spread quickly through a population.

As the immune system tries to halt the spread of the virus, a profuse release of pro-inflammatory cytokines occurs, often called a cytokine storm. It is actually the overabundance of cytokines that is responsible for the devastating effects on the



FIGURE 55-1 *Treponema pallidum*. Electron micrograph showing the colic and periplasmic flagella. (Courtesy of CDC Archives, Atlanta, GA)

more permeable, resulting in dangerously low blood pressure. As the platelet count drops, excessive bleeding occurs from every orifice in the body. Death typically results in one to two weeks after infection.

The cytokine storm is a profound example of the importance of regulation of the immune system. If left unchecked, the cytokines that normally help to overcome infection can have a deleterious effect.

Nucleotides

In DNA, the nitrogen base of a nucleotide—either guanine, adenine, cytosine or thymine—is attached to the 1 carbon of the deoxyribose sugar. The ribose 5 carbon is mono-, di- or triphosphorylated. The ribose 3 carbon carries a hydroxyl group (OH). Positions in the deoxyribose and nitrogen base rings are numbered as shown in Figure 12–2.

Major functions of IgG include the following:

- Providing immunity for the newborn because IgG is the only antibody that can cross the placenta;
- Fixing complement;
- Coating antigen for enhanced phagocytosis (opsonization); (4) neutralizing toxins and viruses; and
- Participating in agglutination and precipitation reactions.

All subclasses are able to participate in the secondary immune response, an enhanced and quicker response to antigen, although their appearance depends upon the triggering antigen. IgG1 and 3 are induced in response to protein antigens, while IgG 2 and 4 are associated with polysaccharide antigens.⁷

There are hundreds of restriction enzymes with unique binding and cleavage sites. The restriction enzymes used in the clinical laboratory (Type II restriction enzymes) recognize palindromic sites. These sites are nucleotide sequences that read the same 5 to 3 on both strands of the DNA. For example,



is the recognition site for the restriction enzyme, EcoRI. Restriction enzymes are named for the organisms from which they were isolated. EcoRI was the first enzyme isolated from

E. coli, strain R. HindIII is the third enzyme isolated from *H. Influenzae*, strain d. In a bacterium, restriction enzymes serve as part of a primitive immune system that allows it to recognize its own DNA and degrade any incoming foreign DNA.

Lymphoblastic Leukemias

Lymphoblastic leukemias are characterized by the presence of lymphoblasts in the peripheral blood. These cells are small and contain little cytoplasm, dense nuclear chromatin, and indistinct nucleoli (Fig. 16–2). Leukemias are generally classified as either acute or chronic. Chronic leukemias are usually slowly progressive and compatible with extended survival. However, they are generally not curable with chemotherapy. By contrast, acute leukemias are generally much more rapidly progressive but have a higher response rate to therapy.

Study Tip 3 The best indication of a current infection is a 4-fold rise in antibody titer when comparing two serum samples collected from a patient during the beginning and later stages of the infection. This is a good time to review the typical antibody response curve shown in Chapter 5 Antibody Structure and Function.

Other Endogenous and Environmental Factors

Hormonal Influence

Tissue Trauma and Release

Women are 2.7 times more likely to acquire an autoimmune disease than men, and that about 78 percent of patients with autoimmune diseases are of female gender.⁸ These observations suggest that there is a hormonal influence on the development of autoimmunity. Studies on the effects of hormones have shown that estrogens tend to direct the immune system in favor of a Th2 type response, resulting in more B cell activation and antibody production, while androgens favor a Th1 type response with activation of CD8+ T cells.

Tissue Trauma and Release of Cryptic Antigens. As we discussed above, immunologic tolerance to self antigens occurs during the early development of lymphocytes in the thy-

Table 5-3 Comparison Of T And B Cells

T CELLS	B CELLS
Identified By Rosette	Product of Activation
Develop in the thymus	Develop in the bone marrow Identified by surface immunoglobulin
Found in blood (60%–80% of circulating lymphocytes), thoracic duct fluid, lymph nodes	Found in bone marrow, spleen, lymph nodes Identified by surface immunoglobulin
Identified by rosette formation with SRBCs	Identified by surface immunoglobulin End product of activation is antibody
End products of activation are cytokines	End product of activation is antibody
Antigens include CD2, CD3, CD4, CD8	Antigens include CD19, CD20, CD21, CD40, MHC class II

SRBC = Sheep red blood cells

mus and bone marrow, and then continues after their release into the periphery. However, during these times, some self antigens may be cryptic, or hidden within the tissues of the host.^{1,4,9}

The Joint Commission (JC), an independent body that certifies and accredits healthcare organizations in the United States, requires that all health-care facilities post evacuation routes and detailed plans to follow in the event of a fire. When a fire is discovered, all employees are expected to take the actions described by the acronym RACE.

Rescue—rescue anyone in immediate danger

Alarm—activate the institutional fire alarm system

Contain—close all doors to potentially affected areas

Extinguish/Evacuate—attempt to extinguish the fire if possible, or evacuate, closing the door.

16-2 Connections

Lymphoblasts and Lymphocytes

The Ebola virus causes one of the most serious and fatal diseases known to humans. This single-stranded RNA virus begins its attack on the body within two to twenty-one days after exposure. Early symptoms include severe headache, fever, muscle pain, fatigue, diarrhea, vomiting, abdominal pain, and unexplained bruising or hemorrhaging. It is extremely infectious and can spread quickly through a population.

As the immune system tries to halt the spread of the virus, a profuse release of pro-inflammatory cytokines occurs, often called a cytokine storm. It is actually the overabundance of cytokines that is responsible for the devastating effects on the body. TNF- α , in particular, causes the blood vessels to become more permeable, resulting in dangerously low blood pressure. As the platelet count drops, excessive bleeding occurs from every orifice in the body. Death typically results in one to two weeks after infection

Fire blankets should be present in the laboratory. Persons whose clothes are on fire should be wrapped in the blanket to smother the flames. The acronym PASS can be used to remember the steps in operating a fire extinguisher:

1. Pull pin
2. Aim at the base of the fire
3. Squeeze handles
4. Sweep nozzle side to side

The Standard System for the Identification of the Fire Hazard of Materials, NFPA 704, is a symbol system used to inform firefighters of the hazards they may encounter when fighting a fire in a particular area. The color-coded areas contain information relating to health hazards, flammability, reactivity, use of water, and personal protection.

SUMMARY

The Standard System for the Identification of the Fire Hazard of Materials, NFPA 704, is a symbol system used to inform firefighters of the hazards they may encounter when fighting a fire in a particular area.

- The basic structural unit for all immunoglobulins is a tetrapeptide composed of two L and two H chains joined together by disulfide bonds.
- The five classes of antibodies are IgM, IgG, IgA, IgD, and IgE. IgG, IgD, and IgE exist as monomers. IgA has a dimeric form, and IgM is a pentamer whose subunits are held together by a J chain.
- Kappa and lambda (L chains) are found in all types of immunoglobulins, but the H chains differ for each immunoglobulin class.

CASE STUDIES

1. A 15-year-old male exhibited symptoms of fever, fatigue, nausea, and sore throat. He went to his primary care physician, and a rapid strep test and a test for infectious mononucleosis were performed in the office. The rapid strep test result was negative, but the test result for infectious mononucleosis was faintly positive. The patient mentioned that he thought he had mononucleosis about two years earlier, but it was never officially diagnosed. His serum was sent to a reference laboratory to test with specific Epstein-Barr viral antigens. The results indicated the presence of IgM only.

Questions

- a. Is this a reactivated case of mononucleosis? Explain your answer.
- b. How do the results relate to the difference between the primary and a secondary response to exposure to the same antigen?

2. A 10-year-old female experienced one cold after another in the springtime. She had missed several days of school, and her mother was greatly concerned. The mother took her daughter to the pediatrician, worried that her daughter might be immunocompromised because she couldn't seem to fight off infections. A blood sample was obtained and sent to a reference laboratory for a determination of antibody levels, including an IgE level. The patient's IgM, IgG, and IgA levels were all normal for her age, but the IgE level was greatly increased.

Questions

- a. What does the increase in IgE signify?
- b. Should there be a concern about the patient being immunocompromised?
- c. What does the increase in IgE signify?

REVIEW QUESTIONS

- Which is characteristic of variable domains of immunoglobulins?
 - They occur on both the H and L chains.
 - They represent the complement binding site.
 - They are at the carboxy-terminal ends of the molecules.
 - All of the above
- All of the following are true of IgM except that it
 - can cross the placenta.
 - fixes complement.
 - has a J chain.
 - is a primary response antibody.
- How does the structure of IgE differ from that of IgG?
 - IgG has a secretory component and IgE does not.
 - IgE has one more constant region than IgG
 - IgG has more antigen-binding sites than IgE
 - IgG has more light chains than IgE
- All of the following are true of IgM except that it
 - can cross the placenta.
 - fixes complement.
 - has a J chain.
 - is a primary response antibody.

See the Answer Key in the Appendix.

The 12 Laboratory Quality System Essentials

QUALITY SYSTEM ESSENTIALS

PROCESSES AND PROCEDURES

The Laboratory QSEs

1. Organization	Personnel roles, responsibilities, and reporting relationships Quality planning and risk assessment Allocation of personnel and material resources Review and assessment of meeting goals
2. Facilities and Safety	Space designed for efficiency Adequate storage space Required safety precautions and equipment availability Housekeeping Safety training
3. Personnel	Qualifications Current job descriptions Orientation of new employees Competency assessment Continuing education

6-3 Feature



The Florida Panther

The Ebola virus causes one of the most serious and fatal diseases known to humans. This single-stranded RNA virus begins its attack on the body within two to twenty-one days after exposure. Early symptoms include severe headache, fever, muscle pain,

FIGURE 2-2

fatigue, diarrhea, vomiting, abdominal pain, and unexplained bruising or hemorrhaging. It is extremely infectious and can spread quickly through a population.

Molecular diagnostic assays are powerful tools used to gain information to aid in diagnosis and monitoring of disease and now play a central role in medicine. These techniques

are based on the detection of specific nucleic acid sequences in microorganisms or particular cells. Such techniques may be an advantage in clinical diagnosis, as detection of nucleic acids can be accomplished long before antibody detection is possible. Immunodeficiency and autoimmune diseases that have a genetic basis can also be identified more quickly. Molecular diagnostics also contribute to therapeutic decisions, transplant selection, drug efficacy, forensics, and disease prognosis.¹ Molecular techniques used in the clinical laboratory to identify unique nucleic acid sequences include enzymatic cleavage of nucleic acids, gel electrophoresis, enzymatic amplification of target sequences, and hybridization with nucleic acid probes. Immunodeficiency and autoimmune diseases that have a genetic basis can also be identified more quickly. Molecular diagnostics also contribute to therapeutic decisions, transplant selection, drug efficacy, forensics, and disease prognosis.

* There are hundreds of restriction enzymes with unique binding and cleavage sites. The restriction enzymes used in the clinical laboratory (Type II restriction enzymes) recognize palindromic sites.

References

1. McPherson, RA, and Massey, HD. Laboratory evaluation of immunoglobulin function and humoral immunity. In McPherson, RA, and Pincus, MR (ed): *Henry's Clinical Diagnosis and Management by Laboratory Methods*, ed. 22. Elsevier Saunders, Philadelphia, 2011, pp. 899–912.
2. Edelman, GM. The structure and function of antibodies. *Sci Am* 1970, 223:34.
3. Owen, JA, Punt, J, and Stranford, SA: *Kuby Immunology*, ed. 7. WH Freeman and Company, New York, 20013, pp. 65–103.
4. Porter, RR. The structure of antibodies. *Sci Am* 1967, 217:81. Immunofluorescent antinuclear antibody tests. In Detrick, B, Hamilton, RG, and Folds, JD (eds): *Manual of Molecular and Clinical Laboratory Immunology*, ed. 7. ASM Press, Washington, DC, 2006, pp. 996–97.
5. unoglobulin function and humoral immunity. In McPherson, RA, and Pincus, MR (ed): *Henry's Clinical Diagnosis and Management by Laboratory Methods*, ed. 22. Elsevier Saunders, Philadelphia, 2011, pp. 899–912.
6. Edelman, GM. The structure and function of antibodies. *Sci Am* 1970, 223:34.
7. Owen, JA, Punt, J, and Stranford, SA: *Kuby Immunology*, ed. 7. WH Freeman and Company, New York, 20013, pp. 65–103.
8. Porter, RR. The structure of antibodies. *Sci Am* 1967, 217:81. Immunofluorescent antinuclear antibody tests. In Detrick, B, Hamilton, RG, and Folds, JD (eds): *Manual of Molecular and Clinical Laboratory Immunology*, ed. 7. ASM Press, Washington, DC, 2006, pp. 996–97.
9. McPherson, RA, and Massey, HD. Laboratory evaluation of immunoglobulin function and humoral immunity. In McPherson, RA, and Pincus, MR (ed): *Henry's Clinical Diagnosis and Management by Laboratory Methods*, ed. 22. Elsevier Saunders, Philadelphia, 2011, pp. 899–912.
10. Edelman, GM. The structure and function of antibodies. *Sci Am* 1970, 223:34.
11. Owen, JA, Punt, J, and Stranford, SA: *Kuby Immunology*, ed. 7. WH Freeman and Company, New York, 20013, pp. 65–103.
1. McPherson, RA, and Massey, HD. Laboratory evaluation of immunoglobulin function and humoral immunity. In McPherson, RA, and Pincus, MR (ed): *Henry's Clinical Diagnosis and Management by Laboratory Methods*, ed. 22. Elsevier Saunders, Philadelphia, 2011, pp. 899–912.
2. Edelman, GM. The structure and function of antibodies. *Sci Am* 1970, 223:34.
3. Owen, JA, Punt, J, and Stranford, SA: *Kuby Immunology*, ed. 7. WH Freeman and Company, New York, 20013, pp. 65–103.
4. Porter, RR. The structure of antibodies. *Sci Am* 1967, 217:81. Immunofluorescent antinuclear antibody tests. In Detrick, B, Hamilton, RG, and Folds, JD (eds): *Manual of Molecular and Clinical Laboratory Immunology*, ed. 7. ASM Press, Washington, DC, 2006, pp. 996–97.
5. unoglobulin function and humoral immunity. In McPherson, RA, and Pincus, MR (ed): *Henry's Clinical Diagnosis and Management by Laboratory Methods*, ed. 22. Elsevier Saunders, Philadelphia, 2011, pp. 899–912.
6. Edelman, GM. The structure and function of antibodies. *Sci Am* 1970, 223:34.
7. Owen, JA, Punt, J, and Stranford, SA: *Kuby Immunology*, ed. 7. WH Freeman and Company, New York, 20013, pp. 65–103.
8. Porter, RR. The structure of antibodies. *Sci Am* 1967, 217:81. Immunofluorescent antinuclear antibody tests. In Detrick, B, Hamilton, RG, and Folds, JD (eds): *Manual of Molecular and Clinical Laboratory Immunology*, ed. 7. ASM Press, Washington, DC, 2006, pp. 996–97.
9. McPherson, RA, and Massey, HD. Laboratory evaluation of immunoglobulin function and humoral immunity. In McPherson, RA, and Pincus, MR (ed): *Henry's Clinical Diagnosis and Management by Laboratory Methods*, ed. 22. Elsevier Saunders, Philadelphia, 2011, pp. 899–912.
10. Edelman, GM. The structure and function of antibodies. *Sci Am* 1970, 223:34.
11. Owen, JA, Punt, J, and Stranford, SA: *Kuby Immunology*, ed. 7. WH Freeman and Company, New York, 20013, pp. 65–103.

Answer Key

Chapter 12 Molecular Diagnostic Techniques

Answers to Case Studies

1. **a.** The presence of IgM only is an indicator of an early acute infection. IgM is the first antibody to appear, followed by IgG. In a reactivated case of mono. **b.** The memory cells triggered by the first exposure to the virus would cause production of IgG in a much shorter time and there would be a greater increase in IgG compared to the amount of IgM present.

2. **a.** The increase in IgE is an indicator that the cold symptoms may actually be due to allergy. This is especially evident in the springtime, when pollen levels are high. The child should be tested for specific allergies to determine the cause of the symptoms. Treatment with antihistamine and avoidance of the allergen will help to relieve the symptoms. **b.** Chronic respiratory infections may be due to a decrease or lack of IgA, but this is not the case here. Normal levels of IgG, IgM, and IgA indicate that this child is not immunocompromised.

Answers to Review Questions

1. a 2. a 3. b 4. d 5. b 6. c 7. a
8. d 9. a 10. a 11. c 12. b 13. a 14. c
15. d 16. b 17. b 18. c 19. b 20. d 21. a
22. c

Chapter 13 Molecular Diagnostic Techniques

Answers to Case Studies

1. **a.** The presence of IgM only is an indicator of an early acute infection. IgM is the first antibody to appear, followed by IgG. In a reactivated case of mono, a small amount of IgM might be present, but IgG would also be present. Thus, the patient is encountering the virus for the first time. **b.** The memory cells triggered by the first exposure to the virus would cause production of IgG in a much shorter time and there would be a greater increase in IgG compared to the amount of IgM present.

2. **a.** The increase in IgE is an indicator that the cold symptoms may actually be due to allergy. This is especially evident in the springtime. **b.** Chronic respiratory infections may be due to a decrease or lack of IgA, but this is not the case here. Normal levels of IgG, IgM, and IgA indicate that this child is not immunocompromised.

Answers to Review Questions

1. a 2. a 3. b 4. d 5. b 6. c 7. a
8. d 9. a 10. a 11. c 12. b 13. a 14. c
15. d 16. b 17. b 18. c 19. b 20. d 21. a

Chapter 14 Molecular Diagnostic Techniques

Answers to Case Studies

1. **a.** The presence of IgM only is an indicator of an early acute infection. IgM is the first antibody to appear, followed by IgG. In a reactivated case of mono, a small amount of IgM might be present, but IgG would also be present. Thus, the patient is encountering the virus for the first time. **b.** The memory cells triggered by the first exposure to the virus would cause production of IgG in a much shorter time and there would be a greater increase in IgG compared to the amount of IgM present.

2. **a.** The increase in IgE is an indicator that the cold symptoms may actually be due to allergy. This is especially evident in the springtime, when pollen levels are high. The child should be tested for specific allergies to determine the cause of the symptoms. Treatment with antihistamine and avoidance of the allergen will help to relieve the symptoms. **b.** Chronic respiratory infections may be due to a decrease or lack of IgA.

Answers to Review Questions

1. a 2. a 3. b 4. d 5. b 6. c 7. a
8. d 9. a 10. a 11. c 12. b 13. a 14. c
15. d 16. b 17. b 18. c 19. b 20. d 21. a

Chapter 15 Molecular Diagnostic Techniques

Answers to Case Studies

1. **a.** The presence of IgM only is an indicator of an early acute infection. IgM is the first antibody to appear, followed by IgG. In a reactivated case of mono, a small amount of IgM might be present, but IgG would also be present. Thus, the patient is encountering the virus for the first time. **b.** The memory cells triggered by the first exposure to the virus would cause production of IgG in a much shorter time and there would be a greater increase in IgG compared to the amount of IgM present.

2. **a.** The increase in IgE is an indicator that the cold symptoms may actually be due to allergy. This is especially evident in the springtime, when pollen levels are high. The child should be tested for specific allergies to determine the cause of the symptoms. Treatment with antihistamine and avoidance of the allergen will help to relieve the symptoms. **b.** Chronic respiratory infections may be due to a decrease or lack of IgA, but this is not the case here. Normal levels of IgG, IgM, and IgA indicate that this child is not immunocompromised.

Answers to Review Questions

1. a 2. a 3. b 4. d 5. b 6. c 7. a
8. d 9. a 10. a 11. c 12. b 13. a 14. c

