Immunodeficiency Disorders in Children: Review Questions

C. Lucy Park, MD

QUESTIONS

Choose the single best answer for each question.

1. **A 7-month-old girl presents with chronic cough for 3 months and post-tussive vomiting for 3 weeks. The infant was born full-term with no neonatal complications, and she has never been exposed to tobacco smoke or pets. There is no history of asthma or recurrent infection in the family. Physical examination reveals a small, emaciated infant (weight at < 5th percentile, height at 10th percentile), extensive oral thrush, generalized lymphadenopathy (including cervical, axillary, inguinal, and suboccipital), bilateral intercostal and subcostal retraction, bilateral crackles, hepatosplenomegaly, and extensive diaper rash. Serum IgG, IgA, and IgM levels are all above normal. What is this patient's most likely diagnosis?**
   (A) Adhesion molecule deficiency
   (B) Asthma
   (C) Bruton's agammaglobulinemia
   (D) HIV infection
   (E) Severe combined immunodeficiency (SCID)

2. **A 20-month-old boy presents with a history of recurrent bruising, bilateral otitis media, pneumonia, and severe eczema. Complete blood count with differential count reveals thrombocytopenia ($50 \times 10^3/mm^3$), low mean platelet volume (5 fL), low serum IgM, and increased IgA and IgE levels. What is this patient's most likely diagnosis?**
   (A) Ataxia-telangiectasia
   (B) DiGeorge syndrome
   (C) Hyperimmunoglobulinemia E syndrome
   (D) Nezelof syndrome
   (E) Wiskott-Aldrich syndrome (WAS)

3. **In which of the following conditions is regular intravenous immunoglobulin (IVIg) replacement therapy an absolute indication?**
   (A) AIDS
   (B) Chronic granulomatous disease
   (C) IgG_2 subclass deficiency
   (D) SCID
   (E) None of the above

4. **A 12-year-old girl presents with history of recurrent pneumonia, otitis media, and sinusitis. She has had bilateral perforated tympanic membranes and mild hearing loss. Chest radiograph reveals bronchiectasis at the left lower and right middle lobes and infiltration at right lower and upper lobes. Total serum IgG, IgA, and IgM levels are normal. Her immunizations are current. Which of the following laboratory tests is the most appropriate next step in this patient's evaluation?**
   (A) Total complement (CH50) and C3 and C4 levels
   (B) HIV serology
   (C) IgG subclass levels
   (D) Serum antibodies to tetanus toxoid and pneumococcal antigens
   (E) CD4/CD8 ratio

5. **Which of the following tests evaluates cell-mediated immune function in vivo?**
   (A) Antibodies to isohemagglutinins and *Haemophilus influenzae*
   (B) Boyden chamber test
   (C) Delayed hypersensitivity skin test (DHST) with candida antigen
   (D) Nitroblue tetrazolium test
   (E) T- and B-cell enumeration

(turn page for answers)

Dr. Park is an associate professor, Department of Pediatrics, University of Illinois at Chicago, Chicago, IL.

ANSWERS AND EXPLANATIONS

1. **(D) HIV infection.** The patient has chronic cough due to chronic viral respiratory infection. Chronic infection, failure to thrive, generalized lymphadenopathy, and hepatosplenomegaly are frequent clinical symptoms and signs of HIV infection in children. Lymphadenopathy and hepatosplenomegaly are not commonly seen in patients with SCID. Bruton's agammaglobulinemia is associated with low immunoglobulin levels in all isotypes (IgG, IgA, and IgM) and paucity of lymphoid tissues; it usually presents with recurrent bacterial infection.
2. **(E) WAS.** WAS is a rare inherited disease characterized by immune dysregulation and microthrombocytopenia. Diagnostic criteria for WAS has been published by the Pan-American Group for Immunodeficiency. Probable criteria include a male patient with thrombocytopenia ($< 70 \times 10^3/mm^3$), low mean platelet volume (< 5.0 fL), and at least 1 of the following: eczema; low level of isohemagglutinins; poor vaccine responses to polysaccharide antigens, recurrent bacterial, viral or opportunistic infections; autoimmune disease; and lymphoreticular malignancy. Many patients with WAS have low levels of IgM and increased levels of IgA, IgD, and IgE.
3. **(D) SCID.** Patients with SCID are unable to produce functional antibodies. Although the basic defect in SCID is T-cell dysfunction, B cells are unable to produce functional antibody due to lack of T-cell help. Therefore, routine IVIg replacement therapy is indicated until more definitive therapy (eg, bone marrow transplantation) can be performed. Isolated IgG_2 subclass deficiency without evidence of functional antibody production deficiency is not an indication for IVIg therapy. The benefit of IVIg in reduction of serious bacterial infection in HIV-infected persons is apparent only in children who do not receive trimethoprim-sulfamethoxazole (TMP-SMX)as prophylaxis for opportunistic infections. IVIg therapy in these patients should be restricted to those who develop recurrent infections despite combination antiviral therapy and prophylactic TMP-SMX.
4. **(D) Serum antibodies to tetanus toxoid and pneumococcal antigens.** Patients with specific antibody deficiency frequently present with recurrent sinopulmonary infection with bacteria. Despite normal levels of total IgG, IgA, or IgM, patients with this deficiency are unable to produce antibodies to specific antigens (specific antibodies or functional antibodies). Evaluation of functional antibody production in patients who have received childhood immunizations should include measurement of serum antibodies to protein antigens (tetanus toxoid, diphtheria toxoid) and carbohydrate antigens (isohemagglutinins, pneumococcal polysaccharide antigens). Evaluation of antibody response to carbohydrate antigens should be performed using unconjugated pneumococcal vaccine (23-valent) since protein-conjugated polysaccharide antigens are recognized and processed by a subset of B cells that respond to protein antigens and they are different from the ones that respond to carbohydrate antigens.
5. **(C) DHST with candida antigen**. DHST can be readily available in any office setting for evaluation of in vivo cell-mediated immune function. Most commonly used antigens are candida, tetanus toxoid, mumps, and trichophyton. The choice of antigens for any particular patient depends on a probable previous sensitization (ie, immunization, natural infection, environmental exposure). The nitroblue tetrazolium test is used to evaluate phagocytic oxidative metabolism. Boyden chamber is an in vivo test of neutrophil chemotaxis. The test for antibodies to isohemagglutinins and *H. influenzae* measures the ability to produce functional antibodies to polysaccharide antigens. T- and B-cell enumeration tests are useful in conditions associated with low percentage of T cells or T-cell subsets.

SUGGESTED READINGS

1. Bonilla FA, Geha RS. 12. Primary immunodeficiency diseases [published erratum appears in J Allergy Clin Immunol 2003;112:267]. J Allergy Clin Immunol 2003; 111(2 Suppl):S571–81.
2. Mouthon L, Lortholary O. Intravenous immunoglobulins in infectious diseases: where do we stand? Clin Microbiol Infect 2003;9:333–8.
3. Tangsinmankong N, Bahna SL, Good RA. The immunologic workup of the child suspected of immunodeficiency. Ann Allergy Asthma Immunol 2001;87:362–9.

ALLERGY AND IMMUNOLOGY

A current list of certification and recertification exam dates and registration information is maintained on the American Board of Allergy and Immunology Web site, at http://www.abai.org.