Allergy and Immunology Review Corner: Chapter 15 of Immunology IV: Clinical Applications in Health and Disease, by Joseph A. Bellanti, MD.

Chapter 15: Clinical Immunology of Parasitic Diseases

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1. Which of the following is an intracellular protozoan that primarily elicits a Th1 response?
   A. Giardia
   B. Schistosoma
   C. Trypanosoma
   D. Leishmania
   E. Ascaris

2. Chronic malaria is seen with which protozoa?
   A. P. falciparum
   B. P. vivax
   C. P. ovale
   D. A and B
   E. B and C

3. What is the most important humoral component of the innate immune response?
   A. Properdin
   B. C4
   C. C3
   D. C2
   E. IL-12

4. With which parasite do adults harbor greater parasite numbers than children?
   A. Whipworm
   B. Taenia solium
   C. Hookworm
   D. Pinworm
   E. Toxoplasma

5. What is the mechanism by which Giardia intestinalis performs immune evasion?
   A. Antigenic modulation
   B. Antigenic variation
   C. Molecular mimicry
   D. Suppression of host immunity
   E. Resistance to complement-mediated lysis

6. Which of the following TLRs (Toll-like receptors) interacts with schistosome double-stranded RNA?
A. TLR1  
B. TLR2  
C. TLR3  
D. TLR4  
E. TLR8

7. Which of the following primary immunodeficiencies is associated with *Giardia* infection?  
A. IgA deficiency  
B. IgM deficiency  
C. Hyper IgM  
D. Autosomal dominant hyper-IgE syndrome  
E. Autosomal recessive hyper-IgE syndrome

8. Red blood cells lacking the Duffy antigen are not susceptible to which of the following parasitic infections?  
A. Plasmodium falciparum  
B. Plasmodium vivax  
C. Trypanosoma cruzi  
D. Trypanosoma gambiense  
E. Trypanosoma rhodesiense

9. Which of the following is the most common cause of pathology observed during helminth infections?  
A. Type I Immediate Hypersensitivity  
B. Type II Cell-Mediated Hypersensitivity  
C. Type III Immune Complex-Mediated Hypersensitivity  
D. Type IVA Delayed-Type Hypersensitivity  
E. Type V Autoimmunity

10. Which of the following is often asymptomatic in immune-competent individuals but can become disseminated and cause shock when patients with chronic infection become immunosuppressed?  
A. Strongyloidiasis  
B. Microsporidia  
C. Cyclospora cayetanensis  
D. Cryptosporidium parvum  
E. Sarcoptes scabiei

**Answers**  
1. D, pages 522-524  
Leishmaniasis is an intracellular protozoa that elicits a Th1 response from the host but can also elicit Th2 in active cutaneous infections. African trypanosomiasis produces waves of progeny and is both blood borne and intracellular. Schistosoma incorporates host antigens on the cell surface of the parasite.
2. E, page 526
P. Vivax and P. Ovale cause chronic infections. P. falciparum causes only acute fulminating form.

3. C, page 529
The most important humoral component of the innate immune response is the C3 component of complement.

4. C, page 537
Hookworm infections are the exception where adults harbor greater parasite numbers than children. This suggests hookworms may have unique mechanisms to evade the host’s response.

5. B, page 547
In Giardia antigenic variation is caused by an exchange of the parasite’s variant surface protein (VSP). Others that utilize antigenic variation are Plasmodium species and trichomonas vaginalis.

6. C, page 521
Schistosome double-stranded RNA (dsRNA) interacts with the dendritic cell TLR3.

7. A, page 528
“A definite study of the human immune response to the parasite [Giardia] has not been possible since most cases of Giardia infection occurs in immunodeficiency patients, particularly those with an IgA deficiency.”

8. B, page 529
“…red blood cells lacking the Duffy antigen are not susceptible to Plasmodium vivax infection.”

9. D, page 544
“Delayed-Type Hypersensitivity Type IVA is the most common cause of pathology observed during helminth infections and is associated with the production by DC4+ T cells of the Th2 cytokines IL-4 and IL-5 and the subsequent recruitment of eosinophils.”

10. A, page 550, Table 15-6, and page 551
“Strongyloidiasis, often asymptomatic in immune, normal individuals, can become disseminated when patients with chronic strongyloidiasis become immunosuppressed. It presents with abdominal pain, distension, shock, pulmonary and neurologic complications, and septicemia, and is potentially fatal.”

Allergy and Immunology Review Corner: Chapter 16 of Immunology IV: Clinical Applications in Health and Disease, by Joseph A. Bellanti, MD.
Chapter 16: Immune Deficiency Disorders

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1. Which of the following is true of Chediak-Higashi Syndrome (CHS)?
A. Neutrophils of patients have multiple primary granules, and have normal bone marrow granulocyte release but decreased circulating granulocyte half-life.
B. CHS is a rare autosomal recessive disease characterized by oculocutaneous albinism, bacterial infections, neurologic abnormalities, and a late onset “accelerated phase” that is a form of hemophagocytic lymphohistiocytosis (HLH).
C. Phagocytosis is diminished, but chemotaxis is normal or increased; in addition, antibody-dependent cell-mediated cytotoxicity (ADCC) is diminished, but NK cell cytotoxicity is intact.
D. Bone marrow transplantation is curative for both the immune defect of CHS, as well as the neurologic abnormalities.

2. Which of the following genes is not associated with Griscelli Syndrome?
A. Myosin Va on Chromosome 15q21
B. Rab27a on Chromosome 15q21
C. MLPH on Chromosome 2q37.3, F-exon of Myosin Va
D. LYST on Chromosome 1q42-43

3. Which of the following is not true of Hyper IgE Syndrome (HIES)?
A. Many cases are attributable to autosomal dominant or sporadic mutations in the signal transducer and activator of transcription 3 (STAT3).
B. Patients may present with recurrent infections caused by Staphylococcus aureus, eczema, elevated IgE level, eosinophilia, delayed shedding of primary teeth, distinct facial features, osteoporosis and fractures, scoliosis, hyperextensible joints, and candidiasis.
C. Adults with IgE levels below 2000 IU/mL do not meet diagnostic criteria for HIES, and do not have susceptibility to infections.
D. Type 2 HIES is an autosomal recessive variant that has been described with elevated IgE, severe eczema, susceptibility to intracellular bacterial and viral infections, and deficiency of tyrosine kinase 2 (TYK2).

4. Presence of which of the following is associated with increased risk of developing diabetes in autoimmune polyendocrine syndrome type 1 (APECED)?
A. HLA-DQ2
B. HLA-DQ6
C. HLA-DQ8
D. None of the above

5. Which of the following is true of Ataxia-Telangiectasia?
A. Patients have elevated levels of serum alpha-fetoprotein, growth retardation, premature aging, chromosomal instability with an increased frequency of lymphoreticular cancers, and hypersensitivity to ionizing radiation.
B. In vitro tests of lymphocyte function generally show normal proliferative responses to T and B cell mitogens.
C. Ataxia typically becomes evident in adolescence.
D. IgA and IgE levels are usually elevated in patients with ataxia-telangiectasia.

6. Severe congenital neutropenia and cyclic neutropenia may both be due to mutations of what gene?
   A. ELA2
   B. BTK
   C. LYST
   D. EVER1

7. Neutrophil-specific granule deficiency is an autosomal recessive disease characterized by reduction of neutrophil-specific granules and lack of defensins. It can be diagnosed on peripheral smear because it shows which of the following?
   A. Giant granules in neutrophils
   B. Platelet clumping
   C. Bilobed neutrophil nuclei
   D. Add

8. All of the following conditions are associated with defects in chemotaxis except for:
   A. Shwachman-Diamond syndrome
   B. LAD II
   C. LAD III
   D. Hyper-IgE Syndrome

9. The complement system provides a bridge between innate immunity and adaptive immunity. Which of the following biologic products is incorrectly paired with the role it plays in immunity?
   A. C3b and opsonization
   B. C5a and chemotactic activity
   C. C7 and anaphylatoxic activity
   D. C5b-C9 and cytotoxicity MAC

10. A defect in XIAP (X-linked inhibitor of apoptosis) results in which of the following immune deficiencies?
    A. XLP-1
    B. XLP-2
    C. ITK
    D. ALPS

Answers
1. B, pages 566-67
“CHS is a rare multisystem autosomal recessive disease with oculocutaneous albinism, frequent bacterial infections, neurologic abnormalities, and a relatively late onset lymphoma-like “accelerated phase” that is a form of hemophagocytic lymphohistiocytosis (HLH). “Giant granules are seen in neutrophils as a result of inappropriate fusion of multiple primary granules”. “Chemotaxis is diminished, but phagocytosis is normal or increased. Impaired bacterial killing is probably due to low levels and impaired mobilization of primary and secondary granule enzymes. NK cell cytotoxicity is diminished, but antibody-dependent cell-mediated cytotoxicity (ADCC) is intact. B cell function appears intact”. “Bone marrow transplantation cures the immune defect in CHS and the accelerated phase but it does not prevent the central or peripheral neurologic problems.”

2. D, page 568, Table 16-2
“Classification of the three types of Griscelli syndrome (GS) in comparison with Chediak-Higashi syndrome (CHS).”

3. C, page 579
“HIES is an immunodeficiency disorder that, in many cases, is transmitted as an autosomal dominant trait (Type 1 HIES), but that occurs sporadically in all racial and ethnic groups. Mutations in STAT3 have been identified as the cause of the autosomal dominant and sporadic forms of HIES. Patients with this disorder present with recurrent infections of the skin and lower respiratory system caused by Staphylococcus aureus, eczema, extremely elevated levels of IgE, eosinophilia, and abnormalities of the connective tissue, skeleton, and teeth with distinctive facial features, osteoporosis and fractures, scoliosis, hyperextensible joints, and candidiasis”. “IgE is greatly elevated at some point in the life of all patients with HIES, but about 20% drop their IgE levels below 2,000 IU/mL as they get older while retaining their susceptibility to infection”. “More than one genotype may account for the HIES phenotype. An autosomal recessive variant (Type 2 HIES) has also been described with elevated IgE, severe eczema, and recurrent infections, but lacking pneumonias, pneumatoceles, and bony abnormalities. A TYK2 deficiency was identified in an AR-HIES patient who presented with susceptibility of intracellular bacterial and viral infections.”

4. B, page 614. Table 16-6
“Clinical and genetic features of the autoimmune polyendocrine syndromes.”

5. A, page 618. “Ataxia typically becomes evident soon after affected children begin to walk; the condition progresses until they are confined to a wheelchair, usually by the age of 10 to 12 years. In addition to cerebellar degeneration, patients with ataxia-relangiectasia have elevated levels of serum alpha-fetoprotein, growth retardation, premature aging, chromosomal instability, as increased frequency of lymphoreticular cancers, and hypersensitivity to ionizing radiation and radiomimetic drugs”. “In vitro tests of lymphocyte function have generally shown moderately depressed proliferative responses to T and B cell mitogens”. “The most frequent humoral immunologic abnormality is the selective absence of IgA, which is present in 50 to 80 percent of these patients. Hyper-catabolism of IgA also occurs. IgE concentrations are usually low,
and the IgM may be of the low molecular weight variety. IgG2 or total IgG levels may be decreased, and specific antibody titers may be decreased or normal.”

6. C, pages 565-566. Thirty percent of cases of SCN have dominant mutations in neutrophil elastase (ELA2). Mutations in this same gene can cause cyclic neutropenia as well. Both are treated with G-CSF. The BTK gene is mutated in XLA, the LYST gene is mutated in Chediak-Higashi (CHS), and the EVER1 gene is mutated in Epidermodysplasia Verruciformis (EV).

7. D, page 569
This condition is characterized by recurrent pyogenic infections of the skin, ears, lungs, and lymph nodes. Neutrophils are slightly larger and paler than normal upon peripheral smear. Also, neutrophil morphology is abnormal with bilobed neutrophil nuclei, known as the pseudo-Pelger-Huet anomaly.

8. D, pages 573-574
There a group of molecular defects that come under the general heading of leukocyte adhesion deficiency which results in defective leukocyte movement from the blood into tissues. LAD II is a rare autosomal recessive disease due to mutations in FUCT1. LAD III is due to mutations in CAL DAG-GEF1. Shwachman-Diamond syndrome is due to a defect in the SBDS gene and is associated with pancytopenia, exocrine pancreatic insufficiency, and chondrodysplasia.

9. C, page 581
The three complement pathways, once activated, result in the cleavage of C3 components and utilize a final common pathway to generate important biologic products. These include C3b (opsonization), C3a and C5a (anaphylatoxic activity), C5a (chemotactic activity), and C5b-C9 (cytotoxicity MAC).

10. B, pages 611-612 and Table 16.5 on 612
Immune dysregulation in patients is expressed not only by their susceptibility to infections but also by an increased risk of allergy, autoimmunity, autoinflammatory disorders, or malignancy. The lymphoproliferative syndromes are each triggered by EBV infection, and include XLP-1, XLP-2, and ITK. A defect in XIAP results in XLP-2.