

Male: Immunology, 8th Edition

Test Bank by Rohit Divekar, MD

MULTIPLE CHOICE

1. A 46-year-old man complaining of an upper respiratory tract infection attends the outpatient clinic for treatment. After assessment of the patient's condition the doctor prescribes him some antibiotics. After 4 days of treatment, the patient notices that whenever he goes outside the house and it's very cold, his hands turn blue and white. He says that he has never had this problem before. If the attending physician suspects that the person has developed Raynaud's phenomenon secondary to the drug administration, what kind of antibodies would be present in this patient causing the symptoms?
- IgG
 - IgM
 - IgA
 - IgD
 - IgE

ANS: B

Drug-induced Raynaud's phenomenon is due to cryoglobulins. Cryoglobulins are IgM antibodies that react at lower temperatures such as those that might be expected when it's cold outside (choice b). Cryoglobulins are also formed in many nonspecific viral illnesses and in mycoplasma infections. IgG antibodies (choice a) are warm agglutinins and will react at only warm temperatures; hence, they would not be responsible for this kind of picture. IgA (choice c) is a secreted antibody and is not responsible for cold agglutinin reaction. IgD (choice d) is membrane-bound antibody seen on B cells; the function of IgD is not yet clear. IgE (choice e) is important for immunity to parasites and also is the cause of anaphylactic and type I hypersensitivity reactions.

PTS: 1

2. A center for autoimmune diseases in a metropolitan area deals with all kinds of autoimmune conditions. The research wing of this institution is divided into cell-mediated autoimmune diseases and antibody-dependent autoimmune diseases. The research personnel receive their human tissue samples and research material from the patients admitted to the hospital. There are blood samples of five patients listed below that need to go to their respective research laboratories. Which of the patient samples would go to the division of antibody-mediated autoimmune diseases?
- Patient A = autoimmune myocarditis
 - Patient B = type 1 diabetes
 - Patient C = insulin-resistant diabetes
 - Patient D = multiple sclerosis
 - Patient E = T-cell-mediated peripheral neuritis

ANS: C

Immune diseases can be basically divided in these groups: T cell mediated autoimmune diseases, immune complex-mediated autoimmune diseases, and antibody-dependent immune conditions. Autoimmune carditis (choice a) is a result of T cells sensitized to myosin antigen, and both multiple sclerosis (choice d) and type 1 diabetes (choice b) are classically CD4 T-cell-mediated autoimmune diseases. T-cell-mediated peripheral neuritis (e.g., Guillain-Barré syndrome) is again not antibody mediated though there might be an elevation of immunoglobulin titer. Insulin resistance (choice c) on the other hand is due to preformed antibodies that react with the insulin receptor and prevent the binding of insulin to the receptor, reducing the efficacy of insulin, leading to diabetes. Thus, this is clearly an example of antibody-dependent disease.

PTS: 1

3. Experimental autoimmune encephalomyelitis (EAE) is the animal model of human multiple sclerosis (MS). Injecting myelin antigen along with a strong adjuvant like CFA can induce the disease in these mice. CFA contains a suspension of mineral oil and killed mycobacteria. What is the purpose of adding the killed bacteria to the emulsion?
- Products of killed bacteria retain the antigen better.
 - Killed bacteria stimulate B cells to stimulate antibody.
 - Inflammation produced by bacteria aids in EAE.
 - Bacterial products migrate to the brain producing severe disease.
 - Killed bacteria stimulate antigen-presenting cells.

ANS: E

The entire concept of adjuvant in immunization is related to retention of antigen at the site long enough so that it will be delivered effectively to the T cells. This is achieved by the emulsion that is formed because of the mineral oil (choice a). Mycobacteria are added to the adjuvant to initiate an inflammatory condition that will stimulate the antigen-presenting cells (APCs), so when they present the antigen, the cells will recognize the antigen in the presence of the up-regulated co-stimulatory molecules. Bacterial inflammation has no direct role to play in induction of EAE (choice c), nor do the antibodies induced by the bacterial products enhance the disease (choice b). In addition, because the bacterial products are injected with the mineral oil they will be retained at the site of injections along with the antigen rather than being circulated to the brain; hence, choice d is wrong.

PTS: 1

4. A 6-year-old child complains of sudden onset of breathlessness and becomes very ill. She is rushed to the emergency department, where the intern attending this patient does a complete physical examination to evaluate the cause. Patient appears very anxious, is hyperventilating, and complains of a dull pain substernally. Pulse = 110 beats per minute, BP = 124/84 mm Hg, and upon auscultation there is a distinct pericardial friction rub. Upon specific questioning, the parent of the child gives a history of an upper respiratory illness preceding this episode. If the physician considers the possibility of acute viral myocarditis, which cell is most likely responsible for the pathogenesis?
- CD4 T cell
 - CD8 T cell
 - Myofibroblast
 - Plasma cells
 - Mast cell

ANS: B

CD4 T cells perform the function of regulating and orchestrating the immune system; they are responsible for production of cytokines. Depending on the nature of the inflammation, these cytokines are meant to activate specific cells of the immune system to carry out their functions. CD4 T cells that secrete IL-12 and IFN-gamma are called T_H1 cells, and those that produce IL-4, IL-5, and IL-13 are called T_H2 cells. CD8 T cells, on the other hand, are responsible for cytotoxic effector functions that get rid of tumor cells and virally infected cells. Myofibroblasts are mesenchymal cells that line the wound during the process of repair; they are modified fibroblasts that have the capacity to contract. They are responsible for wound contraction. Plasma cells are mature and differentiated B cells that produce antibody. They are important in antibody-mediated immune responses. Mast cells are cells of the innate immune system that secrete a variety of immunomodulatory proteins. Degranulation of mast cells causes release of proinflammatory products, notably histamine.

PTS: 1

5. Neutrophils are isolated from the peripheral blood of a patient suffering from an immunodeficiency disease. This individual has a recurrent history of severe infections. Upon analysis it is found that the neutrophils are able to ingest gram-negative organisms but are unable to kill them. The nitro blue tetrazolium test (NBT), however, is positive. Which of the following is most likely responsible?
- Neutrophil elastase
 - NADPH oxidase
 - Nitric oxide synthase
 - Toll-like receptors (TLRs)
 - Perforin

ANS: A

One of the mechanisms of microbicidal killing is phagocytosis. The ingested bacteria are held in a phagosome that fuses with the lysosome, which contains proteolytic enzymes and a variety of bactericidal molecules. Neutrophil lysosomes are particularly rich in the enzyme neutrophil elastase (choice a), whose primary targets are probably bacterial proteins. Incidentally, neutrophil elastase is also implicated in lung damage in patients who lack the protein to inactivate this elastase, alpha-1 antitrypsin. NK cells such as the cytotoxic T lymphocytes contain a protein known as perforin (choice e). This protein, similar in function to the membrane attack complex of the complement pathway, is inserted into the cell membrane, where it creates pores or channels through which cytoplasmic content can leak out. It also allows for enzymes produced by these cells, called granzymes, to get inside and activate the apoptosis pathway. The other mechanism of bacterial killing is production of reactive oxygen metabolites following a “respiratory burst.” The principal enzyme involved in generation of these free radical oxy-halide molecules (e.g., HOCl) is NADPH oxidase (choice b). Deficiency of NADPH oxidase is one of the causes of chronic granulomatous disease (CGD), in which the neutrophils ingest bacteria but are unable to kill them because of defective free radical production. Cells that lack the ability to generate free oxygen radicals give a negative NBT test. A second method of generating free radicals is by using the nitric oxide synthase enzyme (choice c). This enzyme is absent from macrophages and neutrophils but is rapidly induced upon exposure of these cells to bacterial products such as LPS along with IFN-gamma. The inducible nitric oxide system along with the reactive oxygen system work together for efficient killing of pathogens. Toll-like receptors (choice d) belong to a family of innate receptors that are involved in pattern recognition. They don't have pathogen-specific recognition motifs but can recognize patterns of molecular structure in bacteria. For example, TLR 4 can recognize LPS produced by a variety of bacteria, and TLR 5 bind to bacterial flagellin. TLRs are abundant on macrophages and dendritic cells and are responsible for activation of these cells upon exposure to bacterial products.

PTS: 1

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47. The focus of an immunology researcher is the mechanisms of T-cell activation. He has several mice in his arsenal that have been specifically knocked out for individual proteins on the surface of T cells or APCs. One of these knockout mice is severely deficient in proliferation and isotype switching of B cells in vitro and fails to mount an antigen-specific antibody response. If the deficient protein were normally present on T cells, which of the following proteins has most likely been knocked out?

- a. B7.2
- b. CTLA-4
- c. CD28
- d. CD40L
- e. CD25

ANS: C

The B7 (choice a) family of co-stimulators is the best characterized among the co-stimulatory molecules. These are expressed in large amounts on antigen-presenting cells and bind to CD28 (choice c) like molecules on the surface of T cells. These co-stimulatory molecules engage corresponding molecules on the T cell and provide a second signal for T-cell activation, the first one being TCR–MHC engagement. In absence of co-stimulation T cells that encounter the antigen either fail to respond and die by apoptosis or become anergic. CD28 is the ligand for B7 molecules on the APCs on the T cell and their major function is co-stimulation of naïve cells. CTLA-4 (choice b), on the other hand, is also another CD28-like ligand of B7 molecules, but it is expressed later on the T cells and is responsible for negative regulation of immune responses and functions as a physiologic switch to reduce the activation of activated T cells. The T_H1 cells secrete IFN-gamma that activates macrophages. Engagement of CD40L (choice d) on T cells with CD40 on APCs enhances T-cell activation. The critical role of CD40L-CD40 interaction is to induce a florid expression of B7 molecules on APCs so that the T cell is stimulated adequately. Also, interaction between T cell CD40L and B cell CD40 is important for class switching. IL-2 receptor alpha chain, also called CD25 (choice e), is part of the receptor for autocrine growth factor for T cell interleukin 2. It is up-regulated on activated and antigen experienced T cells and promotes proliferation of antigen activated T cells.

PTS: 1

48. The focus of an immunology researcher is the mechanism of T-cell activation. He has several mice in his arsenal that have been specifically knocked out for individual proteins on the surface of T cells or APCs. One of these knockout mice shows excessive T-cell proliferation, activation, systemic autoimmunity, and severe reduction in numbers of regulatory T cells (Tregs). If the deficient protein were normally present on T cells, which of the following proteins has most likely been knocked out?

- a. B7.2
- b. CTLA-4
- c. CD28
- d. CD40L
- e. CD25

ANS: E

The B7 (choice a) family of co-stimulators is the best characterized among the co-stimulatory molecules. These are expressed in large amounts on antigen-presenting cells and bind to CD28 (choice c) like molecules on the surface of T cells. These co-stimulatory molecules engage corresponding molecules on the T cell and provide a second signal for T-cell activation, the first one being TCR–MHC engagement. In absence of co-stimulation T cells that encounter the antigen either fail to respond and die by apoptosis or become anergic. CD28 is the ligand for B7 molecules on the APCs on the T cell and their major function is co-stimulation of naïve cells. CTLA-4 (choice b), on the other hand, is also another CD28-like ligand of B7 molecules, but it is expressed later on the T cells and is responsible for negative regulation of immune responses and functions as a physiologic switch to reduce the activation of activated T cells. The T_H1 cells secrete IFN-gamma that activates macrophages. Engagement of CD40L (choice d) on T cells with CD40 on APCs enhances T-cell activation. The critical role of CD40L-CD40 interaction is to induce a florid expression of B7 molecules on APCs so that the T cell is stimulated adequately. Also, interaction between T cell CD40L and B cell CD40 is important for class switching. IL-2 receptor alpha chain, also called CD25 (choice e), is part of the receptor for autocrine growth factor for T cell interleukin 2. It is up-regulated on activated and antigen experienced T cells and promotes proliferation of antigen activated T cells. Even though one would expect that removing CD25 will suppress immunity, paradoxically there is enhancement of autoimmunity because knocking out CD25 also gets rid of Tregs, which play an important role in suppressing autoimmune phenomena.

PTS: 1

Male: Immunology, 8th Edition

Test Bank by Louise Thai, MD

MULTIPLE CHOICE

1. A 12-year-old girl has developed hyperemia, itching and tearing on both eyes, and sneezing and rhinorrhea. She has had similar but less severe episodes in the past couple of summers since the family moved to the Midwest. Skin prick test is performed for reaction to common grass pollens, cat fur, and dust mites and produces a wheal-and-flare reaction after 10 minutes. Pathogenesis of her condition involves which of the following?
- Immune complexes
 - CD4⁺ and CD8⁺ T cells
 - T_H2 cells and IgE antibodies
 - IgM and IgG antibodies directed against mucosal epithelium

ANS: C

The patient's symptoms are characteristic of a type I hypersensitivity reaction and, indeed, the skin prick test confirms the presence of allergic behavior.

Type I hypersensitivities are mediated by IgE antibodies bound to sensitized mast cells and basophils as well as the cytokine products of T_H2 cells. The clinical symptoms are tissue-specific. Consequently, presentation in the nasal cavity induces rhinorrhea, but wheal-and-flare lesions are typical of antigen presentation in the skin.

A is not the right answer because immune complexes are components of type III hypersensitivities. The patient's symptoms are not compatible with the chronic, systemic presentation of most type III hypersensitivities. The rapid response of the immune system to the skin prick test also supports a faster, type I mechanism.

B is not the right answer. Although T_H2 cells are a predominant component of a type I hypersensitivity, CD8⁺, or cytotoxic, T cells are not. This answer would be more suited for the expected response to an intracellular pathogen like a virus.

D supports an autoimmune mechanism of injury. Because of the rapid response to foreign antigen in the skin prick test we can assume that the mechanism is indeed not autoimmune.

2. A 40-year-old, HIV-positive man with a CD4⁺ T cell count <200/□L began a prophylactic treatment with trimethoprim/sulfamethoxazole. Shortly after receiving the first dose, he has developed erythematous skin lesions covering 10% of his body surface. The macular lesions have become confluent and showed signs of epidermal detachment with a positive Nikolsky sign. What is the most likely diagnosis?
- Stevens-Johnson syndrome
 - Kaposi sarcoma

- c. Scalded skin syndrome
- d. Toxic shock syndrome
- e. Contact dermatitis

ANS: A

The mechanism is an allergic reaction to the trimethoprim/sulfamethoxazole. Because this is a prophylactic administration of the drug, we can assume that no apparent bacterial infection exists. The positive Nikolsky sign narrows our options down to A and C.

The symptoms are characteristic of the immune response associated with Stevens-Johnson syndrome. The positive Nikolsky sign and lack of bacterial infection make it the correct choice.

B is a common manifestation in HIV-positive men, but the lesions associated with Kaposi sarcoma are quite distinct from those of this patient. This answer would not account for the positive Nikolsky sign.

C would be a credible answer if a staphylococcal infection were present because staphylococcal scalded skin syndrome toxin can cause similar symptoms. Given the situation of our particular patient, however, this is not the best choice.

D is incorrect, primarily because there is no bacterial infection present to cause TSS. Indeed, even if TSS were present in this patient, it would not result in the observed symptoms.

E is an extremely unlikely choice. Contact dermatitis is a much less severe, localized reaction that would not give a positive Nikolsky sign.

3. In preparation for a Peace Corp mission in South America, a 22-year-old man receives immunizations against certain viral diseases, including an inactivated hepatitis A viral vaccine. Which of the following is involved in the mechanism of immunity induced by this vaccine?

- a. Neutrophils and macrophages
- b. MHC class I molecules and CD4⁺ T cells
- c. MHC class II molecules and CD8⁺ T cells
- d. MHC class I molecules and CD8⁺ T cells
- e. MHC class II molecules and CD4⁺ T cells

ANS: E

Rationale: Inactivated, or killed, vaccines prevent intracellular penetration. This bypasses the typical MHC class I presentation of an intracellular pathogen as well as the involvement of CD8⁺ T cells. The general mechanism for hepatitis A immunity due to the inactivated vaccine is humorally mediated.

The vaccine is recognized as an extracellular pathogen and is phagocytized by APCs. The antigen is presented on the surface via a MHC class II molecule. This complex is recognized by a CD4⁺ T cell that stimulates helper T cell differentiation to aid in the humoral immunity.

A is associated with the innate immune response. Immunity, or memory, is not a component of the innate response.

B is incorrect. MHC class I molecules do not associate with CD4⁺ T cells.

C is incorrect. MHC class II molecules do not associate with CD8⁺ T cells.

D would be the expected response of the live hepatitis A virus. The killed vaccine, however, does not maintain the intracellular capabilities necessary for MHC class I presentation.

4. Three weeks after an episode of streptococcal pharyngitis, a 5-year-old girl develops polyarthrititis and heart murmur. Significant laboratory findings include elevated levels of C-reactive protein and erythrocyte sedimentation rate and rising levels of antistreptolysin O and anti-DNAse antibodies. Which of the following is most directly involved in the pathogenesis of this patient's disease?

- CD4⁺ T cells
- Immune complexes
- Cross-reacting antibodies
- Streptolysin O
- Streptococcal pyrogenic exotoxin

ANS: C

Rationale: Because the patient recently had a streptococcal infection, it is logical to suspect rheumatic fever as the cause of the arthritis and heart complications. The presence of antistreptolysin O and anti-DNAse antibodies provides strong support for this diagnosis.

In rheumatic fever, antibodies directed against streptococcal antigens cross-react with self antigens in the heart and joints causing inflammation. The resulting inflammation is responsible for the observed symptoms.

A is not the best choice. Although CD4⁺ T cells play a role in the humoral response, their role is not as pathogenically direct as that of the antibody binding to the tissue.

B would be a good choice because cross-reacting antibodies are indeed a fundamental requirement of the pathogenesis of rheumatic fever. No immune complexes, however, are formed in ARF.

D is wrong. Streptolysin O would have played an important role in the pathogenesis of the initial bacterial infection, but the rheumatic fever is the result of autoimmune processes.

E is wrong for the same reasons as D.

5. A 23-year-old medical student presents with itchy, red, scaly lesions on the scalp, elbows, knees, and lower back. He suspects he might have psoriasis and the dermatologist confirms it. She prescribes triamcinolone, a topical corticosteroid, and explains that psoriasis is an immune-mediated disease characterized by an abundance of IL-2, IL-6, IL-8 and IFN- γ in the skin. Which of the following cells contribute most to production of these cytokines?
- B cells
 - Helper T cells
 - Plasma cells
 - Cytotoxic T cells
 - Macrophages

ANS: B

Psoriasis is an autoimmune disease. The listed cytokines are fairly typical of a type 1 cytokine response.

Although there is recent debate about the individual roles T_H1 and T_H2 cells play in the psoriatic pathogenesis, the fact that helper T cells are involved is well documented. It is also known that TNF- α plays a major role in psoriasis. IL-6 and IL-8 are both secreted in response to this particular cytokine.

A is incorrect as B cells play a subordinate role in cytokine-mediated immunity. Typically, B cells respond only to the messages sent via cytokines from T cells.

C is also wrong. Plasma cells are only a type of B cell and thus have little role in cytokine-mediated inflammation.

D is wrong. Cytotoxic T cells play a less significant role in cytokine secretion than do helper T cells. They do produce TNF, IFN- γ , and LT-alpha to contribute to cellular cytotoxicity, however.

E is also incorrect. IL-6 and IL-8 can be secreted by activated macrophages, but IFN- γ and IL-2 are characteristic of T cells.

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199. A 36-year-old man who has sex with men is evaluated for arthritis, conjunctivitis and keratoderma. His history is positive for HIV and a recent episode of nongonococcal urethritis, for which he received doxycycline. The patient's serum is likely to be positive for antibodies to which of the following organisms?

- a. *Shigella dysenteriae*
- b. Human papillomavirus 4
- c. *Trichomonas vaginalis*
- d. *Chlamydia trachomatis*
- e. *Treponema pallidum*

ANS: D

The patient's nongonococcal urethritis was most likely caused by *C. trachomatis* D-K. This organism is notoriously associated with postinfectious reactive arthritis or Reiter syndrome. The majority of patients with HIV and HLA-B27 genotype will develop Reiter syndrome following *Chlamydia*-NGU.

A is incorrect. As other enteric pathogens, shigellae are notoriously associated with Reiter syndrome. However, this patient has no history of dysentery.

B is incorrect. HPV 4 causes benign skin warts and is not known to be associated with Reiter syndrome.

C is incorrect. *Trichomonas vaginalis* is a sexually transmitted protozoon that is not known to trigger Reiter syndrome.

E is incorrect. *T. pallidum* causes syphilis and is not associated with Reiter syndrome.

200. During prenatal screening, a 30-year-old woman, with known allergy to penicillin, was found to have syphilis. The patient underwent desensitization with increasing doses of intravenous penicillin. The rationale for this therapy is to induce the overriding production of which of the following?

- a. IgA
- b. IgD
- c. IgE

- d. IgG
- e. IgM

ANS: D

During desensitization, increasing quantities of an allergen (penicillin in this case) are injected at regular intervals to induce the production of specific IgG antibodies. During subsequent exposures, the allergen will be neutralized by the IgG before it gets a chance to bind to IgE on the surface of mast cells.

A is incorrect. IgA antibodies are found in a variety of mucosal surfaces. It cannot be induced by specific antigens and thus plays no role in immunotherapy.

B is incorrect. IgD antibodies are found in small quantities in the blood, peritoneum, and pleura. They are present on the surface of many B lymphocytes, but their precise function is unclear. They may play a role in allergic reactions to milk and some medications. Rise in IgD titer would not be beneficial in preventing allergic reactions.

C is incorrect. IgE antibodies mediate immediate hypersensitivity, including anaphylaxis, to penicillin and other beta-lactam antibiotics. The goal of immunotherapy is to reduce the amounts of IgE antibodies.

E is incorrect. IgM antibodies are produced in the early stage of immune response. They bind antigens and are efficient at complement activation, neutralization, and agglutination. IgM antibodies play no role in prevention of allergic reactions.