

- IMMUNOLOGY[dse1]

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Directions (Questions 387-474): Select the ONE lettered answer that is BEST in each question.

387. Which category of hypersensitivity BEST describes hemolytic disease of the newborn caused by Rh incompatibility?

- A. atopic or anaphylactic
- B. cytotoxic
- C. immune complex
- D. delayed

388. The principal difference between cytotoxic (type II) and immune complex (type III) hypersensitivity is

- A. the class (isotype) of antibody.
- B. the site where antigen-antibody complexes are formed.
- C. the participation of complement.
- D. the participation of T cells.

389. A child stung by a bee experiences respiratory distress within minutes and lapses into unconsciousness. This reaction is probably mediated by

- A. IgE antibody.
- B. IgG antibody.
- C. sensitized T cells.
- D. complement.
- E. IgM antibody.

390. A patient with rheumatic fever develops a sore throat from which beta-hemolytic streptococci are cultured. The patient is started on treatment with penicillin, and the sore throat resolves within several days. However, 7 days after initiation of penicillin therapy the patient develops a fever of 103°F, a generalized rash, and proteinuria. This MOST probably resulted from

- A. recurrence of the rheumatic fever.
- B. a different infectious disease.
- C. an IgE response to penicillin.
- D. an IgG-IgM response to penicillin.
- E. a delayed hypersensitivity reaction to penicillin.

391. A kidney biopsy specimen taken from a patient with acute glomerulonephritis and stained with fluorescein-conjugated anti-human IgG antibody would probably show

- A. no fluorescence.
- B. uniform fluorescence of the glomerular basement membrane.
- C. patchy, irregular fluorescence of the glomerular basement membrane.

- D. fluorescent B cells.
- E. fluorescent macrophages.

392. A patient with severe asthma gets no relief from antihistamines. The symptoms are MOST likely to be caused by

- A. interleukin-2.
- B. slow-reacting substance A (leukotrienes).
- C. serotonin.
- D. bradykinin.

393. Hypersensitivity to penicillin and hypersensitivity to poison oak are both

- A. mediated by IgE antibody.
- B. mediated by IgG and IgM antibody.
- C. initiated by haptens.
- D. initiated by Th-2 cells.

394. A recipient of a 2-haplotype MHC-matched kidney from a relative still needs immunosuppression to prevent graft rejection because

- A. graft-versus-host disease is a problem.
- B. minor histocompatibility antigens will not be matched.
- C. minor histocompatibility antigens will be matched.

D. complement components will not be matched.

395. Bone marrow transplantation in immunocompromised patients presents which major problem?

A. potentially lethal graft-versus-host disease

B. high risk of T cell leukemia

C. inability to use a live donor

D. delayed hypersensitivity

396. What is the role of class II MHC proteins on donor cells in graft rejection?

A. They are the receptors for interleukin-2, which is produced by macrophages when they attack the donor cells.

B. They are recognized by helper T cells, which then activate cytotoxic T cells to kill the donor cells.

C. They induce the production of blocking antibodies that protect the graft.

D. They induce IgE which mediates graft rejection.

397. Grafts between genetically identical individuals (i.e., identical twins)

A. are rejected slowly as a result of minor histocompatibility antigens.

B. are subject to hyperacute rejection.

C. are not rejected, even without immunosuppression.

D. are not rejected if a kidney is grafted, but skin grafts are rejected.

398. Penicillin is a hapten in both humans and mice. To explore the hapten-carrier relationship, a mouse was injected with penicillin covalently bound to bovine serum albumin and, at the same time, with egg albumin to which no penicillin was bound. Of the following, which one will induce a secondary response to penicillin when injected into the mouse 1 month later?

- A. penicillin
- B. penicillin bound to egg albumin
- C. egg albumin
- D. bovine serum albumin

399. AIDS is caused by a human retrovirus that kills

- A. B lymphocytes.
- B. lymphocyte stem cells.
- C. CD4-positive T lymphocytes.
- D. CD8-positive T lymphocytes.

400. Chemically-induced tumors have tumor-associated transplantation antigens that

- A. are always the same for a given carcinogen.
- B. are different for two tumors of different histologic type even if induced by the same carcinogen.
- C. are very strong antigens.
- D. do not induce an immune response.

401. Polyomavirus (a DNA virus) causes tumors in "nude mice" (nude mice do not have a thymus, because of a genetic defect) but not in normal mice. the BEST interpretation is that

- A. macrophages are required to reject polyomavirus-induced tumors.
- B. natural killer cells can reject polyomavirus-induced tumors without help from T lymphocytes.
- C. T lymphocytes play an important role in the rejection of polyomavirus-induced tumors.
- D. B lymphocytes play no role in rejection of polyomavirus-induced tumors.

402. C3 is cleaved to form C3a and C3b by C3 convertase. C3b is involved in all of the following EXCEPT

- A. altering vascular permeability.
- B. promoting phagocytosis.
- C. forming alternative-pathway C3 convertase.
- D. forming C5 convertase.

403. After binding to its specific antigen, a B lymphocyte may switch its

- A. immunoglobulin light-chain isotype.
- B. immunoglobulin heavy-chain class.
- C. variable region of the immunoglobulin heavy chain.
- D. constant region of the immunoglobulin light chain.

404. Diversity is an important feature of the immune system. Which one of the following statements about it is INCORRECT?

- A. Humans can make antibodies with about 10⁸ different VH X VL combinations.
- B. A single cell can synthesize IgM antibody, then switch to IgA antibody.
- C. The hematopoietic stem cell carries the genetic potential to create more than 10⁴ immunoglobulin genes.
- D. A single B lymphocyte can produce antibodies of many different specificities, but a plasma cell is monospecific.

405. C3a and C5a can cause

- A. bacterial lysis.
- B. vascular permeability.
- C. phagocytosis of IgE-coated bacteria.
- D. aggregation of C4 and C2.

406. Neutrophils are attracted to an infected area by

- A. IgM.
- B. vascular permeability.
- C. phagocytosis of IgE-coated bacteria.
- D. aggregation of C4 and C2.

407. Complement fixation refers to

- A. the ingestion of C3b-coated bacteria by macrophages.
- B. the destruction of complement in serum by heating at 56°C for 30 minutes.
- C. the binding of complement components by antigen-antibody complexes.
- D. the interaction of C3b with mast cells.

408. The classic complement pathway is initiated by interaction of C1 with

- A. antigen.
- B. factor B.
- C. antigen-IgG complexes.
- D. bacterial lipopolysaccharides.

409. Patients with severely reduced C3 levels tend to have

- A. increased numbers of severe viral infections.
- B. increased numbers of severe bacterial infections.
- C. low gamma globulin levels.
- D. frequent episodes of hemolytic anemia.

410. Individuals with a genetic deficiency of C6 have

- A. decreased resistance to viral infections.
- B. increased hypersensitivity reactions.
- C. increased frequency of cancer.
- D. decreased resistance to Neisseria bacteremia.

411. Natural killer cells are

- A. B cells that can kill without complement.
- B. cytotoxic T cells.
- C. increased by immunization.
- D. able to kill virus-infected cells without prior sensitization.

412. A positive tuberculin skin test (a delayed hypersensitivity reaction) indicates that

- A. a humoral immune response has occurred.
- B. a cell-mediated immune response has occurred.
- C. both the T and B cell systems are functional.
- D. only the B cell system is functional.

413. Reaction to poison ivy or poison oak is

- A. an IgG-mediated response.
- B. an IgE-mediated response.

C. a cell-mediated response.

D. an Arthus reaction.

414. A child disturbs a wasp nest, is stung repeatedly, and goes into shock within minutes, manifesting respiratory failure and vascular collapse. This is MOST likely to be due to

A. systemic anaphylaxis.

B. serum sickness.

C. an Arthus reaction.

D. cytotoxic hypersensitivity.

415. "Isotype switching" of immunoglobulin classes by B cells involves

A. simultaneous insertion of VH genes adjacent to each CH gene.

B. successive insertion of a single VH gene adjacent to different CH genes.

C. activation of homologous genes on chromosome 6.

D. switching of light-chain types (kappa and lambda).

416. Which one of the following pairs of genes is linked on a single chromosome?

A. V gene for lambda chain and C gene for kappa chain

B. C gene for gamma chain and C gene for kappa chain

C. V gene for lambda chain and V gene for heavy chain

D. C gene for gamma chain and C gene for alpha chain

417. Idiotypic determinants are located within

- A. hypervariable regions of heavy and light chains.
- B. constant regions of light chains.
- C. constant regions of heavy chains.
- D. the hinge region.

418. A primary immune response in an adult human requires approximately how much time to produce detectable antibody levels in the blood?

- A. 12 hours
- B. 3 days
- C. 1 week
- D. 3 weeks

419. The membrane IgM and IgD on the surface of an individual B cell

- A. have identical heavy chains but different light chains
- B. are identical except for their CH regions
- C. are identical except for their VH regions
- D. have different VH and VL regions

420. During the maturation of a B lymphocyte, the first immunoglobulin heavy chain synthesized is the

- A. Mu chain.
- B. gamma chain.
- C. epsilon chain.
- D. alpha chain.

421. In the immune response to a hapten-protein conjugate, in order to get anti-hapten antibodies it is essential that

- A. the hapten be recognized by helper T cells.
- B. the protein be recognized by helper T cells.
- C. the protein be recognized by B cells.
- D. the hapten be recognized by suppressor T cells.

422. In the determination of serum insulin levels by radioimmunoassay, which one of the following is NOT needed?

- A. isotope-labeled insulin
- B. anti-insulin antibody made in goats
- C. anti-goat gamma globulin made in rabbits
- D. isotope-labeled anti-insulin antibody made in goats

423. Which one of the following sequences is appropriate for testing a patient for antibody

against the AIDS virus with the ELISA procedure? (The assay is carried out in a plastic plate with an incubation and a wash step after each addition except the final one.)

- A. patient's serum/enzyme substrate/HIV antigen/enzyme-labeled antibody against HIV
- B. HIV antigen/patient's serum/enzyme-labeled antibody against human gamma globulin/enzyme substrate
- C. enzyme-labeled antibody against human gamma globulin/patient's serum/HIV antigen/enzyme substrate
- D. enzyme-labeled antibody against HIV/HIV antigen/patient's serum/enzyme substrate

424. The BEST method to demonstrate IgG on the glomerular basement membrane in a kidney tissue section is the

- A. precipitin test.
- B. complement fixation test.
- C. agglutination test.
- D. indirect fluorescent-antibody test.

425. A woman had a high fever, hypotension, and a diffuse macular rash. When all cultures showed no bacterial growth, a diagnosis of toxic shock syndrome was made. Regarding the mechanism by which the toxin causes this disease, which one of the following is LEAST accurate?

- A. The toxin is not processed within the macrophage.
- B. The toxin binds to both the class II MHC protein and the T cell receptor.
- C. The toxin activates many CD4-positive T cells, and large amounts of interleukins are released.
- D. The toxin has an A-B subunit structure--the B subunit binds to a receptor, and the A subunit

enters the cells and activates them.

426. A patient with a central nervous system disorder is maintained on the drug methyldopa. Hemolytic anemia develops, which resolves shortly after the drug is withdrawn. This is MOST probably an example of

- A. atopic hypersensitivity.
- B. cytotoxic hypersensitivity.
- C. immune-complex hypersensitivity.
- D. cell-mediated hypersensitivity.

427. Which one of the following substances is NOT released by activated helper T cells?

- A. interleukin-1
- B. gamma interferon
- C. interleukin-2
- D. interleukin-4

428. A delayed hypersensitivity reaction is characterized by

- A. edema without a cellular infiltrate.
- B. an infiltrate composed of neutrophils.
- C. an infiltrate composed of helper T cells and macrophages
- D. an infiltrate composed of eosinophils.

429. Two dissimilar inbred strains of mice, A and B, are crossed to yield an F1 hybrid strain, AB. If a large dose of spleen cells from an adult A mouse is injected into an adult AB mouse, which one of the following is MOST likely to occur? An explanation of the answer to this question is given on p. 24.

- A. The spleen cells will be destroyed.
- B. The spleen cells will survive and will have no effect in the recipient.
- C. The spleen cells will induce a graft-versus-host reaction in the recipient.
- D. The spleen cells will survive and induce tolerance of strain A grafts in the recipient.

430. This question is based on the same strains of mice described in the previous question. If adult AB spleen cells are injected into a newborn B mouse, which one of the following is MOST likely to occur? An explanation of the answer to this question is given on p. 24.

- A. The spleen cells will be destroyed.
- B. The spleen cells will survive without any effect on the recipient.
- C. The spleen cells will induce a graft-versus-host reaction in the recipient.
- D. The spleen cells will survive and induce tolerance of strain A grafts in the recipient.

431. The minor histocompatibility antigens on cells

- A. are detected by reaction with antibodies and complement.
- B. are controlled by several genes in the major histocompatibility complex.
- C. are unimportant in human transplantation.
- D. induce reactions that can cumulatively lead to a strong rejection response.

432. Which one of the following is NOT true of class I MHC antigens?

- A. They can be assayed by a cytotoxic test that uses antibody and complement.
- B. They can usually be identified in the laboratory in a few hours.
- C. They are controlled by at least three gene loci in the major histocompatibility complex.
- D. They are found mainly on B cells, macrophages, and activated T cells.

433. An antigen found in relatively high concentration in the plasma of normal fetuses and a high proportion of patients with progressive carcinoma of the colon is

- A. viral antigen.
- B. carcinoembryonic antigen.
- C. alpha-fetoprotein.
- D. heterophil

434. An antibody directed against the idiosyncratic determinants of a human IgG antibody would react with

- A. the Fc part of the IgG.
- B. an IgM antibody produced by the same plasma cell that produced the IgG.
- C. all human kappa chains.
- D. all human gamma chains.

435. Which one of the following is NOT true of the gene segments that combine to make up a heavy-chain gene?

- A. Many V region segments are available.
- B. Several J segments and several D segments are available.
- C. V, D, and J segments combine to encode the antigen-binding site.
- D. A V segment and a J segment are preselected by an antigen to make up the variable-region portion of the gene.

436. When immune complexes from the serum are deposited on glomerular basement membrane, damage to the membrane is caused mainly by

- A. gamma interferon.
- B. phagocytosis.
- C. cytotoxic T cells.
- D. enzymes released by polymorphonuclear cells.

437. If an individual was genetically unable to make J chains, which immunoglobulin(s) would be affected?

- A. IgG
- B. IgM
- C. IgA
- D. IgG and IgM
- E. IgM and IgA

438. The antibody-binding site is formed primarily by

- A. the constant regions of H and L chains.
- B. the hypervariable regions of H and L chains.
- C. the hypervariable regions of H chains.
- D. the variable regions of H chains.
- E. the variable regions of L chains.

439. The class of immunoglobulin present in highest concentration in the blood of a human newborn is

- A. IgG.
- B. IgM.
- C. IgA.
- D. IgD.
- E. IgE.

440. Individuals of blood group type AB

- A. are Rh(d)-negative.
- B. are "universal recipients" of transfusions.
- C. have circulating anti-A and anti-B antibodies.

D. have the same haplotype.

441. Cytotoxic T cells induced by infection with virus A will kill target cells

A. from the same host infected with any virus.

B. infected by virus A and identical at class I MHC loci of the cytotoxic T cells.

C. infected by virus A and identical at class II MHC loci of the cytotoxic T cells.

D. infected with a different virus and identical at class I MHC loci of the cytotoxic cells.

E. infected with a different virus and identical at class II MHC loci of the cytotoxic cells.

442. Antigen-presenting cells that activate helper T cells must express which one of the following on their surfaces?

A. IgE

B. gamma interferon

C. class I MHC antigens

D. class II MHC antigens

443. Which one of the following does NOT contain C3b?

A. classic-pathway C5 convertase

B. alternative-pathway C5 convertase

C. classic-pathway C3 convertase

D. alternative-pathway C3 convertase

444. Which one of the following is NOT true regarding the alternative complement pathway?

- A. It can be triggered by infectious agents in absence of antibody.
- B. It does not require C1, C2, or C4.
- C. It cannot be initiated unless C3b fragments are already present.
- D. It has the same terminal sequence of events as the classic pathway.

445. In setting up a complement fixation test for antibody, the reactants should be added in what sequence? (Ag = antigen; Ab = antibody; C = complement; EA = antibody-coated indicator erythrocytes.)

- A. Ag + EA + C/wait/ + patient's serum
- B. C + patient's serum + EA/wait/ + Ag
- C. Ag + patient's serum + EA/wait/ + C
- D. Ag + patient's serum + C/wait/ + EA

446. Proteins from two samples of animal blood, A and B, were tested by the double-diffusion (Ouchterlony) test in agar against antibody to bovine albumin. Which sample(s) contain horse blood? An explanation of the answer to this question is given on p[dse2] . 24.

- A. sample A
- B. sample B
- C. both samples
- D. neither sample

447. Complement lyses cells by

- A. enzymatic digestion of the cell membrane.
- B. activation of adenylate cyclase.
- C. insertion of complement proteins into the cell membrane.
- D. inhibition of elongation factor 2.

448. Graft and tumor rejection are mediated primarily by

- A. non-complement-fixing antibodies.
- B. phagocytic cells.
- C. helper T cells.
- D. cytotoxic T cells.

449. Which one of the following properties of antibodies is NOT dependent on the structure of the heavy-chain constant region?

- A. ability to cross the placenta
- B. isotype (class)
- C. ability to fix complement
- D. affinity for antigen

450. In which one of the following situations would a graft-versus-host reaction be MOST likely to occur? (Mouse strains A and B are highly inbred; AB is an F1 hybrid between strain A and strain B.)

- A. newborn strain A spleen cells injected into a strain B adult
- B. x-irradiated adult strain A spleen cells injected into a strain B adult
- C. adult strain A spleen cells injected into an x-irradiated strain AB adult
- D. adult strain AB spleen cells injected into a strain A newborn

451. In a mixed-lymphocyte culture, lymphocytes from person X, who is homozygous for the HLA-Dw7 allele, are irradiated and then cultured with lymphocytes from person Z. It is found that DNA synthesis is NOT stimulated. The proper conclusion to be drawn is that

- A. person Z is homozygous for HLA-Dw7.
- B. person Z is homozygous or heterozygous for HLA-Dw7.
- C. person Z is heterozygous for HLA-Dw7.

D. person Z does not carry the HLA-Dw7 allele.

452. A patient skin-tested with purified protein derivative (PPD) to determine previous exposure to *Mycobacterium tuberculosis* develops induration at the skin test site 48 hours later. Histologically, the reaction site would MOST probably show

- A. eosinophils.
- B. neutrophils.
- C. helper T cells and macrophages.
- D. B cells.

453. Hemolytic disease of the newborn caused by Rh blood group incompatibility requires maternal antibody to enter the fetal bloodstream. Therefore, the mediator of this disease is

- A. IgE antibody.
- B. IgG antibody.
- C. IgM antibody.
- D. IgA antibody.

454. An Rh-negative woman married to a heterozygous Rh-positive man has three children. The probability that all three of their children are Rh-positive is

- A. 1:2.
- B. 1:4.
- C. 1:8.

D. zero.

455. Which one of the following statements BEST explains the relationship between inflammation of the heart (carditis) and infection with group A beta-hemolytic streptococci?

- A. Streptococcal antigens induce antibodies cross-reactive with heart tissue.
- B. Streptococci are polyclonal activators of B cells.
- C. Streptococcal antigens bind to IgE on the surface of heart tissue and histamine is released.
- D. Streptococci are ingested by neutrophils that release proteases that damage heart tissue.

456. Your patient became ill 10 days ago with a viral disease. Laboratory examination reveals that the patient's antibodies against this virus have a high ratio of IgM to IgG. What is your conclusion?

- A. It is unlikely that the patient has encountered this organism previously.
- B. The patient is predisposed to IgE-mediated hypersensitivity reactions.
- C. The information given is irrelevant to previous antigen exposure.
- D. It is likely that the patient has an autoimmune disease.

457. If you measure the ability of cytotoxic T cells from an HLA-B27 person to kill virus X-infected target cells, which one of the following statements is CORRECT?

- A. Any virus X-infected target cell will be killed.
- B. Only virus X-infected cells of HLA-B27 type will be killed.
- C. Any HLA-B27 cell will be killed.

D. No HLA-B27 cell will be killed.

458. You have a patient who makes autoantibodies against his own red blood cells, leading to hemolysis. Which one of the following mechanisms is MOST likely to explain the hemolysis?

- A. Perforins from cytotoxic T cells lyse the red cells.
- B. Neutrophils release proteases that lyse the red cells.
- C. Interleukin-2 binds to its receptor on the red cells, which results in lysis of the red cells.
- D. Complement is activated, and membrane attack complexes lyse the red cells.

459. Your patient is a child who has no detectable T or B cells. This immunodeficiency is most probably the result of a defect in

- A. the thymus.
- B. the bursal equivalent.
- C. T cell-B cell interaction.
- D. stem cells originating in the bone marrow.

460. The role of the macrophage during an antibody response is to

- A. make antibody.
- B. lyse virus-infected target cells.
- C. activate cytotoxic T cells.
- D. process antigen and present it.

461. The structural basis of blood group A and B antigen specificity is

- A. a single terminal sugar residue.
- B. a single terminal amino acid.
- C. multiple differences in the carbohydrate portion.
- D. multiple differences in the protein portion.

462. Complement can enhance phagocytosis because of the presence on macrophages and neutrophils of receptors for

- A. factor D.
- B. C3b.
- C. C6.
- D. properdin.

463. The main advantage of passive immunization over active immunization is that

- A. it can be administered orally.
- B. it provides antibody more rapidly.
- C. antibody persists for a longer period.
- D. it contains primarily IgM.

464. On January 15, a patient developed an illness suggestive of influenza, which lasted 1 week.

On February 20, she had a similar illness. She had no influenza immunization during this period. Her hemagglutination inhibition titer to influenza A virus was 10 on January 18, 40 on January 30, and 320 on February 20. Which one of the following is the MOST appropriate interpretation?

- A. The patient was ill with influenza A on January 15.
- B. The patient was ill with influenza A on February 20.
- C. The patient was not infected with influenza virus.
- D. The patient has an autoimmune disease.

465. An individual who is heterozygous for Gm allotypes contains two allelic forms of IgG in serum, but individual lymphocytes produce only one of the two forms. This phenomenon, known as "allelic exclusion," is consistent with

- A. a rearrangement of a heavy-chain gene on only one chromosome in a lymphocyte.
- B. rearrangements of heavy-chain genes on both chromosomes in a lymphocyte.
- C. a rearrangement of a light-chain gene on only one chromosome in a lymphocyte.
- D. rearrangements of light-chain genes on both chromosomes in a lymphocyte.

466. Each of the following statements concerning class I MHC proteins is correct EXCEPT:

- A. They are cell surface proteins on virtually all cells.
- B. They are recognition elements for cytotoxic T cells.
- C. They are codominantly expressed.
- D. They are important in the skin test response to *Mycobacterium tuberculosis*.

467. Which one of the following is the BEST method of reducing the effect of graft-versus-host disease in a bone marrow recipient?

- A. matching the complement components of donor and recipient
- B. administering alpha interferon
- C. removing mature T cells from the graft
- D. removing pre-B cells from the graft

468. Regarding Th-1 and Th-2 cells, which one of the following is LEAST accurate?

- A. Th-1 cells produce gamma interferon and promote cell-mediated immunity.
- B. Th-2 cells produce interleukin-4 and -5 and promote antibody-mediated immunity.
- C. Both Th-1 and Th-2 cells have both CD3 and CD4 proteins on their outer cell membrane.
- D. Before naïve Th cells differentiate into Th-1 or Th-2 cells, they are double-positives; i.e., they produce both gamma interferon and interleukin-4.

469. Each of the following statements concerning the variable regions of heavy chains and the variable regions of light chains in a given antibody molecule is correct EXCEPT:

- A. They have the same amino acid sequence.
- B. They define the specificity for antigen.
- C. They are encoded on different chromosomes.
- D. They contain the hypervariable regions.

470. Each of the following statements concerning class II MHC proteins is correct EXCEPT:

- A. They are found on the surface of both B and T cells.
- B. They have a high degree of polymorphism.
- C. They are involved in the presentation of antigen by macrophages.
- D. They have a binding site for CD4 proteins.

471. Which one of the following statements concerning immunoglobulin allotypes is CORRECT?

- A. Allotypes are found only on heavy chains.
- B. Allotypes are determined by class I MHC genes.
- C. Allotypes are confined to the variable regions.
- D. Allotypes are due to genetic polymorphism within a species.

472. Each of the following statements concerning immunologic tolerance is correct EXCEPT:

- A. Tolerance is not antigen-specific; i.e., paralysis of the immune cells results in a failure to produce a response against many antigens.
- B. Tolerance is more easily induced in T cells than in B cells.
- C. Tolerance is more easily induced in neonates than in adults.
- D. Tolerance is more easily induced by simple molecules than by complex ones.

473. Each of the following statements concerning a hybridoma cell is correct EXCEPT:

- A. The spleen cell component provides the ability to form antibody.
- B. The myeloma cell component provides the ability to grow indefinitely.
- C. The antibody produced by a hybridoma cell is IgM, because heavy-chain switching does not occur.
- D. The antibody produced by a hybridoma cell is homogeneous; i.e., it is directed against a single epitope.

474. Each of the following statements concerning haptens is correct EXCEPT:

- A. A hapten can combine with (bind to) an antibody.
- B. A hapten cannot induce an antibody by itself; rather, it must be bound to a carrier protein to be able to induce antibody.
- C. In both penicillin-induced anaphylaxis and poison ivy, the allergens are haptens.
- D. Haptens must be processed by CD8+ cells to become immunogenic.

Answers (Questions 387-474):

387. D

388. B

389. A

390. D

391. C

392. B

393. C

394. C

395. A

396. B

397. C

398. D

399. C

400. B

401. C

402. A

403. B

404. D

405. B

406. C

407. C

408. C

409. B

410. D

411. D

412. B

413. C

414. A

415. B

416. D

417. A

418. C

419. B

420. A

421. B

422. D

423. B

424. D

425. D

426. B

427. A

428. C

429. C

430. D

431. D

432. D

433. B

434. B

435. D

436. D

437. E

438. B

439. A

440. B

441. B

442. D

443. C

444. C

445. D

446. B

447. C

448. D

449. D

450. C

451. B

452. C

453. B

454. C

455. A

456. A

457. B

458. D

459. D

460. D

461. A

462. B

463. B

464. A

465. A

466. D

467. C

468. D

469. A

470. A

471. D

472. A

473. C

474. D

Directions (Questions 475-535): Select the ONE lettered option that is MOST closely associated with the numbered items. Each lettered option may selected once, more than one, nor not at all.

Questions 475-480

A. T cells

B. B cells

C. Macrophages

D. B cells and macrophages

E. T cells, B cells, and macrophages

475. Major source of interleukin-1

476. Acted on by interleukin-1

477. Major source of interleukin-2

478. Express class I MHC markers

479. Express class II MHC markers

480. Express surface immunoglobulin

Questions 481-484

A. Primary antibody response

B. Secondary antibody response

481. Appears more quickly and persists longer

482. Relatively richer in IgG

483. Relatively richer in IgM

484. Typically takes 7-10 days for antibody to appear

Questions 485-488

A. Blood group A

B. Blood group O

C. Blood groups A and O

D. Blood group AB

485. People with this type have circulating anti-A antibodies.

486. People with this type have circulating anti-B antibodies.

487. People with this type are called "universal donors."

488. People with this type are called "universal recipients."

Questions 489-494

A. Variable region of light chain

B. variable region of heavy chain

C. Variable regions of light and heavy chains

D. Constant region of heavy chain

E. Constant regions of light and heavy chains

489. Determines immunoglobulin class

490. Determines allotypes

491. Determines idiotypes

492. Binding of IgG to macrophages

493. Fixation of complement by IgG

494. Antigen-binding site

Questions 495-498

The following double-immunodiffusion plate contains antibody prepared against whole human serum in the center well. Identify the contents of each peripheral well from the following list (each well to be used once). An explanation of the answer to this question is given on p. 24[dse3]

495. Whole human serum

496. Human IgG

497. Baboon IgG

498. Human transferrin

Questions 499-501

A. Immediate hypersensitivity

- B. Cytotoxic hypersensitivity
- C. Immune-complex hypersensitivity
- D. Delayed hypersensitivity

499. Irregular deposition of IgG along glomerular basement membrane

500. Involves mast cells and basophils

501. Mediated by lymphokines

Questions 502-505

- A. IgM
- B. IgG
- C. IgA
- D. IgE

502. Crosses the placenta

503. Can contain a polypeptide chain not synthesized by a B lymphocyte

504. Found in the milk of lactating women

505. Binds firmly to mast cells and triggers anaphylaxis

Questions 506-509

- A. Agglutination

- B. Precipitin test
- C. Immunofluorescence
- D. Enzyme immunoassay

506. Concentration of IgG in serum

507. Surface IgM on cells in a bone marrow smear

508. Growth hormone in serum

509. Type A blood group antigen on erythrocytes

Questions 510-513

- A. IgA
- B. IgE
- C. IgG
- D. IgM

510. Present in highest concentration in serum

511. Present in highest concentration in secretions

512. Present in lowest concentration in serum

513. Contains 10 heavy and 10 light chains

Questions 514-517

In this double diffusion (Ouchterlony) assay, the center well contains antibody against whole human serum. The peripheral (numbered) wells contain one of the following proteins[dse4] :

- A. Human serum albumin at low concentration
- B. Human serum albumin at high concentration
- C. Human serum transferrin
- D. Sheep serum albumin

514. Which protein is present in well No. 1?

515. Which protein is present in well No. 2?

516. Which protein is present in well No. 3?

517. Which protein is present in well No. 4?

An explanation of the answer to this question is given on p. 24.

Questions 518-521

A. Class I MHC proteins

B. Class II MHC proteins

518. Involved in the presentation of antigen to CD4-positive cells

519. Involved in the presentation of antigen to CD8-positive cells

520. Involved in antibody responses to T-dependent antigens

521. Involved in target cell recognition by cytotoxic T cells

Questions 522-525

A. Fab fragment of IgG

B. Fc fragment of IgG

522. Contains an antigen-combining site

523. Contains hypervariable regions

524. Contains a complement-binding site

525. Is crystallizable

Questions 522-525

A. Severe combined immunodeficiency disease (SCID)

B. X-linked hypogammaglobulinemia

- C. Thymic aplasia
- D. Chronic granulomatous disease
- E. Hereditary angioedema

- 526. Caused by a defect in the ability of neutrophils to kill microorganisms
- 527. Caused by a development defect that results in a profound loss of T cells
- 528. Caused by a deficiency in an inhibitor of the C1 component of complement
- 529. Caused by a marked deficiency of B cells
- 530. Caused by a virtual absence of both B and T cells

Questions 531-535

- A. Systemic lupus erythematosus
- B. Rheumatoid arthritis
- C. Rheumatic fever
- D. Graves' disease
- E. Myasthenia gravis

- 531. Associated with antibody to the thyroid-stimulating hormone (TSH) receptor
- 532. Associated with antibody to IgG
- 533. Associated with antibody to the acetylcholine receptor
- 534. Associated with antibody to DNA
- 535. Associated with antibody to streptococci

Answers (Questions 475-535):

475. C

476. A

477. A

478. E

479. D

480. B

481. B

482. B

483. A

484. A

485. B

486. C

487. B

488. D

489. D

490. E

491. C

492. D

493. D

494. C

495. D

496. C

497. A

498. B

499. C

500. A

501. D

502. B

503. C

504. C

505. D

506. D

507. C

508. D

509. A

510. C

511. A

512. B

513. D

514. B

515. A

516. D

517. C

518. B

519. A

520. B

521. A

522. A

523. A

524. B

525. B

526. D

527. C

528. E

529. B

530. A

531. D

532. B

533. E

534. A

535. C

Directions (Questions 387-474): Select the ONE lettered answer that is BEST in each question.

387. Which category of hypersensitivity BEST describes hemolytic disease of the newborn caused by Rh incompatibility?

- A. atopic or anaphylactic
- B. cytotoxic
- C. immune complex
- D. delayed

388. The principal difference between cytotoxic (type II) and immune complex (type III) hypersensitivity is

- A. the class (isotype) of antibody.
- B. the site where antigen-antibody complexes are formed.
- C. the participation of complement.
- D. the participation of T cells.

389. A child stung by a bee experiences respiratory distress within minutes and lapses into unconsciousness. This reaction is probably mediated by

- A. IgE antibody.
- B. IgG antibody.
- C. sensitized T cells.
- D. complement.
- E. IgM antibody.

390. A patient with rheumatic fever develops a sore throat from which beta-hemolytic streptococci are cultured. The patient is started on treatment with penicillin, and the sore throat resolves within several days. However, 7 days after initiation of penicillin therapy the patient develops a fever of 103°F, a generalized rash, and proteinuria. This MOST probably resulted from

- A. recurrence of the rheumatic fever.
- B. a different infectious disease.
- C. an IgE response to penicillin.
- D. an IgG-IgM response to penicillin.
- E. a delayed hypersensitivity reaction to penicillin.

391. A kidney biopsy specimen taken from a patient with acute glomerulonephritis and stained with fluorescein-conjugated anti-human IgG antibody would probably show

- A. no fluorescence.
- B. uniform fluorescence of the glomerular basement membrane.
- C. patchy, irregular fluorescence of the glomerular basement membrane.
- D. fluorescent B cells.
- E. fluorescent macrophages.

392. A patient with severe asthma gets no relief from antihistamines. The symptoms are MOST likely to be caused by

- A. interleukin-2.

- B. slow-reacting substance A (leukotrienes).
- C. serotonin.
- D. bradykinin.

393. Hypersensitivity to penicillin and hypersensitivity to poison oak are both

- A. mediated by IgE antibody.
- B. mediated by IgG and IgM antibody.
- C. initiated by haptens.
- D. initiated by Th-2 cells.

394. A recipient of a 2-haplotype MHC-matched kidney from a relative still needs immunosuppression to prevent graft rejection because

- A. graft-versus-host disease is a problem.
- B. minor histocompatibility antigens will not be matched.
- C. minor histocompatibility antigens will be matched.
- D. complement components will not be matched.

395. Bone marrow transplantation in immunocompromised patients presents which major problem?

- A. potentially lethal graft-versus-host disease
- B. high risk of T cell leukemia

C. inability to use a live donor

D. delayed hypersensitivity

396. What is the role of class II MHC proteins on donor cells in graft rejection?

A. They are the receptors for interleukin-2, which is produced by macrophages when they attack the donor cells.

B. They are recognized by helper T cells, which then activate cytotoxic T cells to kill the donor cells.

C. They induce the production of blocking antibodies that protect the graft.

D. They induce IgE which mediates graft rejection.

397. Grafts between genetically identical individuals (i.e., identical twins)

A. are rejected slowly as a result of minor histocompatibility antigens.

B. are subject to hyperacute rejection.

C. are not rejected, even without immunosuppression.

D. are not rejected if a kidney is grafted, but skin grafts are rejected.

398. Penicillin is a hapten in both humans and mice. To explore the hapten-carrier relationship, a mouse was injected with penicillin covalently bound to bovine serum albumin and, at the same time, with egg albumin to which no penicillin was bound. Of the following, which one will induce a secondary response to penicillin when injected into the mouse 1 month later?

A. penicillin

- B. penicillin bound to egg albumin
- C. egg albumin
- D. bovine serum albumin

399. AIDS is caused by a human retrovirus that kills

- A. B lymphocytes.
- B. lymphocyte stem cells.
- C. CD4-positive T lymphocytes.
- D. CD8-positive T lymphocytes.

400. Chemically-induced tumors have tumor-associated transplantation antigens that

- A. are always the same for a given carcinogen.
- B. are different for two tumors of different histologic type even if induced by the same carcinogen.
- C. are very strong antigens.
- D. do not induce an immune response.

401. Polyomavirus (a DNA virus) causes tumors in "nude mice" (nude mice do not have a thymus, because of a genetic defect) but not in normal mice. the BEST interpretation is that

- A. macrophages are required to reject polyomavirus-induced tumors.
- B. natural killer cells can reject polyomavirus-induced tumors without help from T lymphocytes.

- C. T lymphocytes play an important role in the rejection of polyomavirus-induced tumors.
- D. B lymphocytes play no role in rejection of polyomavirus-induced tumors.

402. C3 is cleaved to form C3a and C3b by C3 convertase. C3b is involved in all of the following EXCEPT

- A. altering vascular permeability.
- B. promoting phagocytosis.
- C. forming alternative-pathway C3 convertase.
- D. forming C5 convertase.

403. After binding to its specific antigen, a B lymphocyte may switch its

- A. immunoglobulin light-chain isotype.
- B. immunoglobulin heavy-chain class.
- C. variable region of the immunoglobulin heavy chain.
- D. constant region of the immunoglobulin light chain.

404. Diversity is an important feature of the immune system. Which one of the following statements about it is INCORRECT?

- A. Humans can make antibodies with about 10⁸ different VH X VL combinations.
- B. A single cell can synthesize IgM antibody, then switch to IgA antibody.
- C. The hematopoietic stem cell carries the genetic potential to create more than 10⁴ immunoglobulin genes.

D. A single B lymphocyte can produce antibodies of many different specificities, but a plasma cell is monospecific.

405. C3a and C5a can cause

- A. bacterial lysis.
- B. vascular permeability.
- C. phagocytosis of IgE-coated bacteria.
- D. aggregation of C4 and C2.

406. Neutrophils are attracted to an infected area by

- A. IgM.
- B. vascular permeability.
- C. phagocytosis of IgE-coated bacteria.
- D. aggregation of C4 and C2.

407. Complement fixation refers to

- A. the ingestion of C3b-coated bacteria by macrophages.
- B. the destruction of complement in serum by heating at 56°C for 30 minutes.
- C. the binding of complement components by antigen-antibody complexes.
- D. the interaction of C3b with mast cells.

408. The classic complement pathway is initiated by interaction of C1 with

- A. antigen.
- B. factor B.
- C. antigen-IgG complexes.
- D. bacterial lipopolysaccharides.

409. Patients with severely reduced C3 levels tend to have

- A. increased numbers of severe viral infections.
- B. increased numbers of severe bacterial infections.
- C. low gamma globulin levels.
- D. frequent episodes of hemolytic anemia.

410. Individuals with a genetic deficiency of C6 have

- A. decreased resistance to viral infections.
- B. increased hypersensitivity reactions.
- C. increased frequency of cancer.
- D. decreased resistance to Neisseria bacteremia.

411. Natural killer cells are

- A. B cells that can kill without complement.
- B. cytotoxic T cells.
- C. increased by immunization.
- D. able to kill virus-infected cells without prior sensitization.

412. A positive tuberculin skin test (a delayed hypersensitivity reaction) indicates that

- A. a humoral immune response has occurred.
- B. a cell-mediated immune response has occurred.
- C. both the T and B cell systems are functional.
- D. only the B cell system is functional.

413. Reaction to poison ivy or poison oak is

- A. an IgG-mediated response.
- B. an IgE-mediated response.
- C. a cell-mediated response.
- D. an Arthus reaction.

414. A child disturbs a wasp nest, is stung repeatedly, and goes into shock within minutes, manifesting respiratory failure and vascular collapse. This is MOST likely to be due to

- A. systemic anaphylaxis.

- B. serum sickness.
- C. an Arthus reaction.
- D. cytotoxic hypersensitivity.

415. "Isotype switching" of immunoglobulin classes by B cells involves

- A. simultaneous insertion of VH genes adjacent to each CH gene.
- B. successive insertion of a single VH gene adjacent to different CH genes.
- C. activation of homologous genes on chromosome 6.
- D. switching of light-chain types (kappa and lambda).

416. Which one of the following pairs of genes is linked on a single chromosome?

- A. V gene for lambda chain and C gene for kappa chain
- B. C gene for gamma chain and C gene for kappa chain
- C. V gene for lambda chain and V gene for heavy chain
- D. C gene for gamma chain and C gene for alpha chain

417. Idiotypic determinants are located within

- A. hypervariable regions of heavy and light chains.
- B. constant regions of light chains.
- C. constant regions of heavy chains.

D. the hinge region.

418. A primary immune response in an adult human requires approximately how much time to produce detectable antibody levels in the blood?

A. 12 hours

B. 3 days

C. 1 week

D. 3 weeks

419. The membrane IgM and IgD on the surface of an individual B cell

A. have identical heavy chains but different light chains

B. are identical except for their CH regions

C. are identical except for their VH regions

D. have different VH and VL regions

420. During the maturation of a B lymphocyte, the first immunoglobulin heavy chain synthesized is the

A. Mu chain.

B. gamma chain.

C. epsilon chain.

D. alpha chain.

421. In the immune response to a hapten-protein conjugate, in order to get anti-hapten antibodies it is essential that

- A. the hapten be recognized by helper T cells.
- B. the protein be recognized by helper T cells.
- C. the protein be recognized by B cells.
- D. the hapten be recognized by suppressor T cells.

422. In the determination of serum insulin levels by radioimmunoassay, which one of the following is NOT needed?

- A. isotope-labeled insulin
- B. anti-insulin antibody made in goats
- C. anti-goat gamma globulin made in rabbits
- D. isotope-labeled anti-insulin antibody made in goats

423. Which one of the following sequences is appropriate for testing a patient for antibody against the AIDS virus with the ELISA procedure? (The assay is carried out in a plastic plate with an incubation and a wash step after each addition except the final one.)

- A. patient's serum/enzyme substrate/HIV antigen/enzyme-labeled antibody against HIV
- B. HIV antigen/patient's serum/enzyme-labeled antibody against human gamma globulin/enzyme substrate
- C. enzyme-labeled antibody against human gamma globulin/patient's serum/HIV antigen/enzyme substrate

D. enzyme-labeled antibody against HIV/HIV antigen/patient's serum/enzyme substrate

424. The BEST method to demonstrate IgG on the glomerular basement membrane in a kidney tissue section is the

- A. precipitin test.
- B. complement fixation test.
- C. agglutination test.
- D. indirect fluorescent-antibody test.

425. A woman had a high fever, hypotension, and a diffuse macular rash. When all cultures showed no bacterial growth, a diagnosis of toxic shock syndrome was made. Regarding the mechanism by which the toxin causes this disease, which one of the following is LEAST accurate?

- A. The toxin is not processed within the macrophage.
- B. The toxin binds to both the class II MHC protein and the T cell receptor.
- C. The toxin activates many CD4-positive T cells, and large amounts of interleukins are released.
- D. The toxin has an A-B subunit structure--the B subunit binds to a receptor, and the A subunit enters the cells and activates them.

426. A patient with a central nervous system disorder is maintained on the drug methyldopa. Hemolytic anemia develops, which resolves shortly after the drug is withdrawn. This is MOST probably an example of

- A. atopic hypersensitivity.

- B. cytotoxic hypersensitivity.
- C. immune-complex hypersensitivity.
- D. cell-mediated hypersensitivity.

427. Which one of the following substances is NOT released by activated helper T cells?

- A. interleukin-1
- B. gamma interferon
- C. interleukin-2
- D. interleukin-4

428. A delayed hypersensitivity reaction is characterized by

- A. edema without a cellular infiltrate.
- B. an infiltrate composed of neutrophils.
- C. an infiltrate composed of helper T cells and macrophages
- D. an infiltrate composed of eosinophils.

429. Two dissimilar inbred strains of mice, A and B, are crossed to yield an F1 hybrid strain, AB. If a large dose of spleen cells from an adult A mouse is injected into an adult AB mouse, which one of the following is MOST likely to occur? An explanation of the answer to this question is given on p. 24.

- A. The spleen cells will be destroyed.
- B. The spleen cells will survive and will have no effect in the recipient.

- C. The spleen cells will induce a graft-versus-host reaction in the recipient.
- D. The spleen cells will survive and induce tolerance of strain A grafts in the recipient.

430. This question is based on the same strains of mice described in the previous question. If adult AB spleen cells are injected into a newborn B mouse, which one of the following is MOST likely to occur? An explanation of the answer to this question is given on p. 24.

- A. The spleen cells will be destroyed.
- B. The spleen cells will survive without any effect on the recipient.
- C. The spleen cells will induce a graft-versus-host reaction in the recipient.
- D. The spleen cells will survive and induce tolerance of strain A grafts in the recipient.

431. The minor histocompatibility antigens on cells

- A. are detected by reaction with antibodies and complement.
- B. are controlled by several genes in the major histocompatibility complex.
- C. are unimportant in human transplantation.
- D. induce reactions that can cumulatively lead to a strong rejection response.

432. Which one of the following is NOT true of class I MHC antigens?

- A. They can be assayed by a cytotoxic test that uses antibody and complement.
- B. They can usually be identified in the laboratory in a few hours.
- C. They are controlled by at least three gene loci in the major histocompatibility complex.

D. They are found mainly on B cells, macrophages, and activated T cells.

433. An antigen found in relatively high concentration in the plasma of normal fetuses and a high proportion of patients with progressive carcinoma of the colon is

- A. viral antigen.
- B. carcinoembryonic antigen.
- C. alpha-fetoprotein.
- D. heterophil

434. An antibody directed against the idotypic determinants of a human IgG antibody would react with

- A. the Fc part of the IgG.
- B. an IgM antibody produced by the same plasma cell that produced the IgG.
- C. all human kappa chains.
- D. all human gamma chains.

435. Which one of the following is NOT true of the gene segments that combine to make up a heavy-chain gene?

- A. Many V region segments are available.
- B. Several J segments and several D segments are available.
- C. V, D, and J segments combine to encode the antigen-binding site.

D. A V segment and a J segment are preselected by an antigen to make up the variable-region portion of the gene.

436. When immune complexes from the serum are deposited on glomerular basement membrane, damage to the membrane is caused mainly by

- A. gamma interferon.
- B. phagocytosis.
- C. cytotoxic T cells.
- D. enzymes released by polymorphonuclear cells.

437. If an individual was genetically unable to make J chains, which immunoglobulin(s) would be affected?

- A. IgG
- B. IgM
- C. IgA
- D. IgG and IgM
- E. IgM and IgA

438. The antibody-binding site is formed primarily by

- A. the constant regions of H and L chains.
- B. the hypervariable regions of H and L chains.
- C. the hypervariable regions of H chains.

D. the variable regions of H chains.

E. the variable regions of L chains.

439. The class of immunoglobulin present in highest concentration in the blood of a human newborn is

A. IgG.

B. IgM.

C. IgA.

D. IgD.

E. IgE.

440. Individuals of blood group type AB

A. are Rh(d)-negative.

B. are "universal recipients" of transfusions.

C. have circulating anti-A and anti-B antibodies.

D. have the same haplotype.

441. Cytotoxic T cells induced by infection with virus A will kill target cells

A. from the same host infected with any virus.

B. infected by virus A and identical at class I MHC loci of the cytotoxic T cells.

- C. infected by virus A and identical at class II MHC loci of the cytotoxic T cells.
- D. infected with a different virus and identical at class I MHC loci of the cytotoxic cells.
- E. infected with a different virus and identical at class II MHC loci of the cytotoxic cells.

442. Antigen-presenting cells that activate helper T cells must express which one of the following on their surfaces?

- A. IgE
- B. gamma interferon
- C. class I MHC antigens
- D. class II MHC antigens

443. Which one of the following does NOT contain C3b?

- A. classic-pathway C5 convertase
- B. alternative-pathway C5 convertase
- C. classic-pathway C3 convertase
- D. alternative-pathway C3 convertase

444. Which one of the following is NOT true regarding the alternative complement pathway?

- A. It can be triggered by infectious agents in absence of antibody.
- B. It does not require C1, C2, or C4.
- C. It cannot be initiated unless C3b fragments are already present.

D. It has the same terminal sequence of events as the classic pathway.

445. In setting up a complement fixation test for antibody, the reactants should be added in what sequence? (Ag = antigen; Ab = antibody; C = complement; EA = antibody-coated indicator erythrocytes.)

- A. Ag + EA + C/wait/ + patient's serum
- B. C + patient's serum + EA/wait/ + Ag
- C. Ag + patient's serum + EA/wait/ + C
- D. Ag + patient's serum + C/wait/ + EA

446. Proteins from two samples of animal blood, A and B, were tested by the double-diffusion (Ouchterlony) test in agar against antibody to bovine albumin. Which sample(s) contain horse blood? An explanation of the answer to this question is given on p[dse2] . 24.

- A. sample A

- B. sample B
- C. both samples
- D. neither sample

447. Complement lyses cells by

- A. enzymatic digestion of the cell membrane.
- B. activation of adenylate cyclase.
- C. insertion of complement proteins into the cell membrane.
- D. inhibition of elongation factor 2.

448. Graft and tumor rejection are mediated primarily by

- A. non-complement-fixing antibodies.
- B. phagocytic cells.
- C. helper T cells.
- D. cytotoxic T cells.

449. Which one of the following properties of antibodies is NOT dependent on the structure of the heavy-chain constant region?

- A. ability to cross the placenta
- B. isotype (class)

- C. ability to fix complement
- D. affinity for antigen

450. In which one of the following situations would a graft-versus-host reaction be MOST likely to occur? (Mouse strains A and B are highly inbred; AB is an F1 hybrid between strain A and strain B.)

- A. newborn strain A spleen cells injected into a strain B adult
- B. x-irradiated adult strain A spleen cells injected into a strain B adult
- C. adult strain A spleen cells injected into an x-irradiated strain AB adult
- D. adult strain AB spleen cells injected into a strain A newborn

451. In a mixed-lymphocyte culture, lymphocytes from person X, who is homozygous for the HLA-Dw7 allele, are irradiated and then cultured with lymphocytes from person Z. It is found that DNA synthesis is NOT stimulated. The proper conclusion to be drawn is that

- A. person Z is homozygous for HLA-Dw7.
- B. person Z is homozygous or heterozygous for HLA-Dw7.
- C. person Z is heterozygous for HLA-Dw7.
- D. person Z does not carry the HLA-Dw7 allele.

452. A patient skin-tested with purified protein derivative (PPD) to determine previous exposure to Mycobacterium tuberculosis develops induration at the skin test site 48 hours later. Histologically, the reaction site would MOST probably show

- A. eosinophils.

- B. neutrophils.
- C. helper T cells and macrophages.
- D. B cells.

453. Hemolytic disease of the newborn caused by Rh blood group incompatibility requires maternal antibody to enter the fetal bloodstream. Therefore, the mediator of this disease is

- A. IgE antibody.
- B. IgG antibody.
- C. IgM antibody.
- D. IgA antibody.

454. An Rh-negative woman married to a heterozygous Rh-positive man has three children. The probability that all three of their children are Rh-positive is

- A. 1:2.
- B. 1:4.
- C. 1:8.
- D. zero.

455. Which one of the following statements BEST explains the relationship between inflammation of the heart (carditis) and infection with group A beta-hemolytic streptococci?

- A. Streptococcal antigens induce antibodies cross-reactive with heart tissue.
- B. Streptococci are polyclonal activators of B cells.

- C. Streptococcal antigens bind to IgE on the surface of heart tissue and histamine is released.
- D. Streptococci are ingested by neutrophils that release proteases that damage heart tissue.

456. Your patient became ill 10 days ago with a viral disease. Laboratory examination reveals that the patient's antibodies against this virus have a high ratio of IgM to IgG. What is your conclusion?

- A. It is unlikely that the patient has encountered this organism previously.
- B. The patient is predisposed to IgE-mediated hypersensitivity reactions.
- C. The information given is irrelevant to previous antigen exposure.
- D. It is likely that the patient has an autoimmune disease.

457. If you measure the ability of cytotoxic T cells from an HLA-B27 person to kill virus X-infected target cells, which one of the following statements is CORRECT?

- A. Any virus X-infected target cell will be killed.
- B. Only virus X-infected cells of HLA-B27 type will be killed.
- C. Any HLA-B27 cell will be killed.
- D. No HLA-B27 cell will be killed.

458. You have a patient who makes autoantibodies against his own red blood cells, leading to hemolysis. Which one of the following mechanisms is MOST likely to explain the hemolysis?

- A. Perforins from cytotoxic T cells lyse the red cells.
- B. Neutrophils release proteases that lyse the red cells.

- C. Interleukin-2 binds to its receptor on the red cells, which results in lysis of the red cells.
- D. Complement is activated, and membrane attack complexes lyse the red cells.

459. Your patient is a child who has no detectable T or B cells. This immunodeficiency is most probably the result of a defect in

- A. the thymus.
- B. the bursal equivalent.
- C. T cell-B cell interaction.
- D. stem cells originating in the bone marrow.

460. The role of the macrophage during an antibody response is to

- A. make antibody.
- B. lyse virus-infected target cells.
- C. activate cytotoxic T cells.
- D. process antigen and present it.

461. The structural basis of blood group A and B antigen specificity is

- A. a single terminal sugar residue.
- B. a single terminal amino acid.
- C. multiple differences in the carbohydrate portion.

D. multiple differences in the protein portion.

462. Complement can enhance phagocytosis because of the presence on macrophages and neutrophils of receptors for

A. factor D.

B. C3b.

C. C6.

D. properdin.

463. The main advantage of passive immunization over active immunization is that

A. it can be administered orally.

B. it provides antibody more rapidly.

C. antibody persists for a longer period.

D. it contains primarily IgM.

464. On January 15, a patient developed an illness suggestive of influenza, which lasted 1 week. On February 20, she had a similar illness. She had no influenza immunization during this period. Her hemagglutination inhibition titer to influenza A virus was 10 on January 18, 40 on January 30, and 320 on February 20. Which one of the following is the MOST appropriate interpretation?

A. The patient was ill with influenza A on January 15.

B. The patient was ill with influenza A on February 20.

C. The patient was not infected with influenza virus.

D. The patient has an autoimmune disease.

465. An individual who is heterozygous for Gm allotypes contains two allelic forms of IgG in serum, but individual lymphocytes produce only one of the two forms. This phenomenon, known as "allelic exclusion," is consistent with

- A. a rearrangement of a heavy-chain gene on only one chromosome in a lymphocyte.
- B. rearrangements of heavy-chain genes on both chromosomes in a lymphocyte.
- C. a rearrangement of a light-chain gene on only one chromosome in a lymphocyte.
- D. rearrangements of light-chain genes on both chromosomes in a lymphocyte.

466. Each of the following statements concerning class I MHC proteins is correct EXCEPT:

- A. They are cell surface proteins on virtually all cells.
- B. They are recognition elements for cytotoxic T cells.
- C. They are codominantly expressed.
- D. They are important in the skin test response to *Mycobacterium tuberculosis*.

467. Which one of the following is the BEST method of reducing the effect of graft-versus-host disease in a bone marrow recipient?

- A. matching the complement components of donor and recipient
- B. administering alpha interferon
- C. removing mature T cells from the graft
- D. removing pre-B cells from the graft

468. Regarding Th-1 and Th-2 cells, which one of the following is LEAST accurate?

- A. Th-1 cells produce gamma interferon and promote cell-mediated immunity.
- B. Th-2 cells produce interleukin-4 and -5 and promote antibody-mediated immunity.
- C. Both Th-1 and Th-2 cells have both CD3 and CD4 proteins on their outer cell membrane.
- D. Before naïve Th cells differentiate into Th-1 or Th-2 cells, they are double-positives; i.e., they produce both gamma interferon and interleukin-4.

469. Each of the following statements concerning the variable regions of heavy chains and the variable regions of light chains in a given antibody molecule is correct EXCEPT:

- A. They have the same amino acid sequence.
- B. They define the specificity for antigen.
- C. They are encoded on different chromosomes.
- D. They contain the hypervariable regions.

470. Each of the following statements concerning class II MHC proteins is correct EXCEPT:

- A. They are found on the surface of both B and T cells.
- B. They have a high degree of polymorphism.
- C. They are involved in the presentation of antigen by macrophages.
- D. They have a binding site for CD4 proteins.

471. Which one of the following statements concerning immunoglobulin allotypes is CORRECT?

- A. Allotypes are found only on heavy chains.
- B. Allotypes are determined by class I MHC genes.
- C. Allotypes are confined to the variable regions.
- D. Allotypes are due to genetic polymorphism within a species.

472. Each of the following statements concerning immunologic tolerance is correct EXCEPT:

- A. Tolerance is not antigen-specific; i.e., paralysis of the immune cells results in a failure to produce a response against many antigens.
- B. Tolerance is more easily induced in T cells than in B cells.
- C. Tolerance is more easily induced in neonates than in adults.
- D. Tolerance is more easily induced by simple molecules than by complex ones.

473. Each of the following statements concerning a hybridoma cell is correct EXCEPT:

- A. The spleen cell component provides the ability to form antibody.
- B. The myeloma cell component provides the ability to grow indefinitely.
- C. The antibody produced by a hybridoma cell is IgM, because heavy-chain switching does not occur.
- D. The antibody produced by a hybridoma cell is homogeneous; i.e., it is directed against a single epitope.

474. Each of the following statements concerning haptens is correct EXCEPT:

- A. A hapten can combine with (bind to) an antibody.
- B. A hapten cannot induce an antibody by itself; rather, it must be bound to a carrier protein to be able to induce antibody.
- C. In both penicillin-induced anaphylaxis and poison ivy, the allergens are haptens.
- D. Haptens must be processed by CD8+ cells to become immunogenic.

Answers (Questions 387-474):

387. D

388. B

389. A

390. D

391. C

392. B

393. C

394. C

395. A

396. B

397. C

398. D

399. C

400. B

401. C

402. A

403. B

404. D

405. B

406. C

407. C

408. C

409. B

410. D

411. D

412. B

413. C

414. A

415. B

416. D

417. A

418. C

419. B

420. A

421. B

422. D

423. B

424. D

425. D

426. B

427. A

428. C

429. C

430. D

431. D

432. D

433. B

434. B

435. D

436. D

437. E

438. B

439. A

440. B

441. B

442. D

443. C

444. C

445. D

446. B

447. C

448. D

449. D

450. C

451. B

452. C

453. B

454. C

455. A

456. A

457. B

458. D

459. D

460. D

461. A

462. B

463. B

464. A

465. A

466. D

467. C

468. D

469. A

470. A

471. D

472. A

473. C

474. D

Directions (Questions 475-535): Select the ONE lettered option that is MOST closely associated with the numbered items. Each lettered option may selected once, more than one, nor not at all.

Questions 475-480

A. T cells

B. B cells

C. Macrophages

D. B cells and macrophages

E. T cells, B cells, and macrophages

475. Major source of interleukin-1

476. Acted on by interleukin-1

477. Major source of interleukin-2

478. Express class I MHC markers

- 479. Express class II MHC markers
- 480. Express surface immunoglobulin

Questions 481-484

- A. Primary antibody response
 - B. Secondary antibody response
-
- 481. Appears more quickly and persists longer
 - 482. Relatively richer in IgG
 - 483. Relatively richer in IgM
 - 484. Typically takes 7-10 days for antibody to appear

Questions 485-488

- A. Blood group A
 - B. Blood group O
 - C. Blood groups A and O
 - D. Blood group AB
-
- 485. People with this type have circulating anti-A antibodies.
 - 486. People with this type have circulating anti-B antibodies.
 - 487. People with this type are called "universal donors."

488. People with this type are called "universal recipients."

Questions 489-494

- A. Variable region of light chain
- B. variable region of heavy chain
- C. Variable regions of light and heavy chains
- D. Constant region of heavy chain
- E. Constant regions of light and heavy chains

489. Determines immunoglobulin class

490. Determines allotypes

491. Determines idiotypes

492. Binding of IgG to macrophages

493. Fixation of complement by IgG

494. Antigen-binding site

Questions 495-498

The following double-immunodiffusion plate contains antibody prepared against whole human serum in the center well. Identify the contents of each peripheral well from the following list (each well to be used once). An explanation of the answer to this question is given on p. 24[dse3]

495. Whole human serum

496. Human IgG

497. Baboon IgG

498. Human transferrin

Questions 499-501

A. Immediate hypersensitivity

B. Cytotoxic hypersensitivity

C. Immune-complex hypersensitivity

D. Delayed hypersensitivity

499. Irregular deposition of IgG along glomerular basement membrane

500. Involves mast cells and basophils

501. Mediated by lymphokines

Questions 502-505

A. IgM

B. IgG

C. IgA

D. IgE

502. Crosses the placenta

503. Can contain a polypeptide chain not synthesized by a B lymphocyte

504. Found in the milk of lactating women

505. Binds firmly to mast cells and triggers anaphylaxis

Questions 506-509

A. Agglutination

B. Precipitin test

C. Immunofluorescence

D. Enzyme immunoassay

506. Concentration of IgG in serum

507. Surface IgM on cells in a bone marrow smear

508. Growth hormone in serum

509. Type A blood group antigen on erythrocytes

Questions 510-513

A. IgA

B. IgE

C. IgG

D. IgM

510. Present in highest concentration in serum

511. Present in highest concentration in secretions

512. Present in lowest concentration in serum

513. Contains 10 heavy and 10 light chains

Questions 514-517

In this double diffusion (Ouchterlony) assay, the center well contains antibody against whole human serum. The peripheral (numbered) wells contain one of the following proteins[dse4] :

- A. Human serum albumin at low concentration
- B. Human serum albumin at high concentration
- C. Human serum transferrin
- D. Sheep serum albumin

514. Which protein is present in well No. 1?

515. Which protein is present in well No. 2?

516. Which protein is present in well No. 3?

517. Which protein is present in well No. 4?

An explanation of the answer to this question is given on p. 24.

Questions 518-521

- A. Class I MHC proteins
- B. Class II MHC proteins

518. Involved in the presentation of antigen to CD4-positive cells

519. Involved in the presentation of antigen to CD8-positive cells

520. Involved in antibody responses to T-dependent antigens

521. Involved in target cell recognition by cytotoxic T cells

Questions 522-525

A. Fab fragment of IgG

B. Fc fragment of IgG

522. Contains an antigen-combining site

523. Contains hypervariable regions

524. Contains a complement-binding site

525. Is crystallizable

Questions 522-525

A. Severe combined immunodeficiency disease (SCID)

B. X-linked hypogammaglobulinemia

C. Thymic aplasia

D. Chronic granulomatous disease

E. Hereditary angioedema

526. Caused by a defect in the ability of neutrophils to kill microorganisms

527. Caused by a development defect that results in a profound loss of T cells

528. Caused by a deficiency in an inhibitor of the C1 component of complement
529. Caused by a marked deficiency of B cells
530. Caused by a virtual absence of both B and T cells

Questions 531-535

- A. Systemic lupus erythematosus
- B. Rheumatoid arthritis
- C. Rheumatic fever
- D. Graves' disease
- E. Myasthenia gravis

531. Associated with antibody to the thyroid-stimulating hormone (TSH) receptor
532. Associated with antibody to IgG
533. Associated with antibody to the acetylcholine receptor
534. Associated with antibody to DNA
535. Associated with antibody to streptococci

Answers (Questions 475-535):

475. C

476. A

477. A

478. E

479. D

480. B

481. B

482. B

483. A

484. A

485. B

486. C

487. B

488. D

489. D

490. E

491. C

492. D

493. D

494. C

495. D

496. C

497. A

498. B

499. C

500. A

501. D

502. B

503. C

504. C

505. D

506. D

507. C

508. D

509. A

510. C

511. A

512. B

513. D

514. B

515. A

516. D

517. C

518. B

519. A

520. B

521. A

522. A

523. A

524. B

525. B

526. D

527. C

528. E

529. B

530. A

531. D

532. B

533. E

534. A

535. C

For each question, choose the ONE BEST answer or completion.

1. The following properties render a substance immunogenic:
 - A) high molecular weight
 - B) chemical complexity
 - C) sufficient stability and persistence after injection
 - D) All of the above.
 - E) All of the above are essential but not sufficient.
2. The protection against smallpox afforded by prior infection with cowpox represents
 - A) antigenic specificity.
 - B) antigenic cross-reactivity.
 - C) enhanced viral uptake by macrophages.
 - D) innate immunity.
 - E) passive protection.

3. Converting a toxin to a toxoid
 - A) makes the toxin more immunogenic.
 - B) reduces the pharmacologic activity of the toxin.
 - C) enhances binding with antitoxin.
 - D) induces only innate immunity.
 - E) increases phagocytosis.
 4. Haptens
 - A) require carrier molecules to be immunogenic.
 - B) react with specific antibodies when homologous carriers are not employed.
 - C) interact with specific antibody even if the hapten is monovalent.
 - D) cannot stimulate secondary antibody responses without carriers.
 - E) all of the above.
 5. An immunologic adjuvant is a substance that
 - A) reduces the toxicity of the immunogen.
 - B) enhances the immunogenicity of haptens.
 - C) enhances hematopoiesis.
 - D) enhances the immune response against the immunogen.
 - E) enhances immunologic cross-reactivity.
 6. An antibody made against the antigen tetanus toxoid (TT) reacts with it even when the TT is denatured by disrupting all disulfide bonds. Another antibody against TT fails to react when the TT is similarly denatured. The most likely explanation can be stated as follows:
 - A) The first antibody is specific for several epitopes expressed by TT.
 - B) The first antibody is specific for the primary amino acid sequence of TT, whereas the second is specific for conformational determinants.
 - C) The second antibody is specific for disulfide bonds.
 - D) The first antibody has a higher affinity for TT.
-

Answers To Review Questions

- 1. E** All of the properties are essential but not sufficient, since, for immunogenicity, the substance must be foreign to the immunized individual.
- 2. B** The protection against smallpox provided by prior infection with cowpox is an example of antigenic cross-reactivity. Immunization with cowpox leads to the production of antibodies capable of reacting with smallpox because the two viruses share several identical, or structurally similar, determinants.
- 3. B** Conversion of a toxin to a toxoid is performed in order to reduce the pharmacologic activity of the toxin, so that sufficient toxoid can be injected to induce an immune response.
- 4. E** Haptens are substances, usually of low molecular weight and univalent, that, by themselves, cannot induce immune responses (primary or secondary), but can do so if conjugated to high-molecular-weight carriers. The haptens can and do interact with the induced antibodies, without it being necessary that they be conjugated to the carrier.
- 5. D** An immunologic adjuvant is a substance that, when mixed with an immunogen, enhances the immune response against that immunogen. It does not enhance cross-reactivity, nor does it enhance hematopoiesis. An adjuvant does not enhance the immune response against a hapten, which requires its

conjugation to an immunogenic carrier to induce a response against the hapten. The adjuvant has no relevance to possible toxicity of an immunogen.

6. B Antibodies can recognize single epitopes formed by primary sequence structures or secondary, tertiary, and quaternary conformational structures. Denaturing a protein by disrupting disulfide bonds generally destroys conformational determinants. Therefore it is likely that the first antibody reacts with a primary amino acid sequence determinant that is present on both native and denatured TT, while the second antibody sees a conformational determinant only on native TT.

For each question, choose the ONE BEST answer or completion.

1. The class-specific antigenic determinants (epitopes) of immunoglobulins are associated with
 - A) L chains.
 - B) J chains.
 - C) disulfide bonds.
 - D) H chains.
 - E) variable regions.
2. The idiotype of an antibody molecule is determined by the amino acid sequence of the
 - A) constant region of the L chain.
 - B) variable region of the L chain.
 - C) constant region of the H chain.
 - D) constant regions of the H and L chains.
 - E) variable regions of the H and L chains.
3. Injection into rabbits of a preparation of pooled human IgG could stimulate production of
 - A) anti- γ heavy-chain antibody.
 - B) anti- κ chain antibody.
 - C) anti- λ chain antibody.
 - D) anti-Fc antibody.
 - E) All are correct.
4. A polyclonal antiserum raised against pooled human IgA will react with
 - A) human IgM.
 - B) κ light chains.
 - C) human IgG.
 - D) J chain.
 - E) All are correct.
5. An individual was found to be heterozygous for IgG₁ allotypes 3 and 1. The different possible IgG₁ antibodies produced by this individual will never have
 - A) two H chains of allotype 1

- B) two L chains of either κ or λ .
C) two H chains of allotype
D) two H chains, one of allotype 3 and one of allotype 1
6. Papain digestion of an IgG preparation of antibody specific for the antigen hen egg albumin (HEA)
- A) will
- A) lose its antigen specificity.
B) precipitate with HEA.
C) lose all interchain disulfide bonds.
D) produce two Fab molecules and one Fc fragment.
E) None of the above.
7. The first immunoglobulin synthesized by the fetus is
- A) IgA.
B) IgE.
C) IgG.
D) IgM.
E) None; the fetus does not synthesize immunoglobulins.
8. The following properties of human IgG are true except:
- A) It can pass through the placenta.
B) It can be cleaved by pepsin and yet remain divalent.
C) Its half-life is approximately 23 days.
D) It induces the formation of leukocytes.
E) It participates in the activation of complement.
F) It has the longest half-life of all Ig isotypes.
9. The relative level of specific IgM antibodies can be of diagnostic significance because
- A) IgM is easier to detect than the other isotypes.
B) viral infection often results in very high IgM responses.
C) IgM antibodies are more often protective against reinfections than are the other isotypes.
D) relatively high levels of IgM often correlate with a first recent exposure to the inducing agent.
10. The primary and secondary antibody responses differ in
- A) the predominant isotype generated.
B) the number of lymphocytes responding to antigen.
C) the speed at which antibodies appear in the serum.
D) the biologic functions manifested by the Ig isotypes produced.
E) All of the above.

Online Only Review Questions

11. Serum from a patient is analyzed by serum protein electrophoresis. The gamma globulin peak is twenty times lower than that of a normal healthy individual.
- A) this result is normal because not all people have similar levels of IgG.
B) this result may indicate a B cell immunodeficiency
C) this patient probably has an autoimmune disease
D) the patient may have a myeloma protein

Answers to Review Questions

- 1. D** The five classes of Ig molecules are defined by the H chains (γ , μ , α , λ , ϵ).
- 2. E** The idiotype is the antigenic determinant of an Ig molecule, which involves its antigen-combining site, which in turn consists of contributions from the variable regions of both L and H chains.
- 3. E** All are correct statements. Since a pool of IgG is injected, it can be assumed that both κ and λ chains will be present and that antibodies will be made against them, as well as against the other determinants (H chain and Fc region) present in all IgG molecules.
- 4. E** All are correct statements. Antibody to IgA will have antibody specific for κ and λ light chains, which, of course, will react with IgG and IgM, both of which have κ and λ chains. Antibody will also be present against J chain if the IgA used for immunization was dimeric.
- 5. D** In any immunoglobulin produced by a single cell, the two H chains and the two L chains are identical. Therefore, any antibody molecule in this individual would have either allotype 3 H chains or allotype 12 H chains, not a mixture. Similarly, the antibody would have either two κ or two λ chains.
- 6. D** Papain digestion cleaves the IgG molecules above the hinge region, generating two Fab molecules and an Fc fragment. The Fab fragments can still bind to HEA, but since they are not held together by disulfide bonds, they cannot precipitate the antigen. This contrasts with the effects of pepsin treatment of IgG, which cleaves below the hinge region, leaving intact one divalent F(ab')₂ cf152 cf1 molecule capable of precipitating the antigen. Fragments of pepsin-treated HEA-specific antibody will have the same affinity for the antigen as the original Fab regions of the antibody, since the CDR regions of the molecules are preserved.
- 7. D** The first (and only) immunoglobulin synthesized by the fetus is IgM. The IgG present in the fetus is maternal IgG that has passed through the placenta. No other immunoglobulins are found in the fetus.
- 8. D** Human IgG is the only Ig that passes across the placenta. It has a half-life of 23 days, the longest of all Ig isotypes. It can be cleaved by pepsin to yield a divalent antibody portion F(ab')₂ cf152 cf1, and it participates in the activation of complement. It does not induce the formation of leukocytes. Thus all the statements are true except D.
- 9. D** Only the last statement is correct. Relatively high levels of IgM often correlate with first recent exposure to an inducing agent, since IgM is the first isotype synthesized in response to an immunogen. All other statements are not true.
- 10. E** All are correct. The statements are self-explanatory.
- 11. B** Reduction in level of the antibody-containing gamma globulin peak indicates immunodeficiency, which may be in the B-cell compartment (see Figure 4.1).

- Primary interactions between antigens and antibodies involve all of the following except
 - A) covalent bonds.
 - B) van der Waals forces.
 - C) hydrophobic forces.
 - D) electrostatic forces.
 - E) a very close fit between an epitope and the antibody.
- If an IgG antibody preparation specific for hen egg lysosome (HEL) is treated with papain to generate Fab fragments, which of the following statements concerning the avidity of such fragments is true?
 - A) They will have a lower avidity for HEL as compared with the intact IgG.
 - B) They will have a higher avidity for HEL as compared with the intact IgG.
 - C) There will have the same avidity for HEL as the intact IgG.
 - D) They will have lost their avidity to bind to HEL.
 - E) They will have the same avidity but will have a lower affinity for HEL.
- Western assays used to test serum samples for the presence of antibodies to infectious agents, such as HIV, are particularly useful as diagnostic assays because
 - A) they are more sensitive than ELISA.
 - B) antibodies specific for multiple antigenic epitopes can be detected.
 - C) they provide quantitative data for sample analysis.
 - D) they allow multiple samples to be tested simultaneously.
 - E) they are less expensive and take less time to perform as compared with ELISA.
- The major difference between transgenic mice and knockout mice is that
 - A) transgenic mice always employ the use of cloned genes derived from other species.
 - B) transgenic mice have foreign genes that integrate at targeted loci through homologous recombination.
 - C) transgenic mice have a functional foreign gene added to their genome.
 - D) knockout mice always have a unique phenotype.
- SCID mice have a genetic defect that prevents development of functional
 - A) hematopoietic cells.
 - B) B cells and T cells.
 - C) T cells and NK cells.
 - D) pluripotential stem cells.
 - E) myeloid cells.
- Which of the following statements regarding B cell hybridomas is false?
 - A) They are immortal cell lines that produce antibodies of a single specificity.
 - B) They are derived from B cells that are first cloned and grown in cell culture for short periods.
 - C) They contain a large nucleus formed by the fusion of two nuclei.
 - D) They can be used to manufacture diagnostic or therapeutic monoclonal antibodies.
 - E) They are derived by fusing B cells with malignant plasma cells that are unable to secrete immunoglobulin.
- An ELISA designed to test for the presence of serum antibody for a new strain of pathogenic bacteria is under development. Initially, a monoclonal antibody specific for a single epitope of the organism was used

both to sensitize the wells of the ELISA plate and as the enzyme-labeled detecting antibody in a conventional sandwich ELISA. The ELISA failed to detect the antigen despite the use of a wide range of antibody concentrations. What is the most probable cause of this problem?

- A) The antigen is too large.
- B) The antibody has a low affinity for the antigen.
- C) The monoclonal antibody used to sensitize the wells is blocking access of the epitope, thus when the same antibody is enzyme-labeled, it cannot bind to the antigen.
- D) The enzyme-labeled antibody used should have been a different isotype than the sensitizing antibody.
- E) The monoclonal antibody used is probably unstable.

Online Only Review Questions

- The *indirect* Coombs' test (anti-immunoglobulin test) typically uses:
 - A) Patient's red cells to determine whether they will bind IgG
 - B) patient's red cells to determine whether they will bind all immunoglobulins
 - C) patient's serum to determine whether it forms a precipitate with donor plasma
 - D) patient's serum to determine whether it contains antibodies that bind to a variety of reagent red cells
 - E) patient's serum to determine whether it contains antibodies that bind to the patient's red cells

Answers To Review Questions

- 1. A** No covalent bonds are involved in the interaction between antibody and antigen. The binding forces are relatively weak and include van der Waals forces, hydrophobic forces, and electrostatic forces. A very close fit between an epitope and the antibody is required.
- 2. A** Avidity denotes the overall binding energy between antigens and multivalent antigens. Since the valency of the Fab fragments is one as compared with the HEL-specific IgG molecule, which has a valence of 2 (due to the presence of two Fab regions), the avidity of the fragments will be lower. Choice E is incorrect since the affinity of the Fab fragments will be the same as each of the Fab regions of the intact IgG molecule.
- 3. B** In Western assays, electrophoretic separation techniques are used to resolve the molecular mass of a given antigen or mixtures of antigens. Since antibody responses to infectious agents generate polyclonal responses by virtue of the complex antigenic determinants expressed by such agents, Western assays can confirm the presence of these antibodies, which react with the electrophoretically separated antigens of known molecular weights.
- 4. C** Cloned foreign genes from either the same or other species are introduced into mice to generate a transgenic strain. Integration is random and occurs in both somatic and germ line cells. Choice D is incorrect because sometimes knockout mice do not have a phenotype unique caused by the replacement of a functional gene with one that is nonfunctional, probably due to the activity of redundant or compensatory mechanisms.
- 5. B** SCID mice possess an autosomal recessive mutation that causes a disorder in which B and T cells fail to develop. Like their human counterparts, SCID mice are compromised with respect to lymphoid defense mechanisms. Pluripotential stem cells present in SCID mice can give rise to other hematopoietic lineages, including cells in the myeloid lineage and NK cells.
- 6. B** The method used to generate B cell hybridomas employs the fusion of B cells (e.g., from the spleen and lymph nodes) harvested from immunized mice with a selected population of malignant plasma cells

unable to secrete immunoglobulin. Antigen-specific B cells are not cloned first and then fused with such plasma cells.

7. C In a sandwich ELISA, an antibody (often monoclonal) is used to coat ELISA wells followed by blocking with a nonspecific protein to saturate any unbound sites. The antigen is then added, followed by the addition of a second antigen-specific antibody that is enzyme-labeled. A polyclonal, antigen-specific antibody is often used as the enzyme-labeled reagent. This is done because the epitope detected by the coating antibody (a monoclonal antibody in this case) may be blocked by that antibody, thus preventing its access if the same monoclonal were used as the enzyme-labeled detecting antibody.

8. D The indirect Coombs test is generally used to detect the presence in a patient's serum of antibodies that react with antigens expressed on red blood cells (see Figure 5.2).

1. The DNA for an H chain in a B cell making IgG₁ antibody for diphtheria toxoid has the following structure: 5'— V₁₇— D₅ — J₂ C_{γ2}— C_{γ4}— C_ε— C_{α2}— 3' How many individual rearrangements were required to go from the embryonic DNA to this B-cell DNA?
 - A) 1
 - B) 2
 - C) 3
 - D) 4
 - E) none
2. If you had 50 V, 20 D, and 6 J regions able to code for a heavy chain, and 40 V and 5 J region genes able to code for a light chain, you could have a maximum repertoire of
 - A) $76 + 45 = 121$ antibody specificities
 - B) $76 \times 45 = 3420$ specificities
 - C) $(40 \times 5) + (50 \times 20 \times 6) = 6200$ specificities
 - D) $(40 \times 5) \times (50 \times 20 \times 6) = 1,200,000$ specificities
 - E) more than 1,200,000 specificities

3. The antigen specificity of a particular B cell
 - A) is induced by interaction with antigen.
 - B) is determined only by the L-chain sequence.
 - C) is determined by H + L-chain variable region sequences.
 - D) changes after isotype switching.
 - E) is determined by the heavy-chain constant region.
4. If you could analyze, at the molecular level, a plasma cell making IgA antibody, you would find all of the following *except*
 - A) a DNA sequence for V, D, and J genes translocated near the $C\alpha$ DNA exon.
 - B) mRNA specific for either κ or λ light chains.
 - C) mRNA specific for J chains.
 - D) mRNA specific for μ chains.
 - E) a DNA sequence coding for the T-cell receptor for antigen.
5. The ability of a single B cell to express both IgM and IgD molecules on its surface at the same time is made possible by
 - A) allelic exclusion.
 - B) isotype switching.
 - C) simultaneous recognition of two distinct antigens.
 - D) selective RNA splicing.
 - E) use of genes from both parental chromosomes.
6. Which of the following statements concerning the organization of immunoglobulin genes is correct?
 - A) V and J regions of embryonic DNA have already undergone a rearrangement.
 - B) Light-chain genes undergo further rearrangement after surface IgM is expressed.
 - C) V_H gene segments can rearrange with J_κ or J_λ gene segments.
 - D) The VDJ segments coding for an immunoglobulin V_H region may associate with different heavy-chain constant region genes.
 - E) After VDJ joining has occurred, a further rearrangement is required to bring the VDJ unit next to the C_μ gene.
7. Which of the following does not contribute to the generation of diversity of B-cell antigen receptors?
 - A) multiple V genes in the germ line
 - B) random assortment of L and H chains
 - C) imprecise recombination of V and J or V, D, and J segments
 - D) inheritance of multiple C-region genes
 - E) somatic hypermutation
8. Which of the following concerning Ig expression on a B cell is *incorrect*
 - A) The light chains of the IgM and IgD have identical amino acid sequences.
 - B) The constant parts of the heavy chains of the IgM and IgD have different amino acid sequences.
 - C) The IgM and IgD have different antigenic specificities.
 - D) If the B cell is triggered by antigen and T-cell signals to proliferate and differentiate into antibody secreting plasma cells, the cell can potentially secrete IgG, IgE, or IgA antibody.
 - E) The IgM on the surface will have either κ light chains or λ light chains, but not both.
9. Which of the following plays a role in changing the antigen binding site of a B cell *after* antigenic stimulation?:
 - A) junctional diversity
 - B) combinatorial diversity

- C) germ-line diversity
 - D) somatic hypermutation
 - E) differential splicing of primary RNA transcripts
-

Case Study

As a member of a research team studying a tribe found in a remote region of New Guinea, you make the astonishing discovery that they have only two V genes for the L chain and three V genes for the H chain of immunoglobulins. Nevertheless, they seem healthy and able to resist the diversity of pathogenic organisms endemic to the area. Suggest how this might be accomplished.

Answers to Review Questions

- 1. C** Three DNA rearrangements are required. First, D_iJ_i rearrangement occurs, followed by V₁₇—>D₅J₂. This permits synthesis of IgM and IgD molecules using V₁₇ D₅ J₂. The third rearrangement is the class switch of V₁₇ D₅ J₂ C_μ C_δ to V₁₇ D₅ J₂ C_γ2, leading to the synthesis of IgG₂ molecules.
 - 2. E** While 1,200,000 would be the product of all possible combinations of genes, the generation of many more antibody specificities is likely as a result of imprecise recombinations of VJ or VDJ segments, insertional diversity, and somatic hypermutation.
 - 3. C** The antigenic specificity is determined by the sequences and hence the structure formed by the combination of heavy- and light-chain variable regions.
 - 4. D** As a consequence of the rearrangement of the VDJ to C_α in the IgA producing cell, the C_μ gene will have been deleted. The other DNA sequences and mRNA species will be found in the cell.
 - 5. D** The simultaneous synthesis of IgM and IgD is made possible by the alternate splicing of the primary RNA transcript 5'—VDJ—C_γ—C_μ—C_δ—3'
 - 6. D** This is the basis of isotype or class switching.
 - 7. D** The presence of multiple C_H region genes, although the basis for functional diversity, does not contribute to the diversity of antigen-specific receptors.
 - 8. C** The IgM and IgD expressed on a single B cell use the same heavy- and light-chain V(D)J gene units and therefore have the same antigenic specificity.
 - 9. D** Of the mechanisms described for generating diversity of Ig molecules, only somatic hypermutation affects the antigen binding site *after* antigen stimulation.
-

Answer to Case Study

Despite the paucity of V-region genes, these individuals presumably retain other mechanisms for generating diversity. These include the presence of multiple J and D gene segments in the germ line, junctional diversity due to deletion or insertion of bases at joining sites, random assortment of H and L

chains, and somatic hypermutation. It is therefore conceivable that, even with their limited V-gene repertoire, they can generate sufficient diversity of antibody specificity to survive.

- The earliest stages of B-cell differentiation

- A) occur in the embryonic thymus.
- B) require the presence of antigen.
- C) involve rearrangement of κ-chain gene segments.
- D) involve rearrangement of surrogate light-chain gene segments.
- E) involve rearrangement of heavy-chain gene segments.

- Which of the following is expressed on the surface of the mature B lymphocyte?

- A) CD40
- B) MHC class II molecules
- C) CD32
- D) IgM and IgD
- E) All of the above.

- Which of the following statements is *incorrect*?

- A) Antibodies in a secondary immune response generally have a higher affinity for antigen than antibodies formed in a primary response.
- B) Somatic hypermutation of V region genes may contribute to changes in antibody affinity observed during secondary responses.
- C) Synthesis of antibody in a secondary response occurs predominantly in the blood.
- D) Isotype switching occurs in the presence of antigen.
- E) Predominantly IgM antibody is produced in the primary response.

- Immature B lymphocytes

- A) produce only μ chains.

- B) are progenitors of T as well as B lymphocytes.
- C) express both IgM and IgD on their surface.
- D) are at a stage of development where contact with antigen may lead to unresponsiveness.
- E) must go through the thymus to mature.

• Antigen binding to the B-cell receptor

- A) transduces a signal through the antigen-binding chains.
- B) invariably leads to B-cell activation.
- C) transduces a signal through the Ig α and Ig β molecules.
- D) results in macrophage activation.
- E) leads to cytokine synthesis, which activates T cells.

• Which of the following would *not* be found on a memory B cell:

- A) Ig α and Ig β
- B) γ heavy chains
- C) ϵ heavy chains
- D) surrogate light chains
- E) κ light chains

Online Only Review Questions

• A 19-year-old African-American presents to her primary care physician with an extranodal mass involving the mandible. Biopsy revealed lymphoma cells with the following characteristics: germline TCR genes, surface IgM+, surface IgD+, CD19+. What normal cell component markers are most similar to those expressed by the lymphoma cell?

- A) Pre-B cell
- B) Immature B cell
- C) Mature B cell
- D) Immature T cell
- E) Mature T cell

• In B cell development when the heavy chain first rearranges it may be expressed on the cell surface prior to light chain rearrangement. If this occurs, the heavy chain is associated with which of the following on the surface of the cell?

- A) invariant chain
- B) surrogate light chains
- C) CLIP
- D) β -2 microglobulin
- E) it is expressed by itself

Answers to Review Questions

1. E The earliest events in B-cell differentiation take place in fetal liver and bone marrow in the adult and involve rearrangement of heavy-chain V, D, and J gene segments.
2. E All the molecules are expressed on the surface of the mature B cell.
3. C Antibody synthesis in secondary responses occurs predominantly in lymph nodes, not blood.
4. D In immature B cells, which express only IgM, contact with antigen leads to unresponsiveness rather than activation.

5 C. The molecules Ig α and Ig β , which are associated with the surface Ig molecule, transduce a signal following antigen binding to surface Ig.

6. D Surrogate light chains are expressed only at the pre-B cell stage of B-cell differentiation.

7. C The surface expression of IgM, IgD, and CD19 is characteristic of mature B cells.

8. C In the early stages of B cell development, the heavy chain is first expressed on the cell surface in association with the non-rearranged molecules VpreB and λ 5, known as the surrogate light chains.

1. All the following are characteristics of both MHC class I and class II molecules *except*:
 - A) They are expressed codominantly.
 - B) They are expressed constitutively on all nucleated cells.
 - C) They are glycosylated polypeptides with domain structure.
 - D) They are involved in presentation of antigen fragments to T cells.
 - E) They are expressed on the surface membrane of B cells.
2. MHC class I molecules are important for which of the following?
 - A) binding to CD8 molecules on T cells
 - B) presenting exogenous antigen (e.g., bacterial protein) to B cells
 - C) presenting viral protein to antigen-presenting cells such as macrophages
 - D) binding to CD4 molecules on T cells
 - E) binding to Ig on B cells
3. Which of the following is *incorrect* concerning MHC class II molecules?
 - A) B cells may express different MHC class II molecules on their surface.
 - B) MHC class II molecules are synthesized in the endoplasmic reticulum of many cell types.
 - C) Genetically different individuals express different MHC class II alleles.
 - D) MHC class II molecules are associated with β 2-microglobulin on the cell surface.
 - E) A peptide that does not bind to an MHC class II molecule will not trigger a CD4 $^{+}$ T cell response.
4. Products of TAP-1 and -2 genes
 - A) bind β 2-microglobulin.
 - B) prevent peptide binding to MHC molecules.
 - C) are part of the proteasome.
 - D) transport peptides into the endoplasmic reticulum for binding to MHC class I.
 - E) transport peptides into the endoplasmic reticulum for binding to MHC class II.
5. Which of the following is *incorrect* concerning the processing of an antigen, such as a bacterial protein, in the acid compartments of the cell?
 - A) It results in production of potentially immunogenic peptides that associate with MHC class II molecules.
 - B) Predominantly exogenous antigens are processed by this pathway.

- C) It may lead to activation of CD4⁺ T cells.
 - D) It may lead to the activation of CD8⁺ T cells.
 - E) Bacterially derived peptides displace a fragment of the invariant chain from the MHC class II binding groove.
6. Which of the following statements about the MHC is *incorrect*?
- A) It codes for complement components.
 - B) It codes for both chains of the MHC class I molecule.
 - C) It codes for both chains of the MHC class II molecule.
 - D) It is associated with susceptibility and resistance to different diseases.
 - E) The total set of MHC alleles on the chromosome is known as the MHC haplotype.

Online Only Review Questions

7. When the sequences of different MHC class I molecules are compared, the variation between molecules is concentrated within which of the following?
- A) Areas of the molecule that bind CD4
 - B) Areas of the molecule that bind to the T cell receptor and to the antigenic peptide
 - C) β -2 microglobulin
 - D) the transmembrane domain of the α chain
 - E) the $\beta 1$ domain (the N terminal domain of the β chain)

Answers to Review Questions

- 1. B** MHC class I molecules are expressed on nearly all nucleated cells, but the constitutive expression of MHC class II molecules is more limited (B cells, dendritic cells, and thymic epithelial cells). MHC class II expression can be induced on other cell types (such as macrophages, endothelial cells, and human T cells) by cytokines.
- 2. A** As described further in Chapters 9 and 10, the interaction of CD8 on the T cell and an invariant region of MHC class I molecule is crucial in the triggering of CD8⁺ T cells.
- 3 D** The MHC class I molecule, not the MHC class II molecule, associates with $\beta 2$ - microglobulin.
- 4. D** The products of the TAP-1 and -2 genes selectively transport peptides 8–9 amino acids in length from the cytoplasm into the ER where they bind to MHC class I molecules.
- 5. D** CD8⁺ T cells are generally not activated by processing in acid compartments; exogenous antigen processing in acid compartments results in the generation of peptides, some of which can displace the CLIP fragment of the invariant chain from the MHC class II binding groove. The peptide—MHC class II complexes move to the cell surface and can interact with a CD4⁺ T cell with the appropriate receptor.
- 6. B** The $\beta 2$ -microglobulin gene is located outside the MHC, on a different chromosome.
- 7. B** Regions in the binding pocket or groove that interact with peptide and the T cell receptor show the greatest variability in allelic variants.

1. Which of the following statements concerning T-cell development is correct?
 - A) Progenitor T cells that enter the thymus from the bone marrow have already rearranged their T cell receptor genes.
 - B) Interaction with thymic non-lymphoid cells is critical.
 - C) Maturation in the thymus requires the presence of foreign antigen.
 - D) MHC class II molecules are not involved in positive selection
 - E) Mature, fully differentiated T cells are found in the cortex of the thymus.
2. The development of self-tolerance in the T-cell compartment is important for the prevention of autoimmunity. Which of the following results in T-cell self-tolerance?
 - A) allelic exclusion
 - B) somatic hypermutation
 - C) thymocyte proliferation
 - D) positive selection
 - E) negative selection
3. Which of the following statements is correct?
 - A) The TCR $\alpha\beta$ chains transduce a signal into a T cell.
 - B) A cell depleted of its CD4 molecule would be unable to recognize antigen.
 - C) T cells with fully rearranged $\alpha\beta$ chains are not found in the thymus.
 - D) T cells expressing the $\gamma\delta$ receptor are found only in the thymus.
 - E) Immature CD4 $^{+}$ CD8 $^{+}$ T cells form the majority of T cells in the thymus.
4. Which of the following is *incorrect* regarding mature T cells that use $\alpha\beta$ as their antigen-specific receptor?
 - A) They coexpress CD3 on the cell surface.
 - B) They may be either CD4 $^{+}$ or CD8 $^{+}$
 - C) They interact with peptides derived from nonself antigens.
 - D) They can further rearrange their TCR genes to express $\gamma\delta$ as their receptor.
 - E) They circulate through blood and lymph and migrate to secondary lymphoid organs.
5. CD4
 - A) binds directly to peptide antigen.
 - B) binds to an invariant portion of MHC class I molecules.
 - C) binds to an invariant portion of MHC class II molecules.
 - D) binds to CD8 on the T cell surface.
 - E) binds to the peptide-binding site of MHC class II.
6. Which of the following statements is *incorrect* concerning TCR and Ig genes?

- A) In both B- and T-cell precursors, multiple V-, D-, J-, and C-region genes exist in an unarranged configuration.
- B) Rearrangement of both TCR and Ig genes involves specific recombinase enzymes that bind to specific regions of the genome.
- C) Both Ig and TCR are able to switch C-region usage.
- D) Both Ig and TCR exhibit allelic exclusion.
- E) Both Ig and the TCR use combinatorial association of V, D, and J genes and junctional imprecision to generate diversity.
7. Which of the following statements is *incorrect* concerning antigen-specific receptors on both B and T cells?
- A) They are clonally distributed transmembrane molecules.
- B) They have extensive cytoplasmic domains that interact with intracellular molecules.
- C) They consist of polypeptides with variable and constant regions.
- D) They are associated with signal transduction molecules at the cell surface.
- E) They can interact with peptides derived from nonself antigens.
1. **B** Interaction of thymocytes with thymic stromal cells—cortical epithelial cells and interdigitating dendritic cells at the corticomedullary junction — is critical in T cell development.
2. **E** Negative selection removes developing T cells with potential reactivity to self-molecules.
3. **E** CD4⁺ CD8⁺ T cells form the majority of cells in the thymus.
4. **D** The genes of T cells that use $\alpha\beta$ as their receptor cannot further rearrange to use $\gamma\delta$ as their receptor; TCR δ gene segments are interspersed with the α locus and are deleted when the α locus rearranges.
5. **C** CD4 expressed on T cells binds to an invariant or nonpolymorphic region of all MHC class II molecules.
6. **C** The ability to change the heavy-chain constant region while retaining the same antigen specificity is a property unique to Ig. The other features are common to both the TCR and Ig.
7. **B** Both the TCR and Ig have short cytoplasmic tails. The signal transduction molecules associated with the antigen-binding chains interact with intracellular molecules.

1. The role of the antigen-presenting cell in the immune response is all of the following *except*
 - A) the limited catabolism of polypeptide antigens.
 - B) to allow selective association of MHC gene products and peptides.
 - C) to supply second signals required to fully activate T cells.
 - D) to present non-self peptides associated with MHC class II molecules to B cells.
 - E) to present peptide-MHC complexes to T cells with the appropriate receptor.
2. Which of the following statements about interleukin 2 (IL-2) is *incorrect*?
 - A) It is produced primarily by activated macrophages.
 - B) It is produced by CD4⁺ T cells.
 - C) It can induce the proliferation of CD4⁺ T cells.
 - D) It binds to a specific receptor on CD4⁺ T cells.
 - E) It can activate CD8⁺ T cells in the presence of antigen.
3. CD40 Ligand (CD154) is expressed by which of the following?
 - A) B cells
 - B) dendritic cells
 - C) resting T cells
 - D) activated T cells
 - E) all leukocytes
4. Which of the following statements about the activation of CD4⁺ cells is *incorrect*?
 - A) Binding of peptide + MHC to the TCR results in rapid phosphorylation of tyrosine residues in proteins associated with the TCR.
 - B) Intracellular calcium levels rise rapidly following activation.
 - C) Only peptide bound in the groove of MHC class II activates the CD4⁺ T cells.
 - D) Interaction of B7 and CD28 stabilizes IL-2 mRNA so effective IL-2 translation occurs.
 - E) The activated cell synthesizes IL-2 and a receptor for IL-
5. Which of the following statements about cytokines synthesized by CD4⁺ T_H1 and T_H2 subsets is *incorrect*?
 - A) Cytokines produced by T_H1 cells include IFN- γ and TNF- β .
 - B) Cytokines produced by T_H2 cells are important in allergic responses.
 - C) T_H1 cells secrete cytokines that induce macrophage and NK cell activation.
 - D) T_H2 cells secrete cytokines that activate CD8⁺ T cells.
 - E) T_H2 cell cytokines may inhibit the action of T_H1 cells.
6. Which of the following statements about CD8⁺ CTL is *incorrect*?
 - A) They lyse targets by synthesizing perforin and granzymes.
 - B) They cause target cell apoptosis.
 - C) They cannot kill CD4⁺ T cells.
 - D) They interact with their target through paired cell surface molecules.
 - E) They must be activated before exerting their cytotoxic function.
7. Infection with vaccinia virus results in the priming of virus-specific CD8⁺ T cells. If these vaccinia virus-specific CD8⁺ T cells are subsequently removed from the individual, which of the following cells will they kill *in vitro*?
 - A) vaccinia-infected cells expressing MHC class II molecules from any individual
 - B) influenza-infected cells expressing the same MHC class I molecules as the individual
 - C) uninfected cells expressing the same MHC class I molecules as the individual

- D) vaccinia-infected cells expressing the same MHC class I molecules as the individual
E) vaccinia-infected cells expressing the same MHC class II molecules as the individual
8. Bacterial lipopolysaccharide (LPS), a T-independent antigen, stimulates antibody production in mice. Which of the following is *incorrect*?
- A) The antibody produced will be predominantly IgM.
B) Memory B cells will not be induced.
C) IL-4 and IL-5 are required for the production of antibody during the response.
D) The polymeric nature of the antigen crosslinks B-cell surface receptors.
E) B cell activation involves phosphorylation of intracellular molecules.

Online Only Review Questions

9. When antigen binds to the T cell receptor, which of the following is involved in signal transduction?
- A) CD3
B) CD21
C) LFA-1 (CD11a/CD18)
D) Ig α /Ig β (CD79 α,β)
-

Case Study

Great effort is now being directed at developing vaccines for a variety of diseases. In one study, it was found that antibody to a particular epitope on a protein of the pathogens surface membrane was protective. The structure of this epitope was determined to be a peptide 10 amino acids in length. This peptide was synthesized and used to immunize individuals exposed to the pathogen. Disappointingly, no protection was seen. Can you suggest any reasons for this failure?

Answers to Review Questions

1. **D** The antigen-presenting cell does not present peptide + MHC class II to B cells. The other statements are all features of the antigen-presenting cell.
2. **A** IL-2 is produced almost exclusively by activated T cells.
3. **D** CD40 ligand (CD154) is expressed on the surface of the CD4 $+$ T cells as a consequence of the activation that follows the binding of peptide + MHC class II to the TCR.
4. **C** Agents other than peptides bound to MHC class II can activate CD4 $+$ T cells; these include superantigens, antigens presented by CD1, and polyclonal activators. 5DT $H1$ rather than T $H2$ cells secrete cytokines that activate CD8 $+$ T cells.
6. **C** A CD8 $+$ CTL can kill any cell expressing an MHC class I molecule in association with a non-self peptide, including, for example, a CD4 $+$ T cell infected with HIV.
7. **D** The principle of MHC restriction indicates that the TCR of CD8 $+$ T cells interacts with target cells that express specific peptide bound to self-MHC class I molecules. Thus, vaccinia-primed CD8 $+$ T cells recognize and hence kill only vaccinia-infected targets that express self MHC class I.

8. C T-independent antigens, because they do not generate T cell-derived cytokines, do not produce IL-4 or IL-5. Thus, no isotype switching or memory cell induction occurs in the response to T-independent antigens.

9. A The polypeptide chains of the CD3 complex are involved in signal transduction following peptide +MHC binding to the $\alpha + \beta$ chains of the T cell receptor. CD21 and Ig α /Ig β are signal transduction molecules associated with the B cell receptor for antigen and LFA-1 is an adhesion molecule.

Answer to Case Study

Several possibilities may be considered, such as size and complexity of the peptide, which are required for immunogenicity. The more likely failure, however, was that the response to the pathogen's membrane protein was almost certainly a thymus-dependent response. Therefore, immunization with the epitope seen by the B cells would not work unless epitopes seen by helper T cells were also present.

Attempts at producing synthetic vaccines are now directed toward incorporating the B cell-specific epitopes in carriers containing adequate helper T epitopes that will induce both help and memory responses. This would provide a better possibility for protection following exposure to the pathogen.

1. An individual does not make an immune response to a self-protein because
 - A) self-proteins cannot be processed into peptides.
 - B) peptides from self-proteins cannot bind to MHC class I.
 - C) peptides from self-proteins cannot bind to MHC class II.
 - D) lymphocytes that express a receptor reactive to a self-protein are inactivated by deletion or anergy.
 - E) developing lymphocytes cannot rearrange V genes required to produce a receptor for self-proteins.
2. Which of the following statements is *incorrect*?
 - A) Interaction of Fas and FasL can lead to apoptosis.
 - B) Both Fas and Fas L can be expressed on activated T cells.
 - C) Both Fas and Fas L can be expressed on B cells.
 - D) Cells in immunologically privileged sites can express FasL.
 - E) Fas—FasL-mediated apoptosis prevents uncontrolled T-cell clone growth.
3. Which of the following is *incorrect* concerning immune tolerance?
 - A) Tolerance induction is antigen-specific.
 - B) Tolerance results from inactivation and/or elimination of B and/or T cells.
 - C) Tolerance can be induced in both young and old individuals.
 - D) Immature neutrophils are more susceptible to tolerance than mature neutrophils.
 - E) The breakdown of tolerance can result in autoimmunity.

4. Which of the following statements is *incorrect* concerning the immune response to antigens?
- A) Reactivity is influenced by extremes of age.
 - B) Greater immune responses are produced when antigen is given with adjuvant.
 - C) Impaired nutrition depresses immunity.
 - D) The presence of preexisting antibody does not affect the subsequent response to antigen.
 - E) Different protein antigens stimulate different levels of antibody production.
5. All of the following procedures would be likely to induce tolerance to a protein antigen *except*
- A) intramuscular injection of the antigen in adjuvant.
 - B) intravenous injection of deaggregated protein.
 - C) injection of cyclosporine with the antigen.
 - D) injection of antigen at a stage in development before mature lymphocytes appear.
 - E) intravenous injection of small amounts of antigen.
6. When a tolerogenic injection of a protein antigen is given experimentally, it can be shown that
- A) B-cell tolerance is more rapidly induced than T-cell tolerance.
 - B) B-cell tolerance is lost as new B cells come from the bone marrow.
 - C) B-cell tolerance can be induced only when low doses are used.
 - D) T-cell tolerance can be induced only when high doses are used.
 - E) T-cell tolerance is shorter lasting than B-cell tolerance.
7. Blocking any of the following processes can result in peripheral tolerance in mature T cells *except*
- A) the interaction of costimulatory molecules on T cells with their ligands on APC.
 - B) intracellular signal transduction mechanisms.
 - C) negative selection of thymocytes.
 - D) activation of the IL-2 gene.
 - E) the binding of antigen with MHC molecules.

Online Only Review Questions

8. An individual with a defect in CTLA-4 (CD152) will be most likely to have which of the following?
- A) Type I hypersensitivity
 - B) immunodeficiency
 - C) recurrent Neisseria infections
 - D) lymphoproliferative disease

Answers to Review Questions

- 1. D** Negative selection generally ensures that a lymphocyte expressing a receptor reactive to a self-protein is inactivated by deletion or anergy.
- 2. C** B cells express Fas but not FasL.
- 3. D** Tolerance can be induced only in lymphocytes that express an antigen-specific receptor.
- 4. D** Preexisting antibody may exert a negative feedback on the subsequent response to antigen.
- 5. A** Injection into muscle and in the presence of adjuvant are likely ways to induce activate rather than tolerate the immune response. The remaining procedures generally induce tolerance. The use of cyclosporine in blocking transplantation rejection is discussed further in Chapter 19.

6. B T-cell tolerance is more rapidly achieved, occurs with lower doses, and lasts longer than B-cell tolerance. As new B cells are produced by the bone marrow, tolerance in this compartment wanes. T-cell tolerance, by contrast, persists because the thymus of an adult no longer actively produces new T cells.

7. C Interfering with negative selection of thymocytes disrupts central rather than peripheral T cell tolerance.

8. D CTLA-4, a T-cell surface molecule closely related to CD28, transmits a negative signal to activated T cells, shutting off IL-2 production. Defects in this signaling could lead to a general lymphoproliferative disorder.

1. Which of the following statements regarding the functional properties of cytokines is *false*?
 - A) They typically have pleiotropic properties.
 - B) They often exhibit functional redundancy.
 - C) They often display antigen specificity.
 - D) They exhibit synergistic or antagonistic properties.
 - E) They assist in the regulation and development of immune effector cells.
2. When IL-2 is secreted by antigen-specific T cells activated due to presentation of antigen by APCs, what happens to naive antigen-nonspecific T cells in the vicinity?
 - A) They proliferate due to their exposure to IL-
 - B) They often undergo apoptosis.
 - C) They begin to express IL-2 receptors.
 - D) They secrete cytokines associated with their T_H phenotype.
 - E) Nothing happens.
3. Which of the following cytokines have receptors that exhibit structural similarity that helps to account for their functional redundancy?
 - A) IL-3, IL-15, and GM-CSF
 - B) IL-1, IL-2, and M-CSF
 - C) IL-2, IL-3, and IL-8
 - D) IL-3, TNF- β , and RANTES
 - E) IL-3, IL-4, and IFN- γ

4. What type of immune response is *not* mediated by the T_H subset?
 - A) responses to viral infections
 - B) delayed-type hypersensitivity
 - C) activation of cytotoxic T cells
 - D) activation of IgE synthesis
 - E) responses to intracellular pathogens
5. IL-1, IL-6, and TNF- α are proinflammatory cytokines that are known to
 - A) cause increased vascular permeability.
 - B) act in concert with chemokines to promote migration of inflammatory cells to sites of infection.
 - C) initiate acute-phase responses.
 - D) have endogenous pyrogen properties.
 - E) All of the above.
6. Which of the following cytokines plays a role in terminating inflammatory responses?
 - A) IL-2
 - B) IL-4
 - C) TGF- β
 - D) IFN- α
 - E) IL-3
7. All of the following are induced by the chemokine IL-8 except
 - A) activation of neutrophils.
 - B) attraction of neutrophils to sites of tissue damage.
 - C) wound healing.
 - D) extravasation of neutrophils.
 - E) reduction of cytokine production by T_H cells.
8. Superantigens cause a burst of cytokine production by T cells due to their ability to
 - A) crosslink the V β segments of T cell receptors with class II MHC molecules on APCs.
 - B) crosslink the V α segments of T cell receptors with class II MHC molecules on APCs.
 - C) crosslink T cell receptors and CD
 - D) crosslink multiple cytokine receptors on a large population of T cells.
 - E) crosslink CD

Case Study

A 7-year-old boy with an infected wound on his leg is admitted to the emergency department. His mother states that a high fever with diarrhea occurred during the last 12 hours. Within the last 2 hours he had become very lethargic, was unable to stand, and was very disoriented. The attending physician observes that his blood pressure is dangerously low and suspects that the boy is suffering from bacterial septic shock caused by the wound infection. Discuss the etiology of bacterial septic shock as well as the role of cytokines in the pathogenesis of this disease. Speculate on future therapeutic strategies that might be employed by using monoclonal antibodies or other biologic agents to treat this disease.

Answers to Review Questions

1. C Cytokines secreted by a single lymphocyte following antigen-specific activation do not exhibit antigen specificity. Instead, they regulate the activities of other cells involved in an immune response by binding to cytokine receptors expressed by these cells.

- 2. E** Since these cells have not been activated by antigen, they do not express the high affinity IL-2 receptor. Hence they remain quiescent.
- 3. A** The receptors for IL-3, IL-5, and GM-CSF contain the common γ chain, which is responsible for signal transduction. Therefore, cytokine binding to each of these receptors probably induces a similar activation signal.
- 4. D** The T_H subset is responsible for classical cell-mediated functions (answers A, B, C, and E). Synthesis of IgE is mediated by cytokines produced by $T_{cf15Hcf12}$ cells.
- 5. E** The answer is self-explanatory.
- 6. C** Among the cytokines listed, TGF- β plays a role in terminating inflammatory responses by promoting the accumulation and proliferation of fibroblasts and the deposition of extracellular matrix proteins required for tissue repair.
- 7. E** IL-8 chemotactically attracts and activates neutrophils and induces their adherence to vascular endothelium. Thus, IL-8 also plays an important role in wound healing. It also promotes their extravasation into tissues. It plays no role in regulation of cytokine production by T_H cells—a biologic property ascribed to IL-10 produced by $T_{cf15Hcf12}$ cells.
- 8. A** Superantigens bind simultaneously to class II MHC molecules and to the $V\beta$ domain of the T cell receptor activating all T cells bearing a particular $V\beta$ domain. Thus, they activate large numbers of T cells (between 5;pc and 25;pc), regardless of their antigen specificity causing them to release harmful quantities of cytokines.

Answer to Case Study Bacterial septic shock is a condition that can develop within a few hours following infection by certain gram-negative bacteria, including *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Enterobacter aerogenes*, and *Neisseria meningitidis*. The symptoms are often fatal and include a drop in blood pressure, fever, diarrhea, and widespread blood clotting in various organs. It develops when bacterial cell wall endotoxins stimulate macrophages to overproduce IL-1 and TNF- α . Therapeutic strategies using monoclonal antibodies capable of neutralizing the effects of IL-1 and TNF-

ορ ανταγονιστος συχη ασ IL-1 ρεξεπτορ ανταγονιστ (IL-1R α) μαψ οφφερ ηοπε φορ τηε τρεατμεντ οφ βαχ τεριαλ σεπτιχ σηοχκ ιν ηυμανσ.

1. A patient is admitted with multiple bacterial infections and is found to have a complete absence of C. Which complement-mediated function would remain intact in such a patient?

 - A) lysis of bacteria
 - B) opsonization of bacteria
 - C) generation of anaphylatoxins
 - D) generation of neutrophil chemotactic factors
 - E) None of the above.
2. Which of the following screening tests would be most useful for confirming a presumptive diagnosis of a congenital absence of a complement component?

 - A) quantitation of serum opsonic activity
 - B) quantitation of serum hemolytic activity
 - C) quantitation of C3 content of serum
 - D) quantitation of C1 content of serum
 - E) electrophoretic analysis of patient's serum
3. Complement is required for

 - A) lysis of erythrocytes by lecithinase.
 - B) NK-mediated lysis of tumor cells.
 - C) phagocytosis.
 - D) bacteriolysis by specific antibodies.
 - E) All of the above.
4. Which of the following is associated with the development of systemic lupus erythematosus (SLE)?

 - A) deficiencies in C1, C4, or C2
 - B) deficiencies in C5, C6, or C7
 - C) deficiencies in the late components of complement
 - D) increases in the serum C3 level
 - E) increases in the levels of C1, C4, or C2
5. Active fragments of C5 can lead to the following, except

 - A) contraction of smooth muscle.
 - B) vasodilation.
 - C) attraction of leukocytes.
 - D) attachment of lymphocytes to macrophages.
 - E) All of the above.
6. The alternative pathway of complement activation is characterized by the functions listed below, except

 - A) activation of complement components beyond C3 in the cascade.
 - B) participation of properdin.

- C) generation of anaphylatoxin.
D) use of C
7. Decay-accelerating factor (DAF) regulates the complement system to prevent complement-mediated lysis of cells. This involves
- A) dissociation of C4b2a or the C3bBb enzyme complex.
B) blocking the binding of C3 convertase to the surface of bacterial cells.
C) inhibiting the membrane attack complex from binding to bacterial membranes.
D) acting as a cofactor for the cleavage of C3b.
E) causing dissociation of C5 convertase.
8. The following activate(s) the alternative pathway of complement:
- A) lipopolysaccharides
B) some viruses and virus-infected cells
C) fungal and yeast cell walls (zymosin)
D) many strains of gram-positive bacteria
E) all of the above.
9. Which component(s) of complement could be missing and still leave the remainder of the complement system capable of activation by the alternative pathway?
- A) C1, C2, and C3
B) C3 only
C) C2, C3, and C4
D) C1, C2, and C4
E) C1, C3, and C4
10. An antigen—antibody immune complex in a C3-deficient individual will still result in
- A) anaphylatoxin production.
B) depression of factor B.
C) production of chemotactic factors.
D) activation of C
E) activation of C5.

Answers to Review Questions

- 1. E** All these functions are mediated by complement components that come after C3 and in its absence cannot be activated.
- 2. B** The hemolytic assay would reveal a defect in any one of the complement components, since all are required to effect hemolysis. The tests for specific components are likely to work only if you happen to pick the right one. They are not useful for screening. Electrophoretic analysis is good for the major serum components (albumin and globulin) but unlikely to give information on many of the complement components.
- 3. D** Complement is required for lysis of bacteria by specific anti-bacteria IgM or IgG. Complement is not required for phagocytosis or lysis of erythrocytes by lecithinase. However, the C3b opsonins, that are generated during complement activation, enhance phagocytosis of the opsonized particle. Although some tumor cells can initiate the alternate pathway of complement activation, complement plays no role in NK-mediated lysis of these cells.
- 4. A** Inherited homozygous deficiency of the early proteins of the classical complement pathway (C1, C4, or C2) are strongly associated with the development of systemic lupus erythematosus (SLE). Such deficiencies probably result in abnormal processing of immune complexes in the absence of a functional classical pathway of complement fixation. Serum levels of C3 or C4 decrease in SLE due to the large

number of immune complexes that bind to them. Deficiencies in the late components are associated with recurrent infections with pyogenic organisms.

5. D C5a is an anaphylatoxin, which induces degranulation of mast cells, resulting in the release of histamine, causing vasodilation and contraction of smooth muscles. C5a is also a chemotaxin, attracting leukocytes to the area of its release where the antigen is reacting with antibodies and activates the complement system. It does not promote the attachment of lymphocytes to macrophages.

6. D The alternative pathway of complement activation connects with the classical pathway at the activation of C. Thus, it does not require C1, C4, or C. Properdin is essential for the activation through the alternative pathway, since it stabilizes the complex (C3bBb) formed between C3b and activated serum factor B, which acts as a C3 convertase and activates C. During the activation of the alternative pathway both C3a and C5a are generated; both are anaphylatoxins and cause degranulation of mast cells.

7. A As a cell surface regulator of complement activation, DAF destabilizes both the alternate and classical pathway C3 convertases (C4b2a or C3bBb). Like the other regulators of complement activation (RC

A), including CR1, factor H, and C4bBP, these proteins accelerate decay (dissociation) of C3 convertase, releasing the component with enzymatic activity (C2a or Bb) from the component bound to the cell membrane (C4b or C3b).

8. E Each of the pathogens and particles of microbial origin listed can initiate the alternate pathway of complement activation. Parasites (e.g., trypanosomes) and teichoic acid from gram-positive cell walls can also activate complement using this pathway.

9. D C3 is required for the alternative pathway of complement activation, while C1, C2, or C4 are not required.

10. D The immune complex will activate C2 (and C4) but will not activate C3 or any other components. Since the alternative pathway of complement activation also requires C3, this pathway will not be activated. Anaphylatoxins and chemotactic factor generation require C3, while the synthesis of factor B is not related to C

1. The usual sequence of events in an allergic reaction is as follows:

- A) The allergen combines with circulating IgE, and then the IgE:allergen complex binds to mast cells.
- B) The allergen binds to IgE fixed to mast cells.
- C) The allergen is processed by antigen-presenting cells and then binds to histamine receptors.
- D) The allergen is processed by antigen-presenting cells and then binds to mast cells.
- E) The allergen combines with IgG.

2. Epinephrine

- A) causes bronchodilation.
- B) is effective even after anaphylactic symptoms commence.
- C) relaxes smooth muscle.
- D) decreases vascular permeability.
- E) All of the above.

3. A human volunteer agrees to be passively sensitized with IgE specific for a ragweed antigen (allergen). When challenged with the allergen intradermally, he displayed a typical skin reaction due to an immediate hypersensitivity reaction. If the injection with sensitizing IgE was preceded

by an injection (at the same site) of Fc fragments of human IgE followed by intradermal injection with allergen, which of the following outcomes would you predict?

- A) No reaction would occur because the Fc fragments would interact with the allergen and prevent it from gaining access to the sensitized mast cells.
 - B) No reaction would occur because the Fc fragments would interact with the IgE antibodies making their antigen-binding sites unavailable for binding to antigen.
 - C) No reaction would occur because the Fc fragments would interact with Fc ϵ receptors on mast cells.
 - D) The reaction would be exacerbated due to the increased local concentration of IgE Fc fragments.
 - E) The reaction would be exacerbated due to the activation of complement.
4. The following mechanism(s) may be involved in the clinical efficacy of desensitization therapy to treat patients with allergies to known allergens:
- A) enhanced production of IgG, which binds allergen before it reaches mast cells
 - B) skewing of T cell responses from T $H2$ to T $H1$
 - C) decreased sensitivity of mast cells and basophils to degranulation by allergen
 - D) decreased production of IgE antibody
 - E) All of the above.
5. Immediate hypersensitivity skin reactions
- A) usually occur within 24 hours.
 - B) exhibit a raised wheal due to infiltration by mononuclear cells.
 - C) exhibit a red flare due to vasodilation.
 - D) cannot be elicited by monovalent haptens.
 - E) All are correct.
6. Mast cells
- A) are found circulating in the blood.
 - B) release their granules following lysis.
 - C) are basophilic after complete degranulation.
 - D) are very similar to basophils.
 - E) All are correct.
7. Antihistamines
- A) bind to receptors for histamine, thereby preventing the histamine from exerting a pharmacologic effect.
 - B) are more effective given before, rather than after, the onset of allergic symptoms.
 - C) do not influence the activity of leukotrienes.
 - D) do not affect binding of IgE to mast cells.
 - E) All are correct.
8. In the RAST assay for ragweed pollen
- A) the patient's serum is first mixed with a radiolabeled anti-IgE.
 - B) only IgE anti-ragweed antibodies are detected.
 - C) the patient's serum competitively inhibits binding of the anti-IgE.
 - D) monovalent IgE is used.
 - E) complement is utilized.
9. Which of the following statements is *false*?
- A) IL-4 and IL-13 produced by T cf15Hcf12 cells play a key role in regulating IgE responses.
 - B) Interferon- γ produced by T cf15H cf11 cells can downregulate IgE responses.
 - C) In normal individuals, a balance between Tcf15Hcf11-derived and T cf15Hcf12-derived cytokines helps to maintain normal levels of IgE.
 - D) IL-4 levels are higher in atopic patients.

- E) In IL-4 knockout mice, IgE production is normal following their exposure to parasites due to the regulatory activity of IL-1
10. Anaphylactic reactions
- A) evolve in minutes and abate within 30 minutes.
 - B) may be followed by inflammatory sequelae hours later.
 - C) are the consequences of released pharmacologic agents.
 - D) may involve components of mast-cell granule matrix.
 - E) All of the above.

Online Only Review Questions

11. Michelle is allergic to ragweed pollen. To reduce her allergic response, she has been treated with minute concentrations of ragweed pollen allergen followed by repeated and gradually increasing doses (desensitization or hyposensitization therapy). If this treatment is successful, which of the following is most likely to have occurred?
- A) clearance of antigen-specific IgE immune complexes
 - B) greater production of circulating high affinity IgG antibody
 - C) depletion of the mast cell pool by repeated degranulation
 - D) specific tolerance induction
-

Case Study

While playing tennis on a warm day, a young man felt a wasp on his arm and brushed it off, but still received a mild sting, which he ignored. Ten minutes later he felt dizzy and began to itch under his arms and on his scalp. When he broke out in hives and felt a tightness in his chest, he headed for the hospital. On the way he felt cold and clammy and collapsed on the seat of the taxi. In the emergency unit his pulse was barely detectable. What happened, and why?

Answers To Review Questions

- 1. B** Allergic (also known as atopic) individuals have already made IgE responses to specific allergens. IgE binds passively to cells expressing high-affinity Fc receptors for IgE (e.g., mast cells) and interacts with the allergen when present. This results in crosslinking of the high-affinity Fc ϵ R, resulting in mast-cell degranulation. The allergen does not need to be processed by APCs in order to bind to IgE.
- 2. E** All are effects of epinephrine and make it useful for treatment of acute anaphylactic symptoms.
- 3. C** Since the IgE Fc fragments would bind to the high-affinity Fc ϵ R expressed on the surface of mast cells, the allergen-specific IgE would not have access to these receptors and therefore would not bind to these cells. When the allergen is introduced intradermally, while it would bind to the allergen-specific IgE at the site, this would not result in crosslinking of Fc ϵ R, which are saturated with soluble IgE Fc fragments. Hence no immediate hypersensitivity reaction would take place.
- 4. E** All are considered to be involved to varying degrees in injection therapy.
- 5. E** All are correct statements.

6. D Mast cells release granules physiologically and not by lysing, they are basophilic before but not after they degranulate, and they are not found circulating freely. Mast cells are similar to circulating basophils.

7. E All are correct statements.

8. B The RAST assay measures IgE antibody that is allowed to bind to allergen coupled to an insoluble matrix. It detects IgE anti-ragweed antibodies. It does not utilize monovalent IgE, and complement is not utilized in the test.

9. E IL-4 knockout mice do not make IgE responses when challenged with parasites, such as *Nippostrongylus brasiliensis*. This finding is consistent with the fact that IL-4 plays a key role in the regulation of IgE responses by B cells.

10. E All are true. A and C are true of the classic ``wheal and flare'' type response, while B and D describe features of the ``late-phase'' response, which is a complication of some anaphylactic reactions.

11. B Successful hyposensitization is generally associated with increase in serum levels of allergen-specific IgG. This may bind to the allergen in the circulation and prevent it from reacting with mast-cell bound IgE.

Answer to Case Study

This is a classic case of systemic anaphylaxis. In the emergency room epinephrine was promptly administered and the symptoms due to vascular permeability (hives, low blood pressure) and smooth muscle constriction (difficulty in breathing) were reversed. When he revived sufficiently, he revealed that he had been stung by similar-looking insects in the past, the last time 3 months ago, but without any noticeable effects. These stings were apparently the priming injections building up sufficient levels of IgE antibody to sensitize his mast cells. Thus the last sting, despite the fact that little venom was injected, was sufficient to precipitate a systemic reaction. A careful skin test, involving intradermal injection of very dilute wasp venom, should show an immediate ``wheal and flare'' response, confirming the existence of sensitivity. The young man should be advised to (1) avoid wasps, (2) carry an emergency vial of injectable epinephrine, and (3) undergo desensitization therapy aimed at hyposensitization to the wasp venom antigen.

1. Which of the following clinical diseases is most likely to involve a reaction to a hapten in its etiology?
 - A) Goodpasture's syndrome
 - B) hemolytic anemia after treatment with penicillin
 - C) rheumatoid arthritis
 - D) farmer's lung
 - E) Arthus reaction
2. An IgA antibody to a red blood cell antigen is unlikely to cause autoimmune hemolytic anemia because
 - A) it would be made only in the gastrointestinal tract.
 - B) its Fc region would not bind receptors for Fc on phagocytic cells.
 - C) it can fix complement only as far as C1, C4, C
 - D) it has a too-low affinity.
 - E) it requires secretory component to work.
3. The glomerular lesions in immune complex disease can be visualized microscopically with a fluorescent antibody against
 - A) IgG heavy chains.
 - B) κ light chains.
 - C) C
 - D) C
 - E) All of the above.
4. The lesions in immune complex-induced glomerulonephritis
 - A) are dependent on erythrocytes and complement.
 - B) result in increased production of urine.
 - C) require both complement and neutrophils.
 - D) are dependent on the presence of macrophages.
 - E) require all nine components of complement.
5. Serum sickness occurs only
 - A) when anti-basement membrane antibodies are present.
 - B) in cases of extreme excess of antibody.
 - C) when IgE antibody is produced.
 - D) when soluble immune complexes are formed.
 - E) in the absence of neutrophils.

6. Immune complexes are involved in the pathogenesis of
- A) poststreptococcal glomerulonephritis.
 - B) pigeon breeder's disease.
 - C) serum sickness.
 - D) an edematous hemorrhagic reaction in the skin of a beekeeper, 2 hours after he was stung for the 20th time.
 - E) All of the above.
7. The Arthus reaction and farmer's lung differ because
- A) only the former is due to antigen —antibody complexes.
 - B) the mode of contact with the antigen is different.
 - C) only the former requires complement.
 - D) only the latter can occur in farmers.
 - E) the reactions in farmer's lung are much more rapid.
8. The final damage to vessels in immune complex-mediated arthritis is due to
- A) cytokines produced by T cells.
 - B) histamine and SRS-A.
 - C) the C5, C6, C7, C8, C9 membrane attack complex.
 - D) lysosomal enzymes of polymorphonuclear leukocytes.
 - E) cytotoxic T cells.
9. Serum sickness is characterized by
- A) deposition of immune complexes in blood vessel walls when there is a moderate excess of antigen.
 - B) phagocytosis of complexes by granulocytes.
 - C) consumption of complement.
 - D) appearance of symptoms before free antibody can be detected in the circulation.
 - E) All of the above.
10. Type II hypersensitivity
- A) is antibody-independent.
 - B) is complement-independent.
 - C) is mediated by CD8⁺ T cells.
 - D) requires immune complex formation.
 - E) involves antibody-mediated destruction of cells.
11. A patient is suspected of having farmer's lung. A provocation test involving the inhalation of an extract of moldy hay is performed. A sharp drop in respiratory function is noted within 10 minutes and returns to normal in 2 hours, only to fall again in another 2 hours. The most likely explanation is that
- A) the patient has existing T cell-mediated hypersensitivity.
 - B) this is a normal pattern for farmer's lung.
 - C) the patient developed a secondary response after the inhalation of antigen.
 - D) the symptoms of farmer's lung are complicated by an IgE-mediated reactivity to the same antigen.
 - E) All of the above.
-

Case Study

A technician in a snake venom-producing farm got careless one day and was bitten by a rare lethal Egyptian cobra. He was rushed to the emergency department, and a call went out immediately for

antivenom serum. Fortunately some was located, and within 5 hours he was given 15 ml intravenously. The next day he received another 10 ml, the last available. Within days he was well on the way to recovery and left the hospital a week later. He returned 10 days after leaving the hospital complaining of joint pain, fever, and recurrent itchy hives on his trunk, arms, and legs. What do you suspect is happening, and how would you confirm it?

Answers to Review Questions

- 1. B** Penicillin can function as a hapten, binding to red blood cells and inducing a hemolytic anemia. A, C, and D are examples of immune aggregate (type III) reactions requiring complement and neutrophils for pathologic effects.
- 2. B** Since phagocytic cells have Fc receptors for IgG, bound IgA would not cause engulfment and damage. Thus, A, C, D, and E are false.
- 3. E** The lesions in immune complex disease are dependent on the presence of antigen, antibody, and complement. Hence all can be demonstrated by immunofluorescence at a lesion: A and B, because they are parts of IgG; C and D, because they are the early components of complement activated by the immune aggregated.
- 4. C** Damage by immune complexes requires complement components to attract neutrophils, which are the agents responsible for subsequent tissue damage. Lysis by the final sequence of C6, C7, C8, and C9 is not required.
- 5. D** Anti-basement membrane antibodies may produce damage but can be distinguished from serum sickness lesions by their ribbonlike appearance compared to the lumpy-bumpy appearance of serum sickness lesions. Excess of antibody would clear antigen rapidly with few lesions. IgE antibody is responsible for anaphylactic reactions and neutrophils are required for the lesions typical of serum sickness.
- 6. E** All are examples of type III hypersensitivity reactions: A, by production of antibody, which reacts with normal kidney antigen; B, by inhalation of antigens from pigeon droppings; C, serum sickness is a classical example of an immune complex disease; and D is a description of an Arthus reaction in someone who has been immunized by repeated injection of bee venom.
- 7. B** Both the Arthus reaction and farmer's lung are examples of immune aggregate reactions that require complement and neutrophils. The former involves antigen injected into the skin; the latter involves inhaled antigen.
- 8. D** Neither T cells nor mast cells are responsible for the final tissue damage in immune complex disease. Therefore A, B, and E are eliminated. The final lytic complex of complement is similarly not involved, since complement activation up to C5 is sufficient to bring in the polymorphonuclear leukocytes, whose lysosomal enzymes cause the tissue damage.
- 9. E** All are characteristics of serum sickness.
- 10. E** Type II hypersensitivity reactions occur following development of antibodies against target antigens expressed on normal cells or cells with altered membrane determinants. Antibodies bind to the surface of these cells and mediate damage or destruction by one or more mechanisms, including complement-mediated reactions. CD8⁺ cytotoxic T cells and immune complexes are not involved in these reactions.

11. D The type III response in farmer's lung and similar occupational diseases has an onset of symptoms usually several hours after exposure. The appearance of breathing difficulties within minutes would create a strong suspicion that a type I anaphylactic response is also present. Presumably the patient made both IgE and IgG antibodies to the actinomycete antigens. A positive wheal and flare reaction on skin testing would provide further confirmation.

Answer to Case Study

Most antivenoms of exotic species such as snake, spider, and scorpion would be made in horses. The horse antiserum neutralized the toxin and saved the patient's life. However, being a foreign protein, it induced an immune response with resultant formation of antigen —antibody complexes and the symptoms of type III hypersensitivity, serum sickness. The localization of these complexes in joints and the activation of complement to give anaphylatoxins were responsible for the joint pain, hives, and itching he experienced. It is possible that he could subsequently develop symptoms of glomerulonephritis as well. Treatment would consist of corticosteroid administration for its general antiinflammatory effects. Confirmatory studies of your diagnosis might include looking for depressed levels of serum C3 and C4 as a result of activation in tissue by the antigen —antibody aggregates. In the convalescent stage one might also find antibody to horse Ig as a final definitive proof of your diagnosis.

1. Which of the following does not involve cell-mediated immunity?
 - A) contact sensitivity to lipstick
 - B) rejection of a liver graft
 - C) serum sickness
 - D) tuberculin reaction
 - E) immunity to chicken pox
2. A positive delayed-type hypersensitivity skin reaction involves the interaction of
 - A) antigen, complement, and cytokines.
 - B) antigen, antigen-sensitive lymphocytes, and macrophages.
 - C) antigen —antibody complexes, complement, and neutrophils.
 - D) IgE antibody, antigen, and mast cells.
 - E) antigen, macrophages, and complement.
3. Cell-mediated immune responses are
 - A) enhanced by depletion of complement.
 - B) suppressed by cortisone.
 - C) enhanced by depletion of T cells.
 - D) suppressed by antihistamine.
 - E) enhanced by depletion of macrophages.
4. Delayed skin reactions to an intradermal injection of antigen may be markedly decreased by
 - A) exposure to a high dose of X-irradiation.
 - B) treatment with antihistamines.
 - C) treatment with an antineutrophil serum.
 - D) removal of the spleen.
 - E) decreasing levels of complement.
5. Patients with DiGeorge syndrome who survive beyond infancy would be capable of
 - A) rejecting a bone marrow transplant.
 - B) mounting a delayed-type hypersensitivity response to dinitrochlorobenzene.
 - C) resisting intracellular parasites.
 - D) forming antibody to T-dependent antigens.
 - E) All of the above.
 - F) None of the above.
6. Which of the following statements is characteristic of contact sensitivity?
 - A) The best therapy is oral administration of the antigen.
 - B) Patch testing with the allergen is useless for diagnosis.
 - C) Sensitization can be passively transferred with serum from an allergic individual.
 - D) Some chemicals acting as haptens induce sensitivity by covalently binding to host proteins

- acting as carriers.
- E) Antihistamines constitute the treatment of choice.
7. Positive skin tests for delayed-type hypersensitivity to intradermally injected antigens indicate that
- A) a humoral immune response has occurred.
 - B) a cell-mediated immune response has occurred.
 - C) both T cell and B cell systems are functional.
 - D) the individual has previously made IgE responses to the antigen.
 - E) immune complexes have been formed at the injection site.
8. T cell-mediated immune responses can result in
- A) formation of granulomas.
 - B) induration at the reaction site.
 - C) rejection of a heart transplant.
 - D) eczema of the skin in the area of prolonged contact with a rubberized undergarment.
 - E) All of the above.

Online Only Review Questions

9. A lymph node biopsy shows multiple necrotizing ("caseous") granulomas. A culture of material obtained at the time of biopsy grows *Mycobacterium tuberculosis*. Which substance produced locally is the principal activator or stimulator of the granuloma macrophages?
- A) bradykinin
 - B) interferon- λ
 - C) leukotriene B4
 - D) prostaglandin E2
 - E) the complement trimolecular complex (C567)

Case Study

As a member of an anthropologic research team, you have occasion to visit a primitive tribe in the remote reaches of the Amazon jungle. During your visit the natives conduct a ceremony celebrating the rites of passage for young males. This consists, among other things, of covering their bodies with elaborate patterns of stripes and circles using a variety of colors extracted from local plants. On your return 3 weeks later you are asked to look at a young male who has developed alarmingly itchy and weepy red areas of skin that run in sharply demarcated stripes across his back and on one arm. Remembering your introductory course in immunology, you make an educated guess as to the cause. How, under such primitive conditions, could you confirm your diagnosis?

Answers to Review Questions

- 1. C** Serum sickness is an example of those reactions mediated by an antibody—antigen complex that involves components of the complement system and neutrophils. All others involve cell-mediated immunity to a significant extent.
- 2. B** Cell-mediated reactions result from the triggering of T cells by antigen with recruitment of macrophages. Neither antibody, complement, nor mast cells plays a role in this process, although they do play a role in immediate hypersensitivity responses.

3. B Cortisone has a general antiinflammatory effect and is also lytic for some T cells. Complement plays no role, and antihistamines have little effect on this type of response. Depletion of T cells or macrophages would suppress, not enhance, this type of response, since the response is dependent on these cells.

4. A High doses of X-irradiation will destroy T cells, which are responsible for initiating the response. Histamine, neutrophils, spleen, and complement do not play a role, and any treatment that affects them would not affect a DTH response.

5. F Patients with DiGeorge syndrome have a congenital thymic aplasia and lack all T cell functions. Since A, B, and C are all aspects of a cell-mediated immune response, they would be absent. Additionally, formation of antibody against these antigens is dependent on helper T cells and therefore would not occur in these patients.

6. D Patch testing consists of application of the offending allergen under an occlusive dressing, and a positive DTH response after 24–48 hours is considered evidence of sensitivity; thus B is wrong. The allergens involved are those capable of penetrating skin and binding to host carrier proteins; thus D is correct. Oral ingestion of antigen, which, in certain experimental situations, was shown to induce suppression after subsequent induction of contact sensitivity, has not yet been shown to be an effective therapeutic maneuver in humans; thus A is wrong. Corticosteroids, not antihistamines, constitute the treatment of choice for contact sensitivity; thus E is also incorrect.. Passive transfer of cell-mediated immune responses is accomplished with T cells, not with serum, thus C is wrong.

7.B A delayed-type hypersensitivity reaction, evidenced by erythema and induration within 24—72 hours of antigen injection, indicates that a cell-mediated reaction has occurred. Such reactions do not involve antibody produced by B cells, thus A, C, D, and E are incorrect.

8. E All of these effects are manifestations of cell-mediated immunity. Induration usually takes place at the reaction site. Formation of granulomas is characteristic of a chronic DTH reaction. Rejection of the heart is an example of an allograft response. Some of the chemicals used to cure rubber can induce contact sensitivity after prolonged exposure of the skin to them.

9. B Interferon- λ produced by CD4+ TH1cells is one of the main activators of monocytes and macrophages that participate in this classic delayed type hypersensitivity response.

Answer to Case Study

The appearance of the skin lesion and its sharp demarcations and weepy, itchy nature all suggest contact sensitivity. One of the dyes used to paint the body is most likely the sensitizer and, since it persisted on the skin, was also able to provoke a T cell-mediated reaction after the initial expansion of the specific clones. In the absence of sophisticated testing equipment, a simple patch test using samples of the various dyes applied to healthy areas of skin should show a localized contact reaction 24—48 hours later at the site to which the causative dye was applied. (In the laboratory one might also look for an in vitro proliferative response of the patients peripheral blood lymphocytes to added dye. A biopsy of the lesion should reveal an intense infiltrate of mononuclear cells.)