Chapter 19
Disorders Associated with the Immune System

Hypersensitivity

19-1 Define hypersensitivity.
19-2 Describe the mechanism of anaphylaxis.
19-3 Compare and contrast systemic and localized anaphylaxis.
19-4 Explain how allergy skin tests work.
19-5 Define desensitization and blocking antibody.

Hypersensitivity Reactions
Response to antigens (allergens) leading to damage
Types of reactions
- Anaphylactic
- Cytotoxic
- Immune complex
- Delayed cell-mediated

Types of Hypersensitivity

Type I (Anaphylactic) Reactions
- IgE attached to mast cells and basophils
- Antigen binds to two adjacent IgE
- Mast cells and basophils undergo degranulation, which releases mediators:
  - Histamine
  - Leukotrienes
  - Prostaglandins
9 Type I (Anaphylactic) Reactions
- Systemic anaphylaxis
  - May result in circulatory collapse and death
- Localized anaphylaxis
  - Hives, hay fever, and asthma

12 Preventing Anaphylactic Reactions
- Desensitizing injections of antigen
- Cause production of IgG, so that IgG antibodies will act as blocking antibodies

13 Are all immune responses beneficial? 19-1
- In what tissues do we find the mast cells that are major contributors to allergic reactions such as hay fever? 19-2
- Which is the more dangerous to life: systemic or localized anaphylaxis? 19-3
- How can we tell whether a person is sensitive to a particular allergen, such as a tree pollen? 19-4
- Which antibody types need to be blocked to desensitize a person subject to allergies? 19-5

14 Hypersensitivity
- 19-6 Describe the mechanism of cytotoxic reactions and how drugs can induce them.
- 19-7 Describe the basis of the ABO and Rh blood group systems.
- 19-8 Explain the relationships among blood groups, blood, transfusions, and hemolytic disease of the newborn.
- 19-9 Describe the mechanism of immune complex reactions.
- 19-10 Describe the mechanism of delayed cell-mediated reactions, and name two examples.

15 Type II (Cytotoxic) Reactions
- Involve IgG or IgM antibodies and complement
- Complement activation causes cell lysis or damage by macrophages
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• Complement activation causes cell lysis or damage by macrophages

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19 Type III (Immune Complex) Reactions
• IgG antibodies and antigens form immune complexes that lodge in basement membranes

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21 Type IV (Cell-Mediated) Reactions
• Delayed-type hypersensitivities due to T cells
• Cytokines attract macrophages and TC cells
  • Initiate tissue damage

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24 What Is the Delayed Rash?
25 What Is the Delayed Rash?
• A patient developed a rash 7 days after taking penicillin.
• Was this the patient’s first exposure to penicillin?
• What is the delayed reaction?

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• What, besides an allergen and an antibody, is required to precipitate a cytotoxic reaction? 19-6
• What are the antigens located on the cell membranes of type O blood? 19-7
• If a fetus that is Rh+ can be damaged by anti-Rh antibodies of the mother, why does such damage never happen during the first such pregnancy? 19-8

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• Are the antigens causing immune complex reactions soluble or insoluble? 19-9
• What is the primary reason for the delay in a delayed cell-mediated reaction? 19-10

28 Autoimmune Diseases
• 19-11 Describe a mechanism for self-tolerance.
• 19-12 Give an example of immune complex, cytotoxic, and cell-mediated autoimmune diseases.

29 Autoimmune Diseases
• Clonal deletion during fetal development ensures self-tolerance
• Autoimmunity is loss of self-tolerance

30 Autoimmune Diseases
• Cytotoxic: antibodies react with cell-surface antigens
  • Graves’ disease
• Immune complex: immune complexes of IgM, IgG, and complement deposit in tissues
  • Systemic lupus erythematosus
• Cell-mediated: mediated by T cells
  • Psoriasis

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• What is the importance of clonal deletion in the thymus? 19-11
• What organ is affected in Graves’ disease? 19-12

32 HLA Reactions
• 19-13 Define HLA complex, and explain its importance in disease susceptibility and tissue transplants.
• 19-14 Explain how a transplant is rejected.
• 19-15 Define privileged site.
• 19-16 Discuss the role of stem cells in transplantation.

33 HLA Reactions
• Histocompatibility antigens: self antigens on cell surfaces
Major histocompatibility complex (MHC): genes encoding histocompatibility antigens
Human leukocyte antigen (HLA) complex: MHC genes in humans

Diseases Related to Specific HLAs

Reactions to Transplantation
- Transplants may be attacked by T cells, macrophages, and complement-fixing antibodies
- Transplants to privileged sites do not cause an immune response
- Stem cells may allow therapeutic cloning to avoid rejection
  - Embryonic stem cells are pluripotent
  - Adult stem cells have differentiated to form specific cells

What is the relationship between the major histocompatibility complex in humans and the human leukocyte antigen complex? 19-13
What immune system cells are involved in the rejection of nonself transplants? 19-14
Why is a transplanted cornea usually not rejected as nonself? 19-15
Differentiate an embryonic stem cell from an adult stem cell. 19-16

HLA Reactions
- 19-17 Define autograft, isograft, allograft, and xenotransplant.
- 19-18 Explain how graft-versus-host disease occurs.
- 19-19 Explain how rejection of a transplant is prevented.

Grafts
- Autograft: use of one’s own tissue
- Isograft: use of identical twin’s tissue
- Allograft: use of tissue from another person
- Xenotransplantation product: use of nonhuman tissue
- Hyperacute rejection: response to nonhuman Ag
- Graft-versus-host disease can result from transplanted bone marrow that contains immunocompetent cells

41 **Immunosuppression**
- Prevents an immune response to transplanted tissues
- Cyclosporine and tacrolimus suppress IL-2
- Mycophenolate mofetil inhibits T cell and B cell reproduction
- Sirolimus blocks IL-2
- Basiliximab and daclizumab block IL-2

42
- Which type of transplant is most subject to hyperacute rejection? 19-17
- When red bone marrow is transplanted, many immunocompetent cells are included. How can this be bad? 19-18
- What cytokine is usually the target of immunosuppressant drugs intended to block transplant rejection? 19-19

43 **The Immune System and Cancer**
- Describe how the immune system responds to cancer and how cells evade immune responses.
- Give two examples of immunotherapy.

44 **The Immune System and Cancer**
- Cancer cells have tumor-associated antigens
- Cancer cells are removed by immune surveillance
- CTL (activated TC) cells lyse cancer cells

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46 **Immunotherapy for Cancer**
- Coley’s toxin (gram-negative bacteria) stimulates TNF
- Vaccines used against:
• Marek’s disease
• Feline leukemia
• Human cervical cancer
• Liver cancer (hepatitis B virus)
• Cervical cancer (HPV vaccine)
• Monoclonal antibodies
• Herceptin

47 Immunotherapy for Cancer
• Treatment of cancer using immunologic methods
• Tumor necrosis factor, IL-2, and interferons may kill cancer cells
• Immunotoxins link poisons with a monoclonal antibody directed at a tumor antigen
• Vaccines contain tumor-specific antigens

48
• What is the function of tumor-associated antigens in the development of cancer? 19-20
• Give an example of a prophylactic cancer vaccine that is in current use. 19-21

49 Immunodeficiencies
• 19-22 Compare and contrast congenital and acquired immunodeficiencies.

50 Immunodeficiencies
• Congenital: due to defective or missing genes
• Acquired: develop during an individual’s life
  • Due to drugs, cancers, and infections

51 Immunodeficiencies
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• Is AIDS an acquired or a congenital immunodeficiency? 19-22
19-23 Give two examples of how infectious diseases emerge.
19-24 Explain the attachment of HIV to a host cell.
19-25 List two ways in which HIV avoids the host’s antibodies.
19-26 Describe the stages of HIV infection.
19-27 Describe the effects of HIV infection on the immune system.

19-28 Describe how HIV infection is diagnosed.
19-29 List the routes of HIV transmission.
19-30 Identify geographic patterns of HIV transmission.
19-31 List the current methods of preventing and treating HIV infection.

AIDS

1981: in United States, cluster of Pneumocystis pneumonia and Kaposi’s sarcoma discovered in young homosexual men
   - The men showed loss of immune function
1983: discovery of virus causing loss of immune function

The Origin of AIDS

- Crossed the species barrier into humans in Africa between 1884 and 1924
- Patient who died in 1959 in Congo is the oldest known case
- Spread in Africa as a result of urbanization
- Spread worldwide through modern transportation and unsafe sexual practices
- Norwegian sailor who died in 1976 is the first known case in Western world
Clades (Subtypes) of HIV

- HIV-1
  - M (main)
    - B (North and South America, Europe)
    - C (India, eastern and southern Africa)
    - E (southeast Asia)
  - O (outlier)
  - N (non-M or non-O)

The Stages of HIV Infection

- Phase 1: asymptomatic or chronic lymphadenopathy
- Phase 2: symptomatic; early indications of immune failure
- Phase 3: AIDS indicator conditions

Diseases Associated with AIDS

- Cryptosporidium hominis
- Toxoplasma gondii
- Isospora belli
- Cytomegalovirus
- Herpes simplex virus
- Varicella-zoster virus
- Mycobacterium tuberculosis
• M. avium-intracellulare

19  Diseases Associated with AIDS
  • Pneumocystis jirovecii
  • Histoplasma capsulatum
  • Cryptococcus neoformans
  • Candida albicans
  • Kaposi’s sarcoma
  • Hairy leukoplakia
  • Cervical dysplasia

20  Survival with HIV Infection
  • Exposed, but not infected
    • CCR5 mutation
  • Long-term nonprogressors
    • Low viral load
    • Effective CTLs

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  • On what continent did the HIV-1 virus arise? 19-23
  • What is the primary receptor on host cells to which HIV attaches? 19-24
  • Would an antibody against the coat of HIV be able to react with a provirus? 19-25
  • Would a CD4+ T cell count of 300/μl be diagnostic of AIDS? 19-26
  • Which cells of the immune system are the main target of an HIV infection? 19-27

22  Diagnostic Methods
  • Seroconversion takes up to 3 months
  • HIV antibodies detected by ELISA
  • Viruses detected by:
    • Western blotting
    • APTIMA (RNA testing)
• Plasma viral load (PVL) is determined by PCR or nucleic acid hybridization

23 HIV Transmission
• HIV survives 6 hours outside a cell
• HIV survives less than 1.5 days inside a cell
• Infected body fluids transmit HIV via:
  • Sexual contact
  • Breast milk
  • Transplacental infection of fetus
  • Blood-contaminated needles
  • Organ transplants
  • Artificial insemination
  • Blood transfusion

24 AIDS Worldwide
• Heterosexual intercourse (85%)
• Women comprise 42% of infected
• Injected drug use (IDU) (eastern Europe, central and southeast Asia)

25 Preventing AIDS
• Use of condoms
• Use of sterile needles (IDUs)
• Health care workers use universal precautions
  • Wear gloves, gowns, masks, and goggles
  • Do not recap needles
  • Risk of infection from infected needlestick injury is 0.3%

26 Vaccine Difficulties
• Mutations
• Clades
• Antibody-binding sites are “hidden”
• Infected cells are not susceptible to CTLs
• Proviruses
• Latent viruses

29 **Chemotherapy**

• Reverse transcriptase inhibitors
  • Nucleoside reverse transcriptase inhibitors
    • Tenofovir and emtricitabrine
  • Non-nucleoside reverse transcriptase inhibitors
    • Efavirenz

30 **Chemotherapy**

• Protease inhibitors
  • Atazanavir, indinavir, and saquinavir
• Cell entry inhibitors
  • Block fusion
  • Enfuvirtide and maraviroc
• Integrase inhibitors
  • Enzyme to form HIV provirus
    • Raltegravir

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33 **HAART**

• Highly active antiretroviral therapy
• Combinations of nucleoside reverse transcriptase inhibitors plus
  • Non-nucleoside reverse transcriptase inhibitor or
- Protease inhibitor

- What form of nucleic acid is detected in a plasma viral load test for HIV? 19-28
- What is considered to be the most dangerous form of sexual contact for transmission of HIV? 19-29
- What is the most common mode, worldwide, by which HIV is transmitted? 19-30
- Does circumcision make a man more or less likely to acquire HIV infection? 19-31