Chapter 32

Drugs for Immune System Modulation

Nonspecific Body Defenses
- First line of defense
- Barrier to microbes or environmental hazards
- Deny entrance of pathogens
  - General responses that are not specific to a particular threat
- Examples
  - Skin, phagocytes, natural killer cells
  - Complement system, fever, interferons, inflammation

Specific Body Defenses
- Second line of defense: specific activation and effectiveness
- Known as immune response
- Lymphocytes interact with antigens
- Two major divisions of immune system
  - Antibody-mediated (humoral)
  - Cell-mediated

Antibody-Mediated (Humoral) Immunity
- Initiated when antigen encounters B cell
  - Activated B cell divides and becomes plasma cell
- Plasma cells secrete antibodies (immunoglobulins)
  - Neutralize foreign agent (antigen)
  - Mark it for destruction by other defense cells
  - Peak production occurs in about ten days
  - Memory B cells can speed a future defense against a specific antigen
Cell-Mediated Immunity

- Activation of specific T cells
  - Helper T cells (CD4 receptor)
    - Activate most other immune cells
  - Cytotoxic T cells (CD8 receptor)
    - Travel through body, killing bacteria, parasites, viruses, cancer cells

Cell-Mediated Immunity (continued)

- Cytokines secreted by T cells
  - Hormonelike proteins that regulate intensity and duration of immune response
  - Mediate cell-to-cell communication
  - Examples: interferon, interleukins, and perforin

Immune Response in Organ Transplant

- Transplanted organs have antigens that trigger immune response
  - Called transplant rejection
  - Often humoral response (acute response)
  - Antibodies destroy transplanted tissue within days
- Cell-mediated response is slower, about two weeks after surgery
- Chronic rejection can occur months to years later

Immunosuppressants

- Inhibit client’s immune system
- Used to treat severe autoimmune disease
- Prevent tissue rejection following organ transplantation
  - Would be impossible without immunosuppressants
- Toxic to bone marrow
- Increase risk of infections and lymphoma

Immunosuppressants

- Glucocorticoids
- Antimetabolites
- Antibodies
- Calcineurin inhibitors
**Glucocorticoids**

- Inhibit inflammation
- Used for short-term therapy of severe inflammation

**Antimetabolites**

- Inhibit aspects of lymphocyte replication
- **Examples:** sirolimus (Rapamune) and azathioprine (Imuran)

**Calcineurin Inhibitors**

- Cyclosporine (Sandimmune, Neoral) and tacrolimus (Prograf)
  - Bind to calcineurin and disrupt T cells
- Used to treat of psoriasis

**Antibodies**

- Created in other species to fight human T cells
- Muromonab-CD3 (Orthoclone OKT3)
  - Prevents rejection of kidney, heart, and liver transplants
  - Depletes bone marrow of T cells prior to marrow transplant

**Antibodies (continued)**

- Basiliximab (Simulect) and daclizumab (Zenapax)
  - Prevent acute rejection of kidney transplants
- Infliximab (Remicade)
  - Suppresses inflammation in autoimmune disorders
- Suffix “ab” in generic name refers to antibody

**Active Immunity**

- Immune system is stimulated to produce antibodies
  - Exposure to antigen produces active immunity
  - Vaccines boost antibody production; produce active immunity
Passive Immunity

- Preformed antibodies transferred from one person to another
  - Maternal antibodies cross the placenta
  - Immune globulin
  - Antivenom
  - Treatment for botulism, tetanus, and rabies

Passive Immunity (continued)

- For people who are exposed or have high risk of exposure
- For immunosuppressed people

Role of the Nurse

- Monitoring client’s condition
- Providing client education
- Obtaining medical, surgical, and drug history
- Assessing lifestyle and dietary habits
- Obtaining detailed description of symptomology and current therapies

Immunization Agents

- Assess for risk-based precautions: pregnancy, diabetes, heart disease, renal failure
- Provide education on importance of receiving vaccinations
- Answer questions and concerns regarding risks and benefits of vaccines
- Instruct on recommended immunization schedule and follow-up vaccines

Immunostimulants

- Assessment of infections and cancer verifies need for these drugs
- Contraindicated for clients with renal or liver disease and those who are pregnant
- Obtain results of lab tests to provide baseline data
- Keep client well hydrated
- Assess for changes in mental status, including suicidal ideation

Immunosuppressants

- Contraindicated in clients with leukemia, metastatic cancer, active infection, renal or liver disease, or those who are pregnant
- Obtain vital signs and results of lab testing to provide baseline data
- Monitor for indications of infection
Immunosuppressants (continued)

- Monitor degree of bone-marrow suppression (thrombocytopenia and leukopenia)
- Monitor clients taking azathioprine (Imuran) for development of secondary malignancies

Immunosuppressant—Calineurin Inhibitor

- **Prototype drug**: cyclosporine (Neoral, Sandimmune)
- **Mechanism of action**: to inhibit helper T cells
- **Primary use**: for transplant recipients
- **Adverse effects**: 75% of clients experience reduction in urine flow
  - Infections, tremor, hypertension, elevated hepatic enzymes

Immunosuppressant—Cyclosporin A

- **Prototype drug**: cyclosporine (Neoral, Sandimmune)
- **Mechanism of action**: to inhibit helper T cells
- **Primary use**: for transplant recipients
- **Adverse effects**: 75% of clients experience reduction in urine flow
  - Infections, tremor, hypertension, elevated hepatic enzymes

Immunosuppressant—Tacrolimus

- **Prototype drug**: tacrolimus (Prograf)
- **Mechanism of action**: to inhibit T-cell activation
- **Primary use**: for transplant recipients
- **Adverse effects**: liver dysfunction, dermatitis, gingival hyperplasia

Immunosuppressant—sirolimus (rapamycin)

- **Prototype drug**: sirolimus (Rapamune)
- **Mechanism of action**: to inhibit mTOR
- **Primary use**: for transplant recipients
- **Adverse effects**: hyperlipidemia, hypertension, hyperkalemia, anemia

Immunosuppressant—Mycophenolate

- **Prototype drug**: mycophenolate mofetil (CellCept, Myfortic)
- **Mechanism of action**: to inhibit lymphocyte proliferation
- **Primary use**: for transplant recipients
- **Adverse effects**: GI symptoms, infections, hematologic abnormalities

Immunosuppressant—Methotrexate

- **Prototype drug**: methotrexate (Trexall)
- **Mechanism of action**: to inhibit folic acid metabolism
- **Primary use**: for transplant recipients
- **Adverse effects**: hematologic suppression, mucositis, oral ulcers

Immunosuppressant—MyD88 inhibitors

- **Prototype drug**: belimumab (Benlysta)
- **Mechanism of action**: to inhibit B-cell activity
- **Primary use**: for transplant recipients
- **Adverse effects**: infections, diarrhea, nausea, vomiting

Immunosuppressant—JAK inhibitors

- **Prototype drug**: tofacitinib (Xeljanz)
- **Mechanism of action**: to inhibit JAK family kinases
- **Primary use**: for transplant recipients
- **Adverse effects**: infection, diarrhea, nausea, headache

Immunosuppressant—mAbs

- **Prototype drug**: rituximab (Rituxan)
- **Mechanism of action**: to target and eliminate B cells
- **Primary use**: for transplant recipients
- **Adverse effects**: infections, hypogammaglobulinemia

Immunosuppressant—Calcineurin Inhibitor

- **Prototype drug**: cyclosporine (Neoral, Sandimmune)
- **Mechanism of action**: to inhibit helper T cells
- **Primary use**: for transplant recipients
- **Adverse effects**: 75% of clients experience reduction in urine flow
  - Infections, tremor, hypertension, elevated hepatic enzymes
Immune Globulin Preparations

- Provide passive immunity following exposure to hepatitis
- Administered when
  - Client has already been exposed to virulent pathogen or is at very high risk of exposure
  - There is not sufficient time to develop active immunity

Immune Globulin Preparations (continued)

- Clients who are immunosuppressed may receive these agents to prevent infections
  - No memory cells are produced, and protective effects last only two to three weeks

Vaccines

- Biological agents used to stimulate immune system
- Vaccination is administration of modified, harmless microorganism or its toxoid so immune response occurs
- Goal is to prevent serious infections

Three Types of Vaccines

1. Killed microbes
2. Attenuated (weakened) microbes
3. Toxoids (modified bacterial toxins)

- Some need booster (follow-up vaccination) for continuous protection
- Titers measure amount of antibodies produced in the body
- See Table 32.2 for common vaccines and schedules
- Pharmacotherapy Illustrated 32.1 (p. 459) shows development of immunity

Mechanisms of Active and Passive Immunity

- Biologic response modifiers
  - Interferons and interleukins
- Boost client’s immune system
- Used to treat certain viral infections, immunodeficiencies, and specific cancers

Immunostimulants
Interferons

- Secreted by lymphocytes and macrophages that have been infected with a virus
- Slow spread of viral infections and enhance activity of leukocytes
- Two major classes
  - Interferon alpha: used to treat leukemia, AIDS, and hepatitis B or C
  - Interferon beta: used to treat multiple sclerosis, granulomatous disease, and severe osteoporosis

Interleukins

- Used to treat metastatic renal carcinoma
- Stimulate platelet production in immunosuppressed clients
- Enhance capabilities of immune system
- Stimulate cytotoxic T cells

Interleukins (continued)

- Increase B-cell and plasma-cell production
- Promote inflammation

Immunosuppressants

- Inhibit immune response
- Used for clients receiving transplanted tissues or organs
- Used in short-term therapy for severe inflammation

Vaccine Schedules

- Nurses play key role in vaccination process

Vaccine Schedules (continued)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dosage and Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria, tetanus, pertussis (DPT, Tri-Immunol, Tripedia, Acel-Imune, Infanrix, Certiva)</td>
<td>IM: 0.5 mL at ages 2 months, 4 months, 6 months, and 18 months</td>
</tr>
<tr>
<td>Haemophilus type B conjugate (HibTITER, ActHIB, PedvaxHIB)</td>
<td>IM: 0.5 mL at ages 2 months, 4 months, 6 months, and 15 months. Children ages 12–14 months who have not been vaccinated receive single dose</td>
</tr>
</tbody>
</table>
### Vaccine Schedules (continued)

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B (Recombivax HB, Engerix-B)</td>
<td>Given to children: 2.5–5 mcg at birth; then 0.5 mL at 1–4 months and 6–18 months. Adults: 0.5 mL in three doses, with second dose 30 days after first and final dose six months after first.</td>
</tr>
<tr>
<td>Influenza vaccine (Fluzone, FluShield, Fluvirin)</td>
<td>Given to children: IM, two doses one month apart; then annual dose. Adults: IM, single annual dose</td>
</tr>
<tr>
<td>Measles, mumps, and rubella (MMR II)</td>
<td>Given subcutaneously: 0.5 mL single dose at age 15 months to puberty</td>
</tr>
<tr>
<td>Pneumococcal, polyvalent (Pneumovax 23, Pneumovax 23) or 7-valent (Prenvar)</td>
<td>Given to children (Prenvar): IM, four doses at ages 2 months, 4 months, 6 months, and 12–15 months. Adults (Pneumovax 23 or Pneumovax 23): subcutaneously or IM; 0.5 mL as single dose</td>
</tr>
</tbody>
</table>

### Immunostimulant Drug Therapy (continued)

#### Immunostimulant Drug Therapy

- **Assessment**
  - Obtain complete health history
  - Assess history of cytomegalovirus and any malignancies
  - Obtain lab work: complete blood count, electrolytes, and liver enzymes
  - Obtain weight and vital signs, especially blood pressure
  - Assess mental alertness

- **Planning—client will**
  - Experience increased immune-system function
  - Demonstrate understanding of drug’s action
  - Report effects
    - Fever, chills, sore throat, unusual bleeding
    - Chest pain, palpitations, dizziness, change in mental status
  - Demonstrate ability to self-administer IM or subcutaneous injection
Immunostimulant Drug Therapy (continued)

- Implementation
  - Monitor for leukopenia, neutropenia, thrombocytopenia, anemia, increased liver enzymes
  - Ensure that drug is properly administered
  - Monitor vital signs
  - Monitor for common side effects
    - Muscle aches, fever, weight loss, anorexia
    - Nausea and vomiting, arthralgia

Immunostimulant Drug Therapy (continued)

- Implementation (continued)
  - Monitor blood-glucose levels
  - Monitor for changes in mental status

Immunostimulant Drug Therapy (continued)

- Evaluation
  - Laboratory studies reveal improvement in immune-system status
  - Client accurately states drug’s action and side effects
  - Client verbalizes potential side effects and when to notify health-care provider
  - Client demonstrates correct procedure to self-administer IM and subcutaneous injections

Immunosuppressant Drug Therapy

- Assessment
  - Obtain complete health history
  - Assess for presence of metastatic cancer, active infection, renal or liver disease, pregnancy
  - Assess skin integrity
  - Obtain results of laboratory work
  - Obtain vital signs

Immunosuppressant Drug Therapy (continued)

- Nursing diagnoses
  - Risk for infection
  - Risk for injury

Immunosuppressant Drug Therapy (continued)

- Planning—client will
  - Experience no symptoms of organ or allograft rejection
  - Immediately report elevated temperature, unusual bleeding, sore throat, mouth ulcers, and fatigue to health-care provider
  - Demonstrate understanding of drug’s action
Immunosuppressant Drug Therapy (continued)

• Implementation
  – Assess renal function
  – Monitor liver-function tests
  – Watch for signs and symptoms of infection
  – Monitor for hirsutism, leukopenia, gingival hyperplasia, gynecomastia, sinusitis, and hyperkalemia
  – Have client avoid ingesting grapefruit juice
  – Assess nutritional status

Immunosuppressant Drug Therapy (continued)

• Evaluation—client
  – Is free of signs of infection or organ rejection
  – Accurately states signs and symptoms to be reported
  – Accurately states drug’s action and side effects

Immune Globulin Preparations

Table 32.1 Immune Globulin Preparations

Immunostimulants

Table 32.3 Immunostimulants

Immunosuppressants

Table 32.4 Immunosuppressants

Immunosuppressants

Table 32.4b Immunosuppressants
Immunosuppressants

Table 32.4c Immunosuppressants

Table 32.4d Immunosuppressants