Chapter 47

Drugs for Bone and Joint Disorders

Calcium

- Adequate levels in body necessary
  - To transmit nerve impulses
  - To prevent muscle spasms
  - To provide stability and movement
- Also important for blood coagulation and myocardial activity
- Body also needs adequate levels of
  - Vitamin D, parathyroid hormone (PTH), and calcitonin

Control of Calcium by Endocrine System

- Parathyroid—secretes PTH
  - Stimulates osteoclasts
  - Accelerates bone resorption
  - Causes breakdown of bone
  - Consequently, calcium increases in blood

Thyroid

- Secretes calcitonin
  - Stimulates bone deposition
    - Builds up bone
    - Consequently, calcium is removed from blood
**PTH and Calcitonin**

- Control calcium homeostasis
- Influence three targets
  - Bones
  - Kidneys
  - GI tract

**Vitamin D**

- Necessary for effective absorption of calcium
- Synthesized from precursor molecules

**Vitamin D introduced in two ways**

- Cholecalciferol in **skin** activated by sunlight (UV light)
- Cholecalciferol obtained in **gastrointestinal tract** from dairy products and fortified foods
- First converted to intermediate form—calcifediol
- Then metabolized to calcitriol (active form of vitamin D)

**Hypercalcemia**

- Sodium permeability decreases across cell membrane
- Dangerous for nervous system
Hypocalcemia

- Cell membranes become excitable
- May produce convulsions or tetany

Disorders of Vitamin D and Calcium Metabolism

- Hypocalcemia
  - Osteomalacia
  - Osteoporosis
  - Paget’s disease

Therapies

- Calcium and vitamin D supplements
- Bisphosphonates
- Miscellaneous agents

Hypocalcemia (continued)

- Symptoms
  - Nerve and muscle excitability
  - Tremor or cramping
  - Numbness or tingling of extremities
  - Convulsions, confusion, abnormal behavior

Treatment of Hypocalcemia

- Severe—IV administration of calcium salts
- Mild—oral supplements of calcium and vitamin D

Essential to find cause
- Hyposerection of PTH
- Digestive-related malabsorption disorders
- Vitamin D deficiencies
Osteomalacia

- Called rickets in children
- Characterized by softening of bones
- No alteration in basic bone structure
- Cause
  - Lack of vitamin D and calcium in diet
  - Kidney failure
  - Malabsorption of calcium from GI tract

Osteomalacia (continued)

- Symptoms
  - Hypocalcemia, muscle weakness and spasms, bone pain
  - Rickets symptoms: bowlegs, pigeon breast, slight fever, restlessness at night

Pharmacotherapy of Osteomalacia

- Calcium supplements
- Vitamin D (inactive, intermediate, active forms)
  - Dose depends on amount of exposure to sunlight
  - Fat soluble, so hypercalcemia may occur
  - Increase intake after age 70

Pharmacotherapy of Osteomalacia

<table>
<thead>
<tr>
<th>Calcium Supplements and Vitamin D Therapy</th>
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<tr>
<td>Drug (Dosage and Administration)</td>
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<td>Calcium Carbonate</td>
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<tr>
<td>Calcium Citrate</td>
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<tr>
<td>Calcium Gluconate</td>
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<tr>
<td>Calcium Phosphate</td>
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<tr>
<td>Vitamin D (inactive, intermediate, active forms)</td>
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Role of the Nurse

- Monitor client’s condition
- Provide client education
- Obtain medical, surgical, drug history
- Assess lifestyle and dietary habits
- Obtain description of symptomology and current therapies

Calcium-Supplement Therapy

- Assess for signs and symptoms of hypercalcemia
  - Drowsiness, lethargy, weakness
  - Headache, anorexia, nausea, vomiting
  - Thirst, increased urination
Calcium-Supplement Therapy (continued)

- Signs and symptoms to assess for hypocalcemia
  - Facial twitching, muscle spasms, paresthesias, seizures
- Obtain baseline and periodic vital signs, labs, ECG
- History of fracture should be investigated

Calcium-Supplement Therapy (continued)

- Calcium supplements contraindicated in some clients
  - History of renal calculi
  - Digoxin toxicity
  - Dysrhythmias
  - Hypercalcemia

Vitamin D Therapy

- Assess liver function, intake of fat-soluble vitamins, current medications
- Assess sclera, skin pigment, bowel movements
- Monitor liver-function tests; serum calcium, magnesium, phosphate levels

Vitamin D Therapy

- Monitor urinary calcium and phosphate levels
- Emphasize including extra dietary vitamin D in children and pregnant women

Osteoporosis

- Most common metabolic bone disease
- Responsible for 1.5 million fractures per year
- Related to bone deterioration—bone resorption outpaces bone deposition
  - Lack of dietary calcium and vitamin D
  - Disrupted bone homeostasis
Risk Factors for Osteoporosis

- Onset of menopause: most common risk factor
- High alcohol or caffeine consumption
- Anorexia nervosa
- Tobacco use
- Physical inactivity

(continued)

- Testosterone deficiency
- Lack of vitamin D or calcium
- Drugs that lower calcium in blood
  - Corticosteroids, anticonvulsants, immunosuppressants

Pharmacotherapy of Osteoporosis

- Calcium supplements and vitamin D
- Bisphosphonates
- Selective estrogen receptor modulators (SERMs)
- Calcitonin
- Hormone replacement therapy (HRT)
- Slow-release sodium fluoride
- PTH analog

Bisphosphonates

- Most common treatment
- Block bone resorption by inhibiting osteoclast activity
- Adverse effects: GI problems
- Take on empty stomach as tolerated
- Once-weekly dosing effective because of extended duration of action

Selective Estrogen Receptor Modulators (SERMs)

- Decrease bone resorption
- Increase bone density
- Bind to estrogen receptors
- May be estrogen agonists or antagonists
  - Depends on drug or tissue involved

Calcitonin

- Approved for women more than 5 years postmenopause
- Increases bone density; reduces risk of vertebral fractures
- Available as nasal spray or injectable form
- Also indicated for Paget’s disease and hypercalcemia
Hormone Replacement Therapy (HRT)

- No longer recommended for osteoporosis
- Until recently, was common treatment
- Research shows increased risks
  - Uterine cancer, thromboembolic disease
  - Breast cancer, other chronic disorders

Pharmacology of Osteoporosis

<table>
<thead>
<tr>
<th>TABLE 47.2</th>
<th>Selected Drug for Osteoporosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HORMONAL AGENTS</td>
<td>[\text{Example-Agent} ]</td>
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<tr>
<td>\text{bisphosphonates}</td>
<td>\text{etanercept}</td>
</tr>
<tr>
<td>\text{calcitonin}</td>
<td>\text{parathyroid hormone}</td>
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</table>

Paget's Disease

- Chronic, debilitating disorder with enlarged, abnormal bones
- Abnormally rapid bone resorption and deposition occurs continually
  - New bone is weak and brittle
  - Deformities and fractures develop

Paget's Disease: Symptoms

- May be asymptomatic for many years
- Joint inflammation, hip and femur pain
- Headaches, facial pain
- Hearing loss, compressed vertebrae
- Diagnosis: elevated alkaline phosphatase (ALP) confirms disease

Pharmacotherapy of Paget's Disease

- Bisphosphonates and calcitonin
  - Slow down rate of bone resorption
  - Encourage deposition of strong bone

Pharmacotherapy of Paget's Disease (continued)

- Surgery needed in some cases
  - Severe bone deformity, degenerative arthritis, or fractures
- Recommendations
  - Daily calcium and vitamin D
  - Adequate exposure to sunlight
Osteoarthritis

- Degenerative, age-onset disease
- Characterized by wearing away of cartilage at articular joint surfaces
- Symptoms
  – Muscle spasms

Osteoarthritis (continued)

- Localized pain and stiffness
- Joint and bone enlargement
- Etiology poorly understood
  – Thought to be due to excessive wear of weight-bearing joints
    - Hip, knee, spine

Rheumatoid Arthritis

- Systemic autoimmune disorder
- Characterized by inflammation of multiple joints
- Autoantibodies (rheumatoid factors) activate inflammatory response in joints.

Pharmacotherapy of Osteoarthritis (continued)

- COX-2 inhibitors
- Tramadol (Ultram)
- Intra-articular glucocorticoids
- Sodium hyaluronate (Hyalgan) injections into joint

Rheumatoid Arthritis (continued)

- Other extra-articular systemic manifestations may develop
  – Infections, pulmonary disease
  – Pericarditis, blood abnormalities
  – Metabolic dysfunction
Pharmacotherapy of Osteoarthritis

- Goal is reduction of pain and inflammation
  - Topical medications (capsaicin cream)
  - NSAIDs (including aspirin)
  - Acetaminophen

Pharmacotherapy for Rheumatoid Arthritis

- Includes same classes of drug used for osteoarthritis
- Additional drugs used for severe inflammation and immune aspects
  - Glucocorticoids
  - Disease-modifying antirheumatic drugs
  - Immunosuppressants

Pharmacotherapy for Rheumatoid Arthritis (continued)

- Several months may be needed before therapeutic results are achieved

Gout

- Characterized by buildup of uric acid in blood or joint cavities
- Primary gout inherited (most commonly observed in Pacific Islanders).
- Secondary gout due to certain drugs, diabetic ketoacidosis, or kidney failure

Symptoms of Acute Attacks

- Red, swollen tissue
  - Often in big toes, ankles, fingers, wrists, knees, elbows
- Triggered by diet, injury, or other stress
- Attacks often occur at night
Pharmacotherapy of Gout

- Goals: termination of acute attacks; prevention of future attacks
- NSAIDs for pain and inflammation
  - Example: indomethacin (Indocin)

Pharmacotherapy of Gout (continued)

- Uric acid–inhibiting drugs
  - Block accumulation of uric acid in blood and uric acid crystals in joints
- Glucocorticoids
  - Short-term relief; injected into joint

Nonpharmacological Therapy for Arthritis

- Nonimpact and passive range of motion (ROM)
- Splinting
- Thermal therapies
- Meditation, visualization
- Distraction techniques
- Massage therapy

Nonpharmacological Therapy for Arthritis (continued)

- Proper body mechanics and posturing
- Consultation with physical and occupational therapists is appropriate
- Surgical techniques
  - Joint replacement and reconstructive surgery
  - Sometimes necessary when other methods ineffective

Role of the Nurse

- Monitor client’s condition
- Provide client education
- Obtain medical, surgical, drug history
- Assess lifestyle and dietary habits
- Obtain description of symptomology and current therapies

Bisphosphonate Drug Therapy

- Obtain thorough history
  - Assess any history of fractures
- Correct preexisting vitamin D deficiency or hypocalcemia prior to initiating bisphosphonate therapy
Bisphosphonate Drug Therapy (continued)

- Complete physical examination
  - CBC, pH, chemistry panel
  - Renal-, liver-function studies
  - Vital signs, bone density studies (DXA scan)

Drug Therapy with Antigout Medications

- Obtain thorough history
  - CBC, platelets
  - Liver- and renal-function studies
  - Uric acid levels, urinalysis

Calcium Supplements

- **Prototype drug:** calcium gluconate (Kalcinate)
- **Mechanism of action:** to return serum calcium levels to normal
- **Primary use:** used to correct hypocalcemia; for osteoporosis and Paget’s disease
- **Adverse effects:** hypercalcemia
  - IV administration of calcium may cause hypotension, bradycardia, dysrhythmias, cardiac arrest

Vitamin D Therapy

- **Prototype drug:** calcitriol (Calcijex, Rocaltrol)
- **Mechanism of action:** as active form of vitamin D
  - Promotes intestinal absorption of calcium
  - Reduces bone resorption
  - Elevates serum levels of calcium

Vitamin D Therapy (continued)

- **Primary use:** for impaired kidney function or hypoparathyroidism
  - Also useful in treating rickets
- **Adverse effects:** hypercalcemia
  - Headache, weakness, dry mouth, thirst
  - Increased urination, muscle or bone pain

Calcitriol Animation

Click here to view an animation on the topic of calcitriol.
Bisphosphonates

- **Prototype drug:** etidronate disodium (Didronel)
- **Mechanism of action:** strengthens bones by slowing bone resorption
- **Primary use:** for Paget's disease and to treat hypercalcemia due to malignancy

Bisphosphonates (continued)

- **Adverse effects:** diarrhea, nausea, vomiting
  - GI irritation, metallic- or altered-taste perception
  - Pathologic fractures, nephrotoxicity

Selective Estrogen Receptor Modulators (SERMs)

- **Prototype drug:** raloxifene (Evista)
- **Mechanism of action:** decreases bone resorption
  - Increases bone mass and density by acting through estrogen receptor
- **Primary use:** prevention of osteoporosis in postmenopausal women

Selective Estrogen Receptor Modulators (SERMs) (continued)

- **Adverse effects:** hot flashes, migraine headache, flu-like symptoms
  - Endometrial disorder, breast pain, vaginal bleeding
  - May cause fetal harm when administered to pregnant woman

Disease-Modifying Antirheumatic Drugs

- **Prototype drug:** hydroxychloroquine sulfate (Plaquenil)
- **Mechanism of action:** relieves severe inflammation of arthritis and lupus
  - Mechanism of action not known

Disease-Modifying Antirheumatic Drugs (continued)

- **Primary use:** for rheumatoid arthritis and lupus erythematosus
  - For clients who have not responded well to other anti-inflammatory drugs
- **Adverse effects:** anorexia, GI disturbances, loss of hair
  - Possible ocular effects, headache
  - Mood and mental changes
Uric Acid Inhibitor

• **Prototype drug:** colchicine
• **Mechanism of action:** inhibits synthesis of microtubules
  – Subcellular structures responsible for helping white blood cells infiltrate area
• **Primary use:** to reduce inflammation associated with acute gouty arthritis

Uric Acid Inhibitor (continued)

• **Adverse effects:** nausea, vomiting, diarrhea
  – Gastrointestinal upset, bone marrow toxicity
  – Aplastic anemia, leucopenia
  – Thrombocytopenia or agranulocytosis
  – May also directly interfere with absorption of vitamin B12

Clients Receiving Calcium Supplements

• **Assessment**
  – Obtain complete health history
  – Obtain baseline ECG
  – Obtain baseline vital signs, especially apical pulse and blood pressure
  – Obtain CBC and electrolytes, especially calcium

Clients Receiving Calcium Supplements (continued)

• **Nursing diagnoses**
  – Risk for injury, related to loss of bone mass and side effects of drug
  – Deficient knowledge, related to drug therapy
  – Deficient knowledge, related to signs and symptoms to report to health-care provider
  – Deficient knowledge, related to rationale for baseline data and subsequent laboratory data collection for optimal drug regimen

Clients Receiving Calcium Supplements

• **Planning**—client will
  – Have normal serum calcium levels (8.5–11.5 mg/dl)
  – Demonstrate understanding of drug’s action
  – Immediately report side effects and adverse reactions

Clients Receiving Calcium Supplements (continued)

• **Implementation**
  – Monitor electrolytes throughout therapy
  – Monitor for signs and symptoms of hypercalcemia
  – Initiate seizure precautions for clients at risk for hypocalcemia
  – Monitor for musculoskeletal difficulties
  – Monitor intake and output
  – Use cautiously in client with renal insufficiency
 Clients Receiving Calcium Supplements (continued)

- Monitor cardiac functioning
- Monitor injection site during intravenous administration for infiltration
- Monitor diet

Clients Receiving Calcium Supplements

- Evaluation
  - Calcium levels are normal
  - Client accurately states drug’s action and side effects
  - Client accurately states signs and symptoms to be reported to health-care provider

Clients Receiving Bisphosphonates

- Assessment
  - Obtain complete health history
  - Assess for presence or history of pathologic fractures, hypocalcemia, hypercalcemia
  - Assess nutritional status
  - Obtain CBC, pH
    - Electrolytes and renal-function studies (blood urea nitrogen [BUN], creatinine, uric acid)
    - Serum calcium, phosphorous, magnesium levels

Clients Receiving Bisphosphonates

- Nursing diagnoses
  - Deficient knowledge, related to drug therapy
  - Risk for imbalanced fluid volume, related to adverse reaction to drug
  - Nausea, related to side effects of drug
  - Acute bone pain, related to adverse drug reaction
  - Ineffective therapeutic regimen management, related to fact that therapeutic response may take 1—3 months

Clients Receiving Bisphosphonates

- Planning—client will
  - Demonstrate decreased progression of osteoporosis or Paget’s disease
  - Demonstrate decreased risk for pathologic fractures
  - Remain free of side effects or adverse reactions
  - Demonstrate understanding of drug’s action
  - Demonstrate understanding of dietary needs/modifications
  - Maintain adequate fluid volume

Clients Receiving Bisphosphonates

- Implementation
  - Monitor for pathologic fractures and bone pain
  - Monitor for GI side effects
  - Monitor calcium lab values
Clients Receiving Bisphosphonates (continued)

• Implementation (continued)
  – Monitor kidney function, especially creatinine level
  – Monitor BUN, vitamin D, urinalysis, serum phosphate and magnesium levels
  – Monitor dietary habits
  – Monitor compliance with recommended regimen

• Evaluation (continued)
  – Accurately states signs and symptoms to be reported to health-care provider
  – Verbalizes understanding of dietary requirements and/or modifications
  – Maintains adequate fluid intake
  – Is free of side effects and adverse reactions

Clients Receiving Colchicine

• Nursing diagnoses
  – Activity intolerance, related to joint pain
  – Disturbed body image, related to joint swelling
  – Deficient knowledge, related to effects and side effects of drug therapy

• Planning—client will
  – Report decrease in pain and increase in function in affected joints
  – Demonstrate understanding of drug’s action
  – Immediately report side effects and adverse reactions

Clients Receiving Bisphosphonates

• Evaluation—client
  – Demonstrates decreased progression of osteoporosis or Paget’s disease
  – Is free of pathological fractures
  – Accurately states drug’s action, side effects, precautions
Clients Receiving Colchicine

• Implementation
  – Monitor lab results throughout therapy
  – Perform Coombs test for hemolytic anemia
  – Monitor for signs of toxicity
  – Monitor for signs of renal impairment, such as oliguria
  – Record intake and output
  – Ensure that medication is administered correctly
  – Monitor for pain and mobility

• Evaluation—client
  – Reports decrease in pain and increase in function of affected joints
  – Accurately states drug’s action, side effects, precautions
  – Accurately states signs and symptoms to be reported to health-care provider

Selected Disease-modifying Antirheumatic Drugs

Table 47.3 Selected Disease-modifying Antirheumatic Drugs

Table 47.3b Selected Disease-modifying Antirheumatic Drugs

Uric Acid–inhibiting Drugs for Gout and Gouty Arthritis

Table 47.4 Uric Acid–inhibiting Drugs for Gout and Gouty Arthritis