

Corticosteroids & Bone Strengthening Agents



Elizabeth Staub

Doctor of Pharmacy candidate, 2017

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- **What you (should) already know**
 - Concept of negative feedback
 - Physiology of endogenous steroids
 - Physiology of bone turnover
- **What we will discuss today**
 - Different dosage forms of corticosteroids
 - Indications for corticosteroid (CS) therapy
 - Two major types of activity of corticosteroids
 - Adverse effects(AE) of corticosteroids
 - Common bone-strengthening agents
 - Adverse effects of bone-strengthening agents
 - Clinical applications of these drugs in physical therapy
- **What you should be able to do**
 - Identify severe side effects resulting from CS usage
 - Identify effects of CS withdrawal
 - Recognize the names of bisphosphonates
 - Identify the major AE associated with bisphosphonates
 - Know how to apply this information to your PT practice

What are they, how do they work, and why does it matter?

CORTICOSTEROIDS

Corticosteroids



Oral
e.g. PREDNISONE



Inhaled
e.g. FLUTICASONE



Nasal
e.g. MOMETASONE



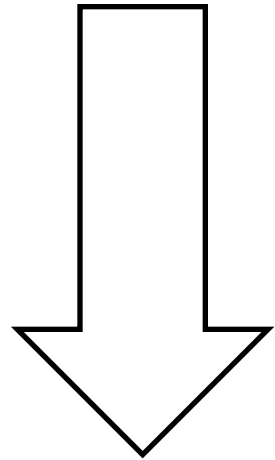
Injectable
e.g. TRIAMCINOLONE



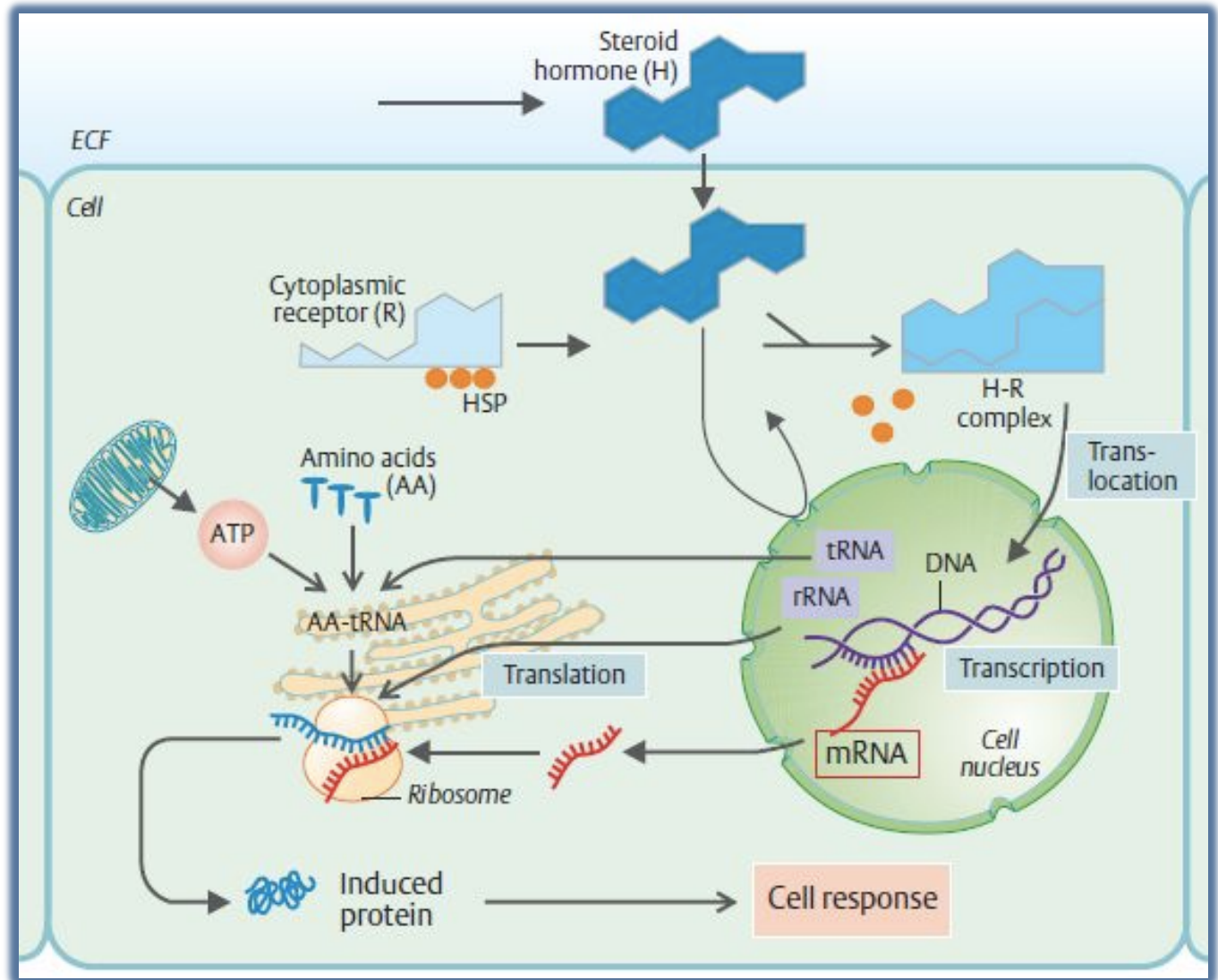
Topical
e.g. HYDROCORTISONE

How do they work?

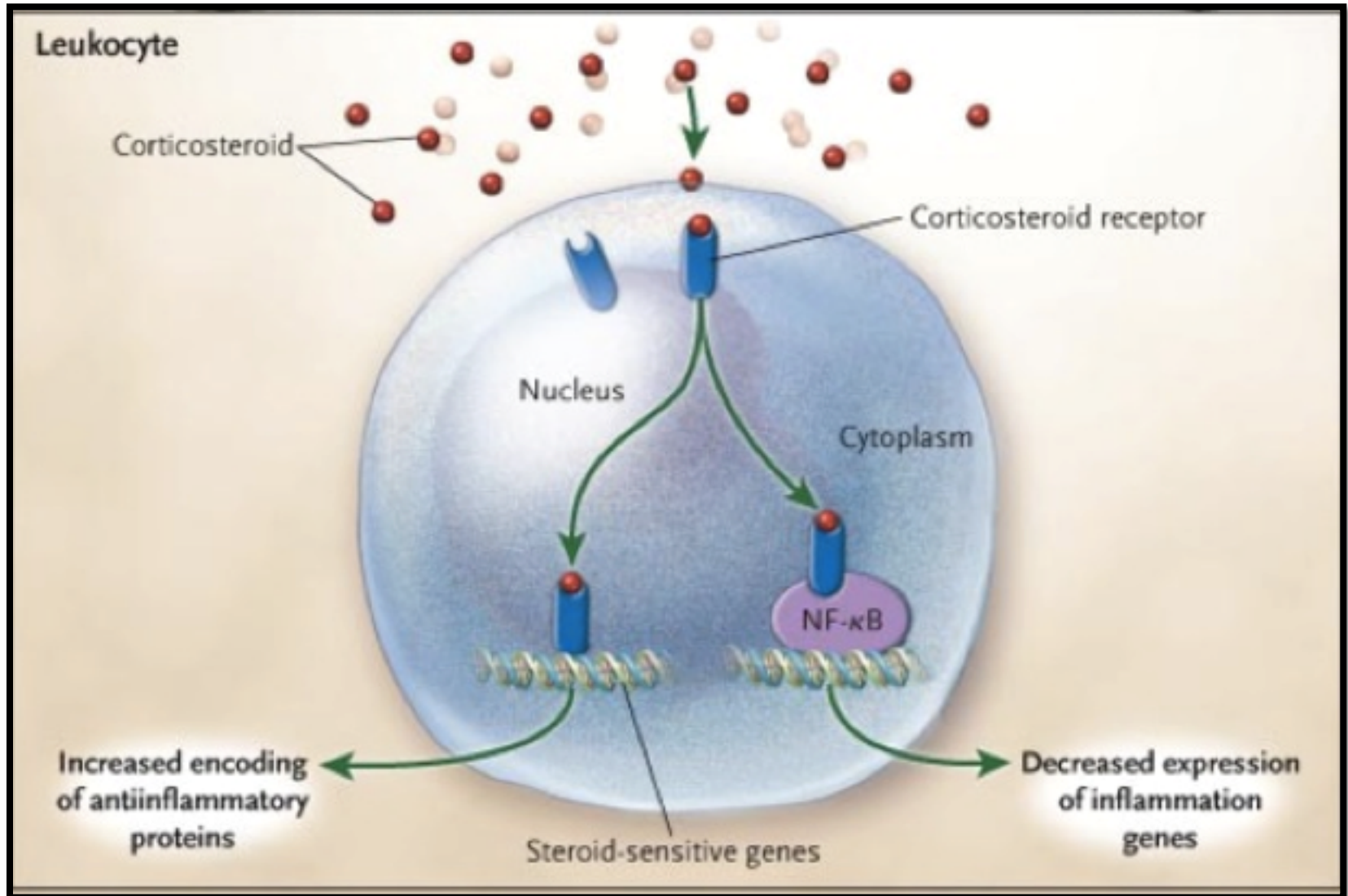
Receptor binding
and altered
protein expression



Physiologic
effect



Decreasing Inflammation

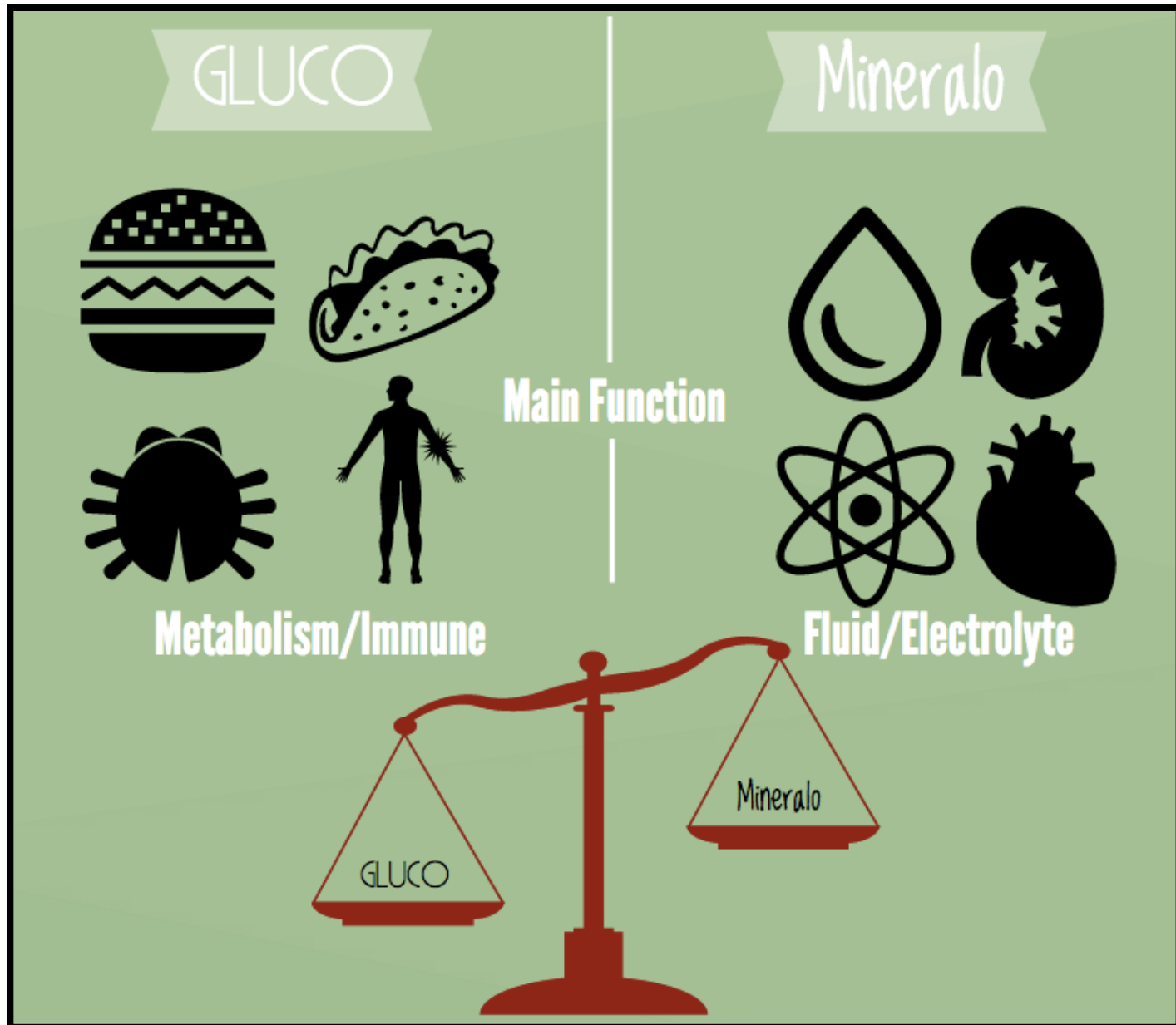


Corticosteroids: Indications

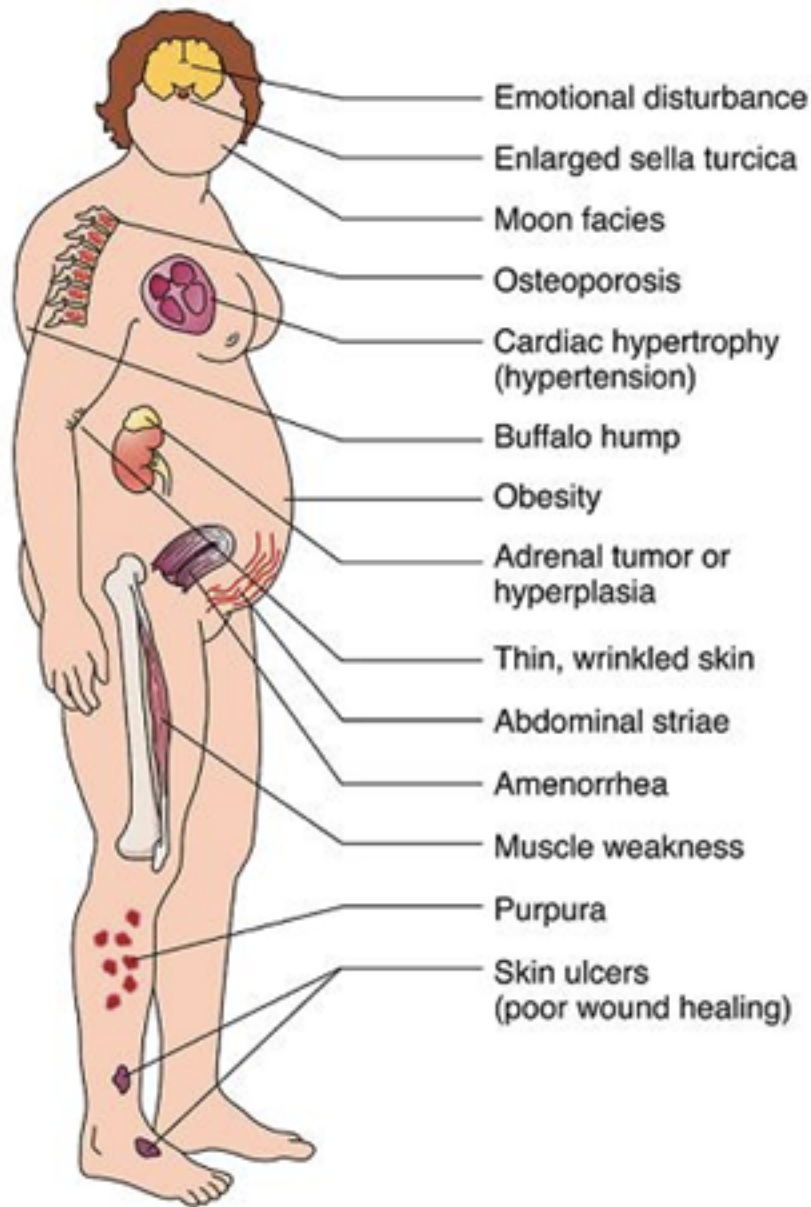
Disorder	Examples
Allergic reactions	Angioneurotic edema, asthma, bee stings, contact dermatitis, drug reactions, allergic rhinitis, serum sickness, urticaria
Collagen-vascular disorders	Giant cell arteritis, lupus erythematosus, mixed connective tissue syndromes, polymyositis, polymyalgia rheumatica, rheumatoid arthritis, temporal arteritis
Gastrointestinal diseases	Inflammatory bowel disease, nontropical sprue, subacute hepatic necrosis
Hematologic disorders	Acquired hemolytic anemia, acute allergic purpura, leukemia, autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, multiple myeloma
Systemic inflammation	Acute respiratory distress syndrome (sustained therapy with moderate dosage accelerates recovery and decreases mortality)
Inflammatory conditions of bones and joints	Arthritis, bursitis, tenosynovitis
Neurologic disorders	Cerebral edema (large doses of dexamethasone are given to patients following brain surgery to minimize cerebral edema in the postoperative period), multiple sclerosis
Organ transplants	Prevention and treatment of rejection (immunosuppression)
Pulmonary diseases	Aspiration pneumonia, bronchial asthma, prevention of infant respiratory distress syndrome, sarcoidosis
Skin diseases	Atopic dermatitis, dermatoses, lichen simplex chronicus (localized neurodermatitis), mycosis fungoides, pemphigus, seborrheic dermatitis, xerosis

Main Theme: Decrease inflammatory/immune responses

Two Types of Steroid Activity



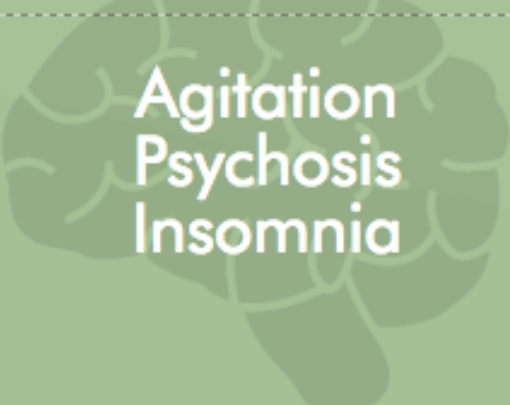
Corticosteroids: Adverse Effects



- Result of **prolonged steroid activity**
 - ↑ blood glucose
 - ↑ BP
 - ↓ immune response
- **Melt everything**
(your muscles, your skin, your bones...)

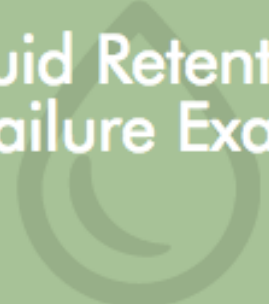
Physical Therapy Relevant Side Effects

NEUROLOGIC



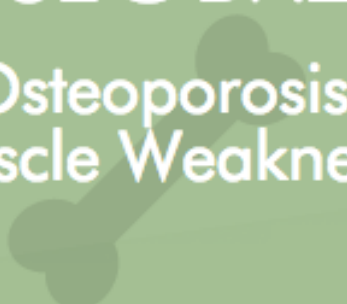
Agitation
Psychosis
Insomnia

FLUID EFFECTS



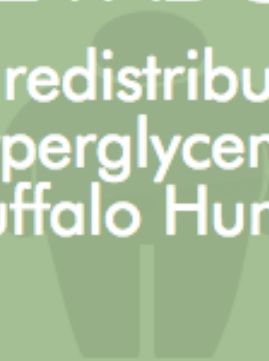
Fluid Retention
Heart Failure Exacerbation

MUSCULOSKELETAL



Osteoporosis
Muscle Weakness

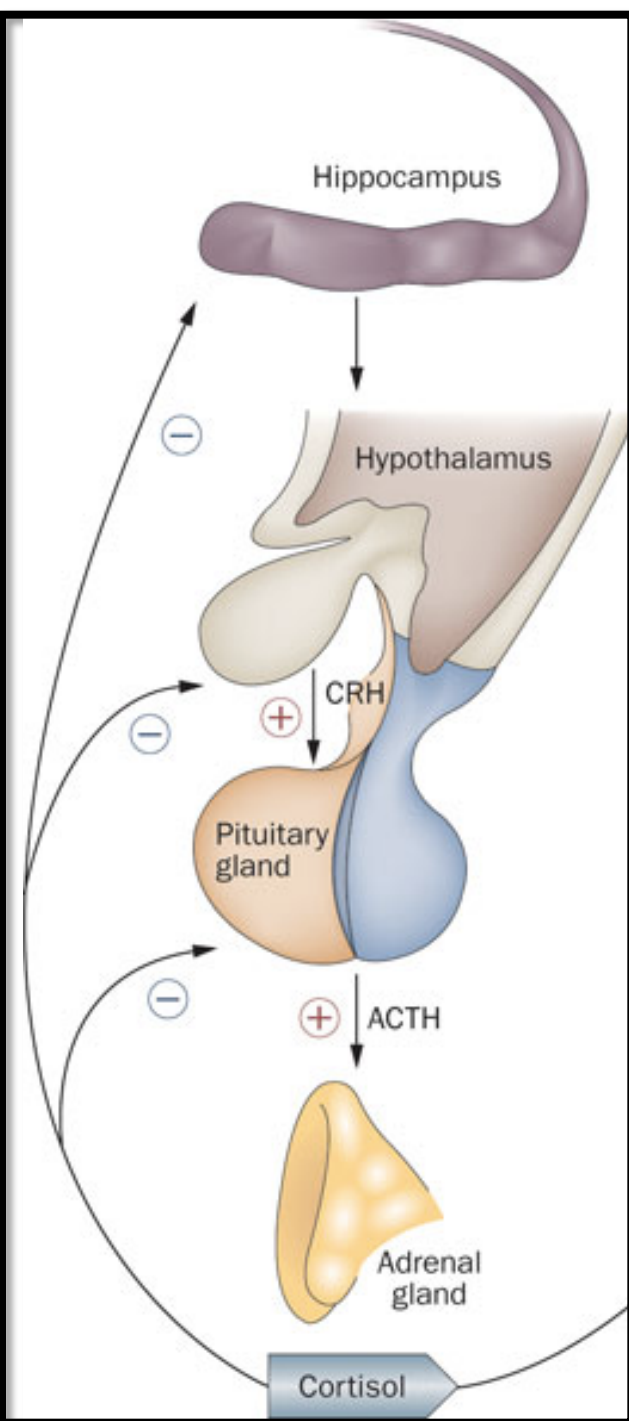
METABOLIC



Fat redistribution
Hyperglycemia
Buffalo Hump

Corticosteroid Withdrawal

- Prolonged use → adrenal atrophy
- Can experience symptoms of steroid deficiency:
 - Fatigue
 - Depression
 - Nausea
 - Hypotension
 - Hypoglycemia
 - Muscle weakness
- Patients less capable of handling stress physically and mentally
- Must be carefully tapered



Corticosteroids:

Clinical Relevance in Physical Therapy

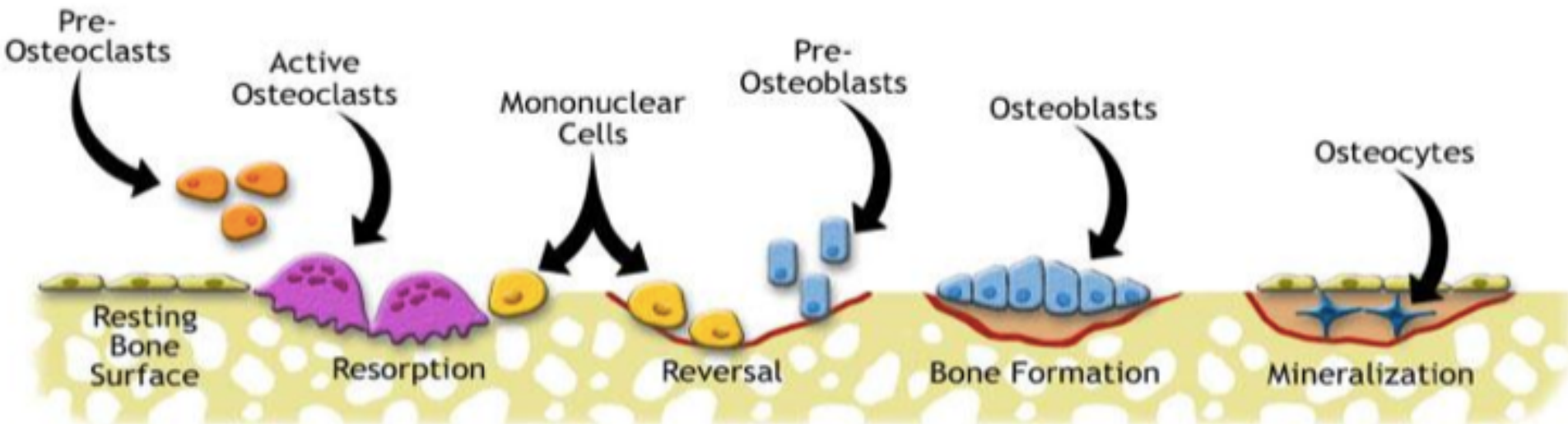
- CS local injections **reduce inflammation** and can improve function in patients with orthopedic dysfunctions
- **Adverse effects** (agitation, hyperglycemia, osteoporosis) of CS therapy may affect PT
- Patients on CS therapy may have **decreased endurance**
- CS **withdrawal symptoms** (orthostatic hypotension, muscle weakness) could affect a patient's PT and lead to medical emergencies

Battling long term effects of steroid use

OSTEOPOROSIS

Osteoporosis: Background

Bone Breakdown >>> Bone Formation



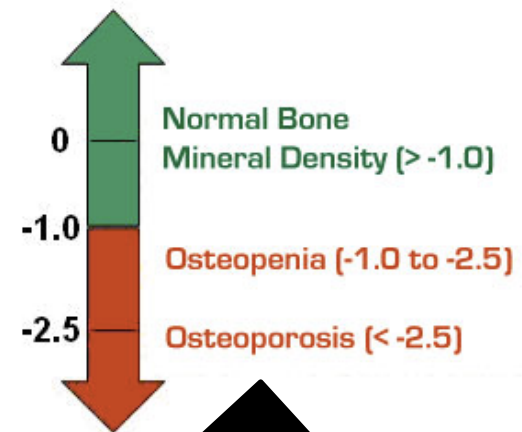
Deterioration of bone tissue



Complications:

- Fractures
- Immobility
- Lower back pain

Diagnosis: DXA Scan



Bone Strengthening Agents

Bisphosphonates

-dronates

Alendronate
Risedronate
Ibandronate

Selective Estrogen
Receptor Modulators
(SERMs)

Raloxifene

Parathyroid Agents

Calcitonin
Teriparatide

Others

Denosumab
Calcium
Vitamin D

Bisphosphonates

alendronate, risendronate, ibandronate

- **Mechanism of action**

- Acts on osteoclasts and osteoclast precursors to inhibit bone resorption

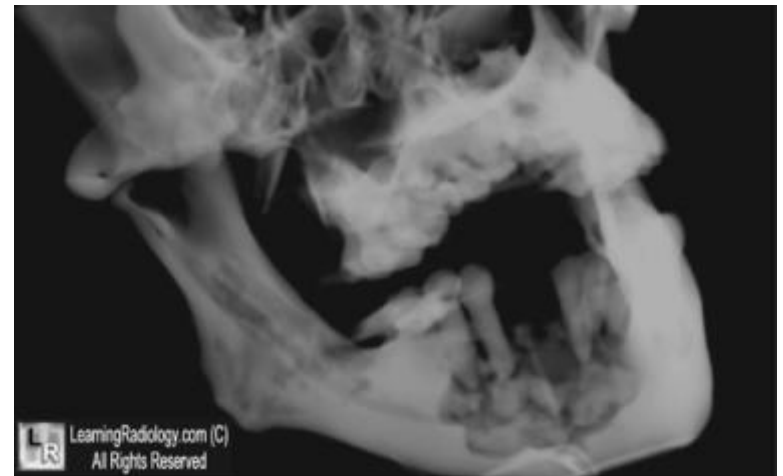
- **Effect**

- Decreased bone resorption

- **Place in therapy**

- Osteoporosis prevention and treatment

Adverse effects
• GI upset • Heartburn • Bone, muscle, or joint pain • Osteonecrosis of the jaw • Abnormal fractures



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Selective estrogen receptor modulators (SERMs)

raloxifine (Evista)

- **Mechanism of action**

- Affects some of the same receptors as estrogen (selective)
- Acts like estrogen in the bone

- **Effect**

- Increase bone production

- **Place in therapy**

- Prevention and treatment of osteoporosis in postmenopausal women
- Risk reduction for invasive breast cancer

Adverse effects
• Hot flashes • Leg cramps • Peripheral edema • Increased risk of venous thromboembolism and stroke

Parathyroid agents

calcitonin (Fortical), teriparatide (Forteo)

- **Mechanism of action**

- calcitonin: normally secreted by thyroid gland
- teriparatide: mimic of parathyroid hormone

- **Effect**

- calcitonin: inhibits osteoclasts
- teriparatide: increase calcium levels and activating osteoblast activity

- **Place in therapy**

- Glucocorticoid induced osteoporosis
- Osteoporosis in men and postmenopausal women

Adverse effects
calcitonin: • Rhinitis • Flushing
teriparatide: • Dizziness • Nausea



<https://healthy.kaiserpermanente.org/static/drugency/images/ATX08230.JPG>

<http://png.tradefindia.com/01525205/b/1/Teriparatide-Injection.jpg>

Others

denosumab (Xgvia)

- **Mechanism of action**

- Monoclonal antibody

- **Effect**

- Prevents osteoclast activation

- **Place in therapy**

- Treat osteoporosis/bone loss
- Treat tumors
- Treat hypercalcemia of malignancy

Adverse effects
• Weakness • Fatigue • Headache • Nausea • Vomiting • Diarrhea • Dyspnea • Infection

Bone-Strengthening Agents:

Clinical Relevance in Physical Therapy

- Physical therapy is an important aspect of **treatment and prevention** of osteoporosis
- Many of your patients with osteoporosis will be on these **bone-strengthening agents**
- PT sessions may exacerbate common **adverse effects** of these medications (GI upset, hot flushes, dyspnea)



References

- Panus PC, Katzung B, Jobst EE, et al. Pharmacology for the Physical Therapist. McGraw Hill. 2009.
- Marti Larriva, PharmD
- Stephanie Hsia, PharmD