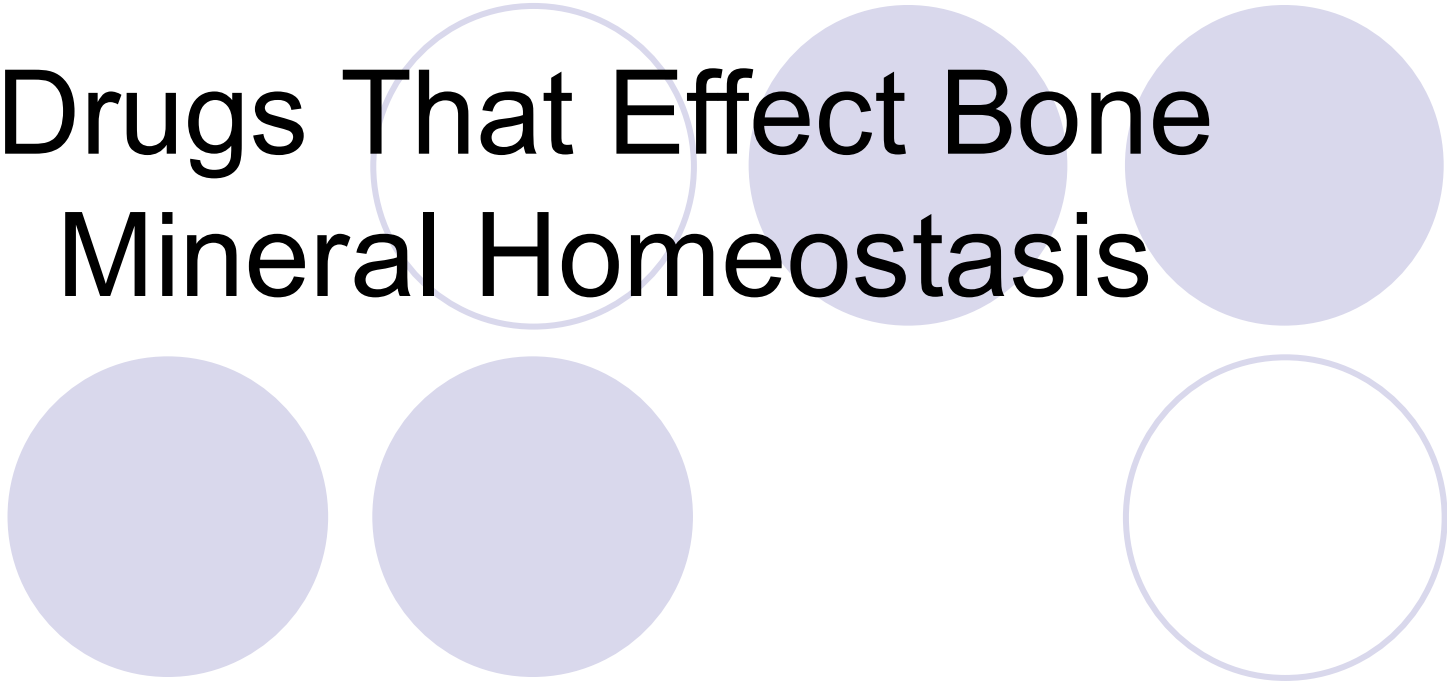


Drugs That Effect Bone Mineral Homeostasis

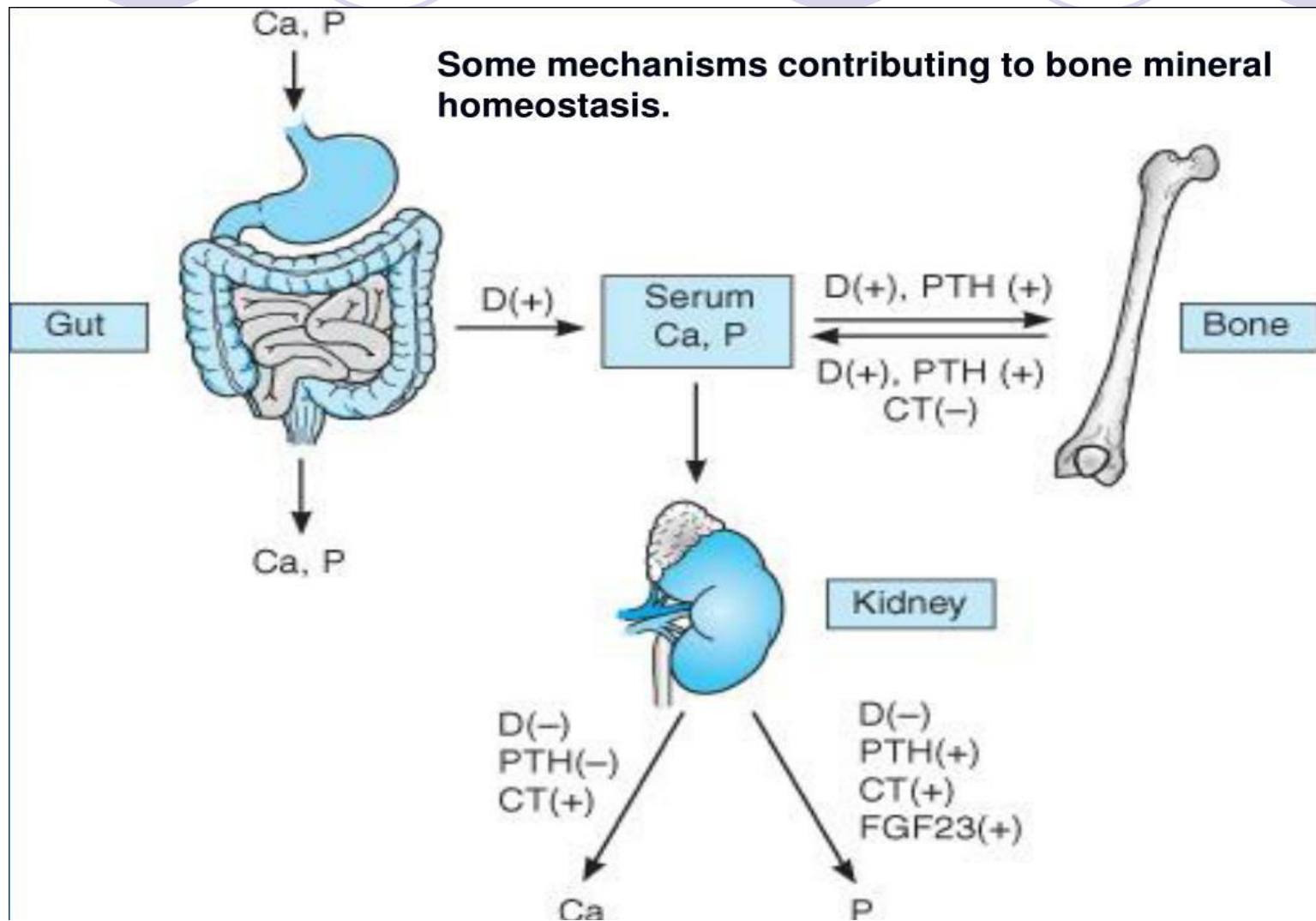
The slide features a title centered in the upper half. Below the title, there are five circles of varying shades of light purple. One circle is a thin outline, while the others are solid. They are arranged in a way that some overlap the text and others are positioned below it.

Introduction

The slide features decorative circles at the top. On the left, there is a solid light purple circle and an outlined light purple circle. On the right, there are three circles: a solid light purple circle, an outlined light purple circle, and another solid light purple circle.

- Calcium and phosphorus are the main two elements of bone.
- Parathyroid hormone (PTH) and vitamin D are primary regulators, whereas calcitonin, glucocorticoids and estrogen play secondary roles.

Some mechanisms contributing to bone mineral homeostasis.

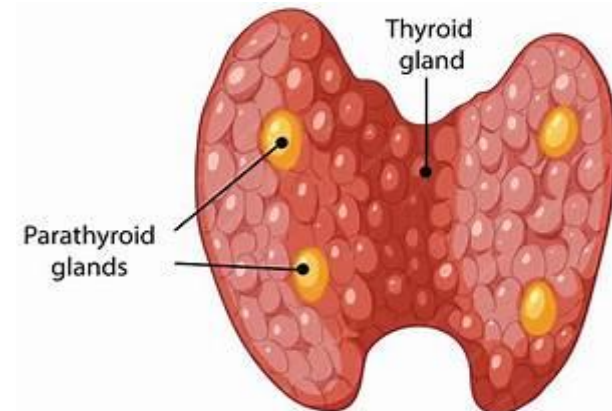


Hormonal Regulators of Bone Mineral Homeostasis

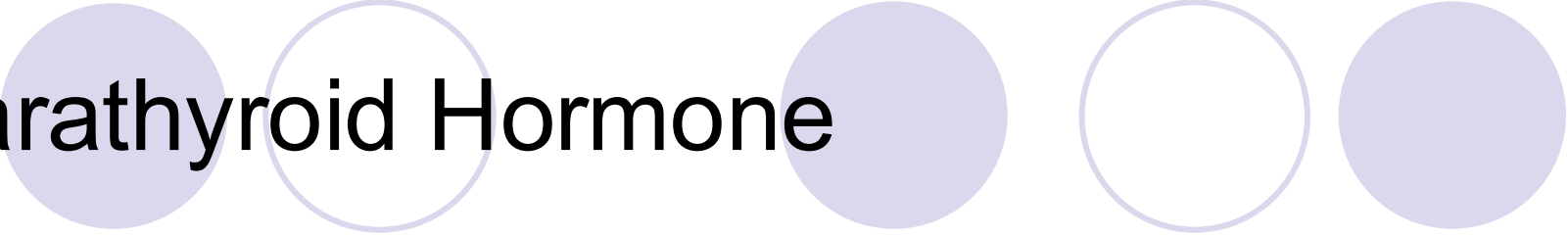
- PTH
- Vitamin D
- Calcitonin
- Estrogen
- Glucocorticoids

Parathyroid Hormone

- 84- amino acid peptide
- In **kidney**: -inhibit Ca excretion , promote phosphate excretion and stimulate the production of vitamin D.
- In **Intestine**: Indirectly increase calcium and phosphorus absorption due to the production of Vitamin D.



Parathyroid Hormone



- In **Bone**: Increase calcium and phosphate resorption by increasing the activity of both osteoclast and osteoblast. So, increase bone turnover.
- The net result is: ↑ Serum calcium
↓ Serum Phosphate
↑ Bone resorption

Parathyroid Hormone

- At moderate doses: ↑ Bone formation. As a result: **Teriparatide** is a drug modified from PTH used in treatment of osteoporosis.



Vitamin D

- Can be synthesized in the skin from 7-dehydrocholesterol under influence of ultraviolet light.
- Absorb from the diet (Cholecalciferol) or from the plant (Ergocalciferol).
- Active metabolites form in liver (25 hydrovitamin D or calcidiol) and Kidney (1,25 dihydrovitamin D or calcitriol).



Vitamin D

- It has a great effect in increasing the absorption of calcium and phosphate from the gastrointestinal tract.
- 1^α - hydroxyvitamin D (**Doxercalciferol**) is a prodrug that is converted in the liver to 1,25-dihydroxyvitamin D. Therefore, it is useful in patients with chronic kidney disease (CKD), where renal activation of vitamin D is impaired.
- Clinical use Mainly used for:
- Secondary hyperparathyroidism
- in CKD patients.





- **Paricalcitol** and **Calcipotriene** are analogs of calcitriol.
- These drugs causes less hypercalcemia than calcitriol.
- Paricalcitol suppress PTH hormone secretion. Unlike calcitriol, it has much less effect on intestinal calcium and phosphate absorption. Therefore, it lowers PTH without markedly increasing serum calcium or phosphate. Clinical use: Secondary hyperparathyroidism in patients with chronic kidney disease.

Vitamin D



- **Over dose of vitamin D:**

- Hypercalcemia
- Hyperphosphatemia
- Hypercalciuria

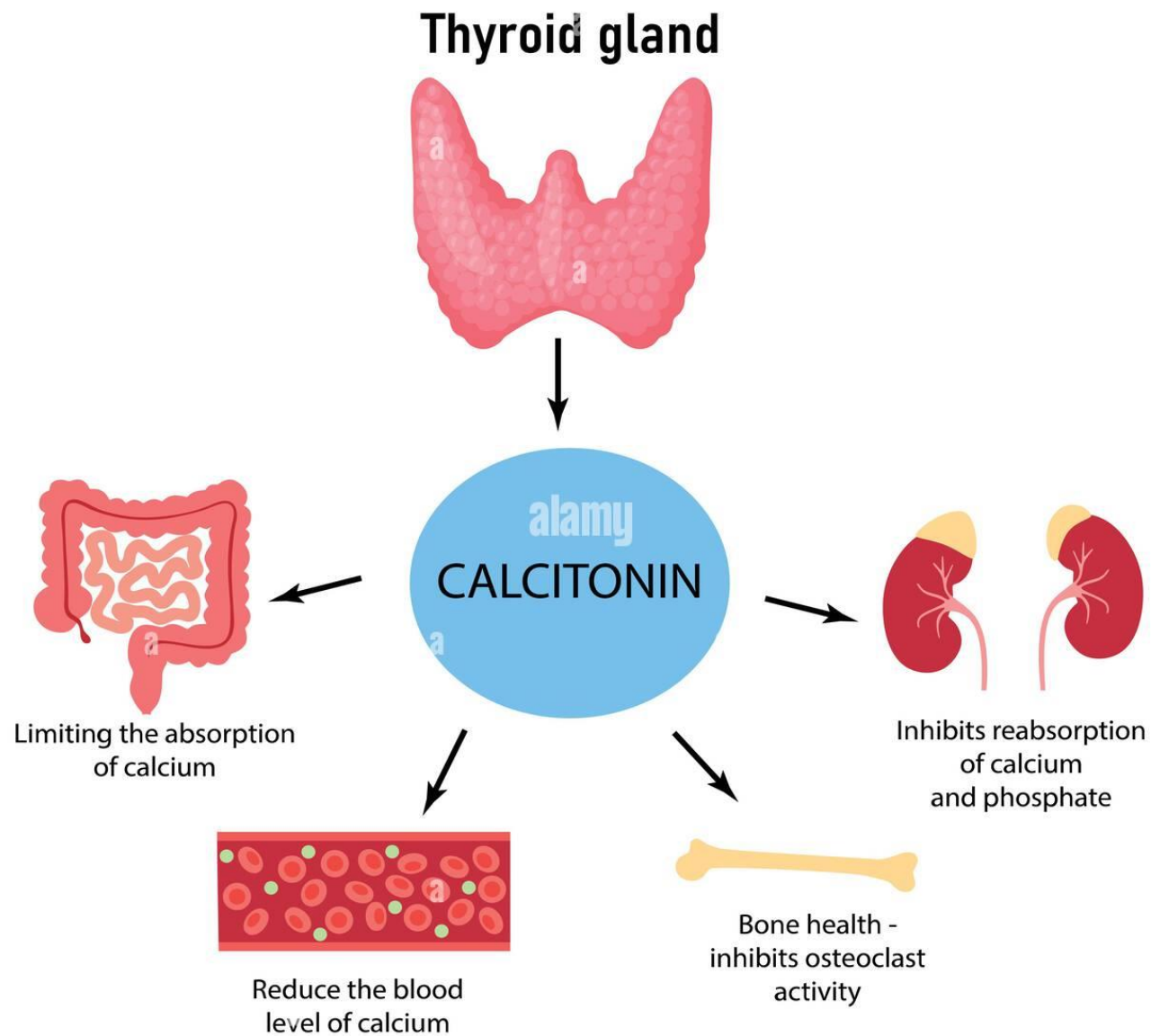
Patients may develop

- kidney stones
- constipation
- confusion
- Arrhythmias **WHY???**



Calcitonin

- Peptide hormone secreted by thyroid gland.
- ↓ Calcium and Phosphate in serum by inhibition of bone resorption.
- Used in acute conditions where high serum calcium should be decreased.
- Used in treatment of osteoporosis.



Calcitonin

- **Salmon calcitonin** is used by injection and nasal spray because of its high half life and potency.

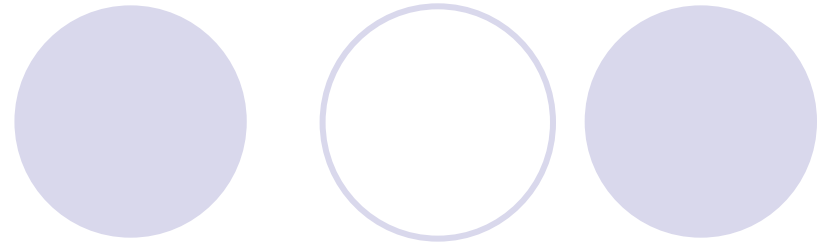


Estrogens

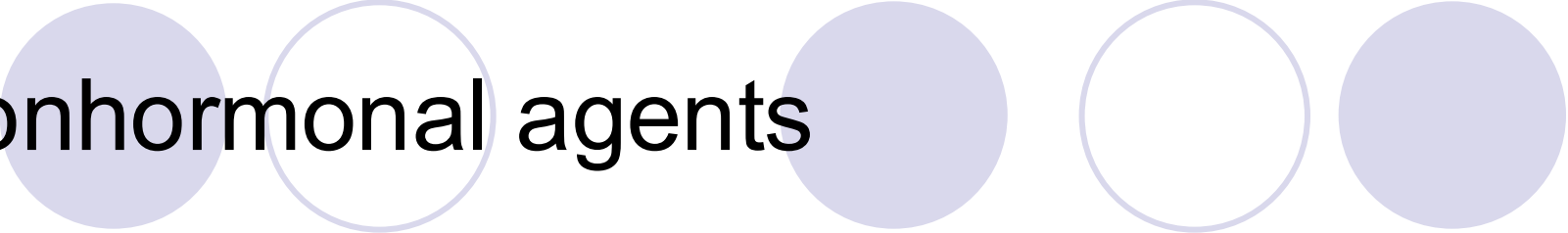
- Estrogens and selective estrogen receptor modulators (**Raloxifene**) prevent and delay bone loss in postmenopausal women.
- Their action involve the inhibition of PTH-stimulated bone resorption.
- Estrogens may cause breast and endometrial cancers where raloxifene does not cause it.



Glucocorticoids



- Inhibit bone mineral maintenance.
- Chronic use of glucocorticoids (Cortisone and prednisolone) is a common cause of osteoporosis.
- Might be useful in ↓ hypercalcemia.
- Decrease osteoblast activity, increase osteoclast survival, decrease intestinal calcium absorption, and increase renal calcium excretion.

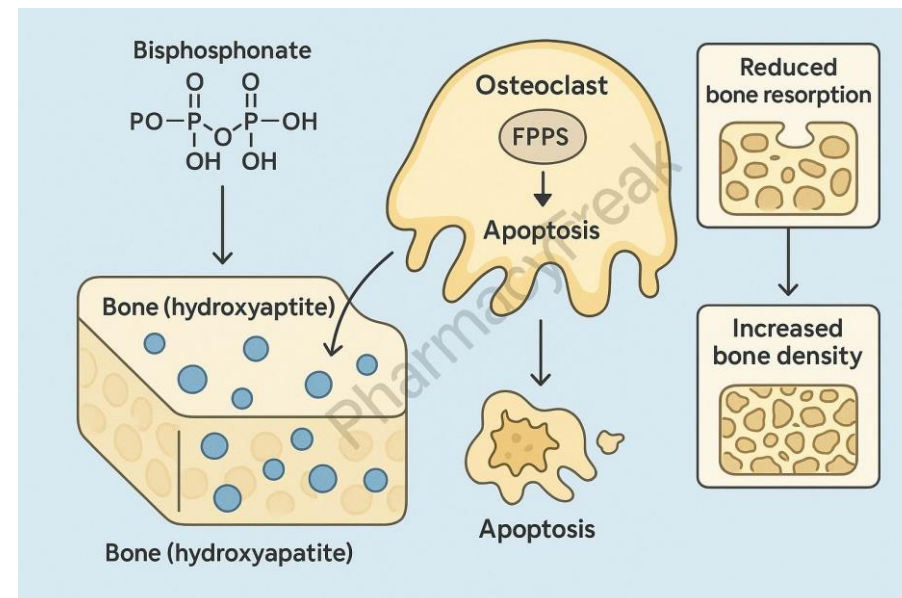


Nonhormonal agents

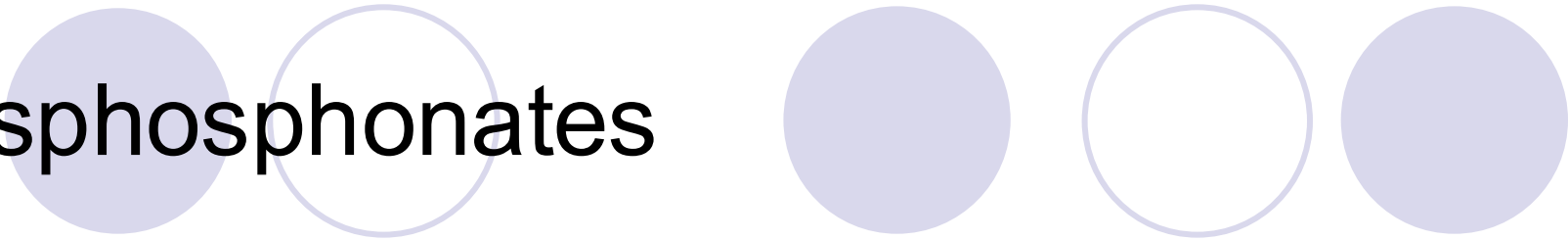
- Bisphosphonates
- Calcimimetics

Bisphosphonates

- Reduce both bone formation and resorption of the bone.
- Has a direct effect on the osteoclast cell by inhibition of farnesyl pyrophosphate which play a role in the survival of the osteoclast.



Bisphosphonates



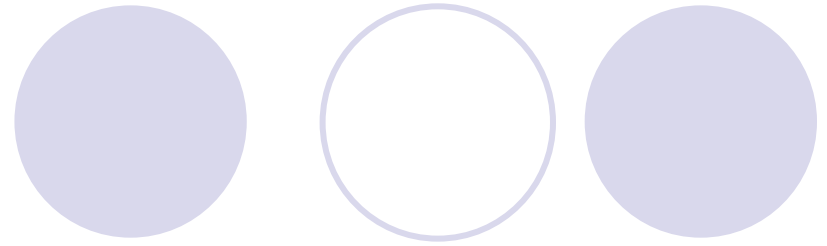
- Is used for management of hypercalcemia.
- Chronic administration of bisphosphonate is used in treatment of all kinds of osteoporosis.
- **The primary toxicity of bisphosphonate is gastric and esophageal irritation.** To reduce the irritation, patient is advised to take a large quantity of water and avoid situations which permit esophageal reflux.

Bisphosphonates

- Examples of bisphosphonate: Alendronate and pamidronate.



Calcimimetics



- Lower the parathyroid hormone by activation of calcium-sensing receptor in the parathyroid gland. The gland thinks calcium is high >>>> ↓Less PTH secretion>>>>> ↓Lower calcium. Uses: Secondary hyperparathyroidism, and parathyroid carcinoma.
- Reduce serum calcium.
- Toxicity: hypocalcemia.
- Example: Cinacalcet

