



Endocrine  
System

**PHARMACOLOGY**  
**432 TEAM**



## drugs used in calcium & vitamin D disorders

### Learning Objectives:

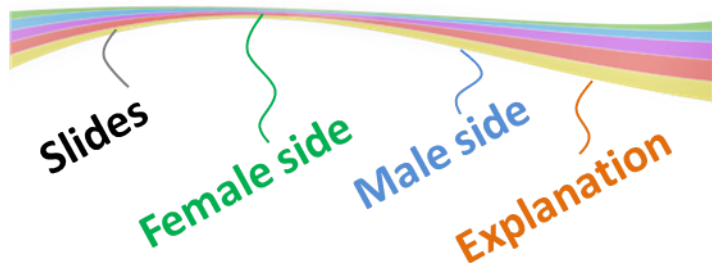
1. Recognize the common drugs used in calcium & vitamin D disorders
2. Classify them according to sources & Pharmacological effects
3. Detail the pharmacology of each drug , regarding , Mechanism, clinical utility in affecting calcium & vitamin D

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**BONE:**

Is a dynamic organ undergoes continuous remodeling process involving resorption of old bone by osteoclast & formation of new bone by osteoblast

**The principal agents involved in calcium metabolism & bone remodeling are :**

Parathyroid hormone ( PTH)

Teriparatide

calcitonin

vitamin D

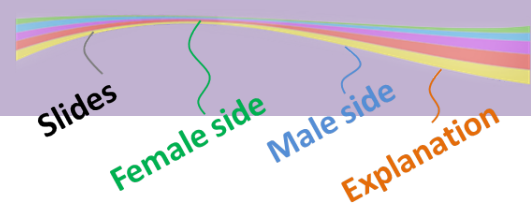
**The target tissues :**

Bone

kidney

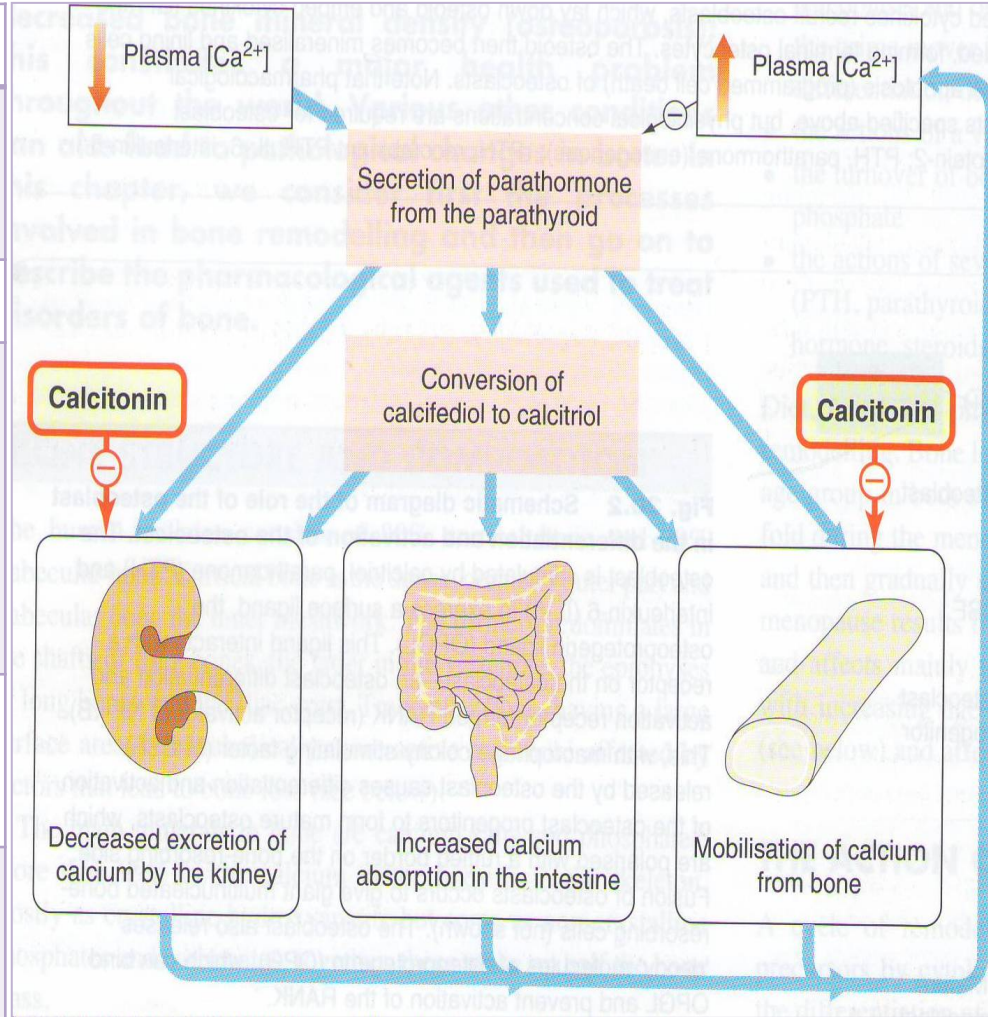
Intestine

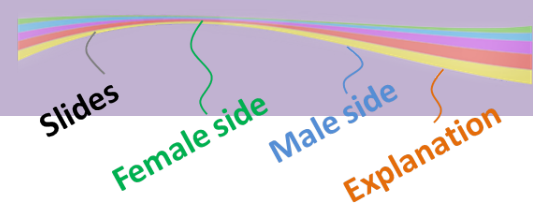




**Physiologically:**

<b><u>Produced by</u></b>	<b>Parathyroid cells.</b>
<b><u>Released when</u></b>	There is an <b>decreased level of Ca<sup>2+</sup> in the blood (hypocalcemia).</b>
<b><u>Effects:</u></b>	
<b>BONE</b>	<p><b>Mobilization of Ca<sup>2+</sup> and PO<sub>4</sub><sup>3-</sup> from bone to blood</b></p> <p>In response to <b>hypocalcemia</b> , PTH <b>stimulates osteoclast</b> cells to increase the outward flux of calcium to restore serum calcium level.</p>
<b>Kidney</b>	<p>↑ Ca<sup>2+</sup> reabsorption</p> <p>↑ formation of calcitriol (which is the active form of Vit. D)</p>
<b>GIT</b>	<p>↑ absorption of Ca<sup>2+</sup></p> <p>( effect mediated via calcitriol )</p>

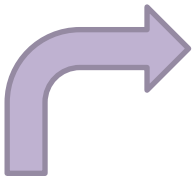




**As a drug;**

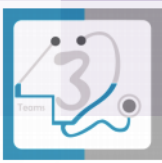
When given as infusion the action depends on whether it is **INTERMITTENT** (in sever cases for ( 1 or 2 hour only )) or **CONTINUOUS** (it's usual action)

PTH	
<u>Intermittent</u>	<u>Continuous</u>
↑ osteoblast number/function	↑ Osteoclast (Mobilization of Ca and PO4 from bone)
↑ bone formation	↑ bone resorption
↑ <u>bone mass/strength</u>	↑ <u>serum Ca<sup>++</sup></u>

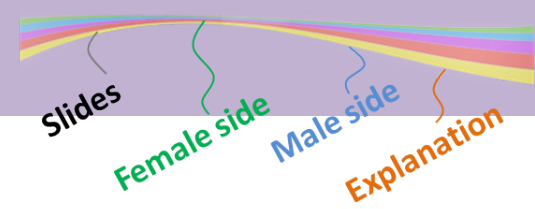


**INTERMITTENT** → used for severe osteoporosis when other drugs fail

“**Not** the drug of choice in treating osteoporosis  
Only if: very sever or if there is a resistant to other drugs”



## 2) Teriparatide

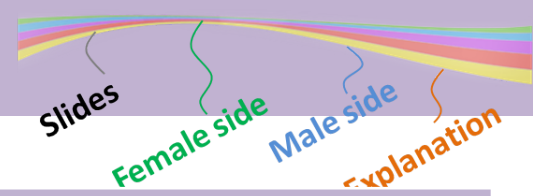


Teriparatide	Skeletal effects	uses	S/E	Contraindications
<p>Synthetic polypeptide form of PTH ( <b>PTH analogue</b> ).</p> <p>Given, once / daily / <u>subcutaneous injection</u></p>	<p>Stimulates <b>new bone formation</b> on trabecular and cortical bone surfaces by stimulating <b>osteoblastic</b> activity over osteoclastic activity.</p> <p>The <b>anabolic effects</b> of teriparatide are manifested as an <u>increase in skeletal mass &amp; strength.</u></p>	<p><b>Osteoporosis in :</b></p> <ul style="list-style-type: none"> <li>- in postmenopausal women at high risk of fracture.</li> <li>-Hypogonadal men at high risk of fracture.</li> </ul> <p><b>-Used in sever osteoporosis or patients not responding to other drugs.</b></p>	<ul style="list-style-type: none"> <li>-Diarrhea, heart burn, nausea, headache, leg cramps</li> <li>-Hypotension when standing .</li> <li>-Elevated serum calcium can occur in some cases leading to kidney stones <b>If percipetated</b></li> <li><b>-Carcinogenic effect (osteosarcoma)</b></li> </ul>	<p>Should not be used by people with increased risk for bone tumors <b>((osteosarcoma))</b> <b>including :</b></p> <ul style="list-style-type: none"> <li>- <u>Paget's disease of bone*</u></li> <li>- <u>Radiation treatment involving bones</u></li> </ul>

**\*Paget's disease :** is a chronic disorder that can result in enlarged and misshapen bones. Paget's is caused by the excessive breakdown and formation of bone, followed by disorganized bone remodeling



### 3) Vitamin D:



#### **Vitamin D2; Ergocalciferol**

Vitamin D2 is the prescription form of vitamin D & is also used as food additive  
In diet, it is rich in milk, egg yolk, fish oils

#### **Vitamin D3; Cholecalciferol**

Vitamin D3 is the form present in vitamin D-fortified milk & foods & also available in drug combination products.  
**Generated in the skin from 7- dehydrocholesterol by the action of ultraviolet radiation (sunshine).**

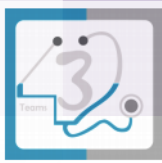
They initially transforms in **liver** to **25-(OH)D3 ( Calcifediol )** the main storage form of Vit D in our body

In the **kidney**, **parathyroid hormone** stimulates the formation of **ACTIVE** form of vitamin D ( **Calcitriol** ) { **1,25-(OH)2 D3** }

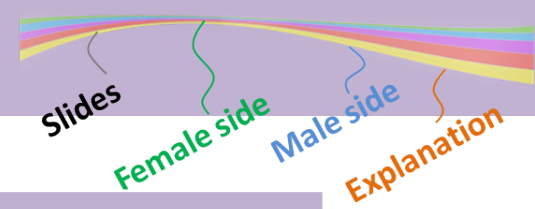
#### **Mechanism of Action**

<b><u>GIT</u> :</b>	Increased absorption of $\text{Ca}^{2+}$ & $\text{PO}_4$
<b><u>Kidney</u> :</b>	Increased reabsorption of $\text{Ca}^{2+}$ & $\text{PO}_4$ . (decrease its excretion)
<b><u>Bone</u> :</b>	Activation of osteoblast cells & increase bone mineralization
<b><u>PTH</u>:</b>	decreases the production of PTH by the parathyroid glands

The overall effect of vitamin D is to increase plasma  $\text{Ca}^{2+}$  concentrations



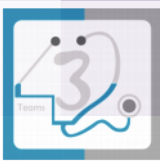
## : 4) Calcitonin



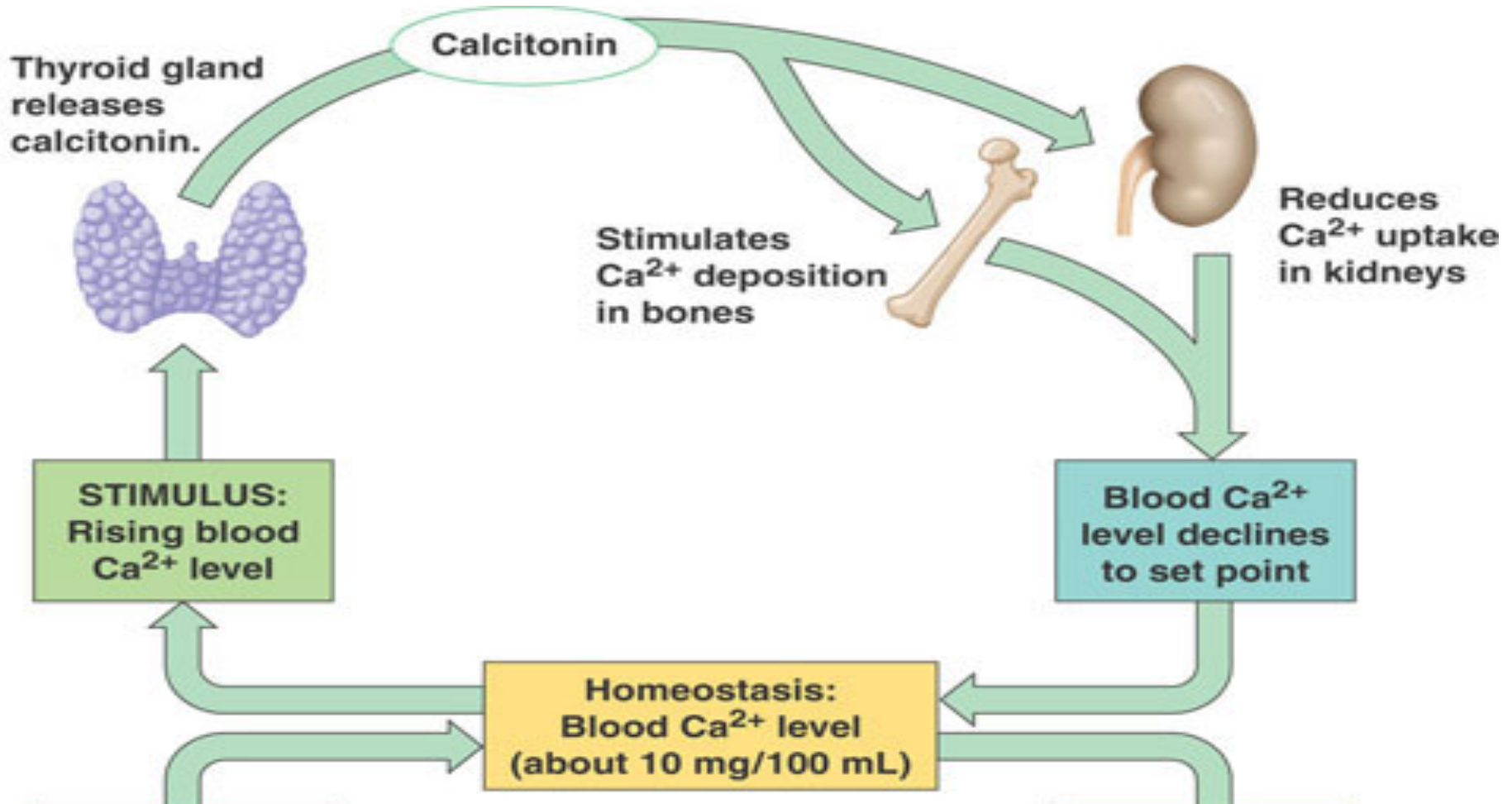
<b>Produced by</b>	the parafollicular cells (C cells) of the thyroid gland .
<b>released when</b>	there is an <b>elevated level of Ca<sup>2+</sup></b> in the blood(hypercalcemia) .
<b>Effects</b>	
<b>Bone :</b>	Stimulates calcium deposition
<b>Kidney :</b>	Decreases reabsorption of Ca <sup>2+</sup>

### As a drug;

<b>Administered</b>	S.C. or Nasal spray ( salmon calcitonin)
<b>Mechanism of Action</b>	<b>Bone :</b> Decrease bone resorption by inhibiting osteoclast activity
<b>Uses</b>	<ol style="list-style-type: none"> <li>1- Osteoporosis</li> <li>2- Hypercalcemia (<b>short-term treatment of hypercalcemia of malignancy</b>) <u>Ex:</u> Pagets disease</li> </ol>
<b>Adverse effects</b>	<ol style="list-style-type: none"> <li>1- Nausea</li> <li>2- Local inflammation ( at the side of injection )</li> <li>3- Flushing of face &amp; hands</li> <li>4- Nasal irritation</li> </ol>



**Calcitonin does not appear to be critical for the regulation of calcium homeostasis even if thyroid gland is removed !!!**







**Q1) Parathyroid hormone is synthesized as a response to:**

- A. High  $\text{Ca}^{++}$
- B. Low  $\text{Ca}^{++}$

**Q2) Which of the following is a mechanism of action of teriparatide in treatment of osteoporosis?**

- A. it increases bone remodeling rate
- B. it decreases serum calcium by inhibition of bone resorption
- C. it increases intestinal absorption of phosphate
- D. it decreases renal excretion of phosphate

**Q3) Which one of the following anti-osteoporosis drugs is contraindicated in a patient with previous osteosarcoma?**

- A. Vitamin D Supplement
- B. Calcitonin nasal spray
- C. Teriparatide

Answers:

1=B 2=B 3=C



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