IMPERIAL

Regulation of calcium and phosphate

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Session plan

Calcium and phosphate homeostasis

- Roles of calcitriol and parathyroid hormone (PTH) in calcium and phosphate balance
- Vitamin D synthesis
- Regulation of parathyroid hormone
- Role of calcitonin in calcium balance

Vitamin D deficiency

- Vitamin D synthesis
- Causes of vitamin D deficiency
- Clinical features of vitamin D deficiency

Hypercalcaemia and hypocalcaemia

- Clinical features of hypocalcaemia and hypercalcaemia

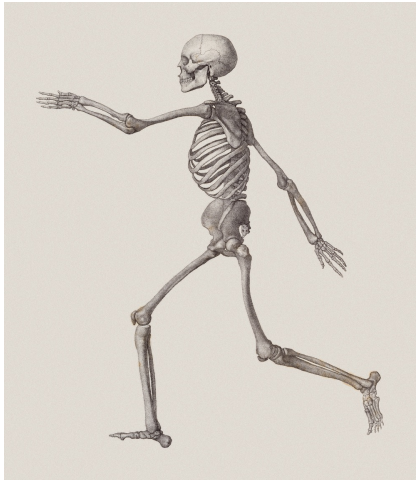
Calcium

- Most abundant **metal** in the body
- Diet should meet **all requirements**

Calcium & phosphate: Outline calcium and phosphate homeostasis and the causes and effects of dysregulation.

Calcium distribution in the body

- 99% resides in **skeleton and teeth** as calcium hydroxyapatite crystals
- Extracellular calcium (tiny amount of total body calcium) is **tightly regulated**
- **'Unbound' ionised calcium =** biologically active component



Total body calcium

- **Skeleton** (99%)
- **Intracellular** (1%)
- **Extracellular** (0.1%) This is what we measure in a blood test to measure calcium

Hormonal control of calcium

INCREASE

- **Parathyroid hormone (PTH)** (secreted by parathyroid glands)
- **Vitamin D**
  - Synthesised in skin or intake via diet

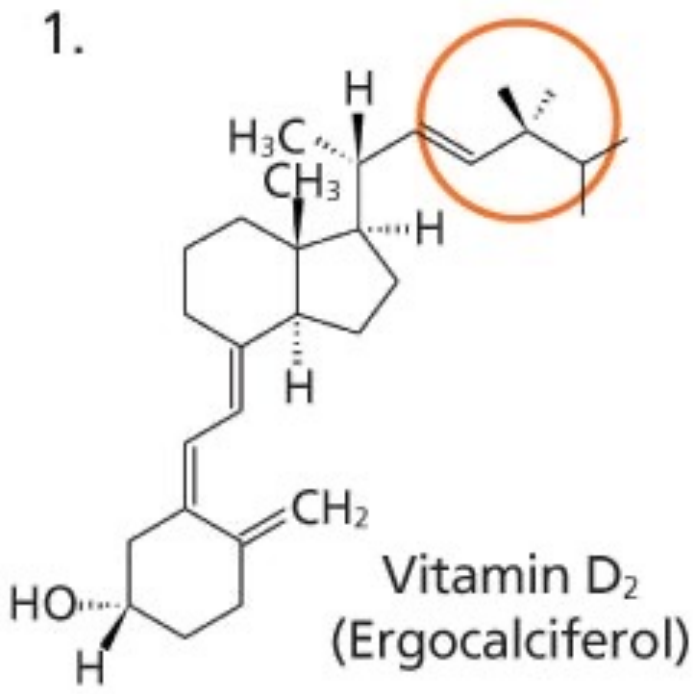
DECREASE

- **Calcitonin** (secreted by thyroid parafollicular cells)
- Can reduce calcium acutely, but no negative effect if parafollicular cells are removed eg thyroidectomy

Calcium & phosphate: Outline calcium and phosphate homeostasis and the causes and effects of dysregulation.

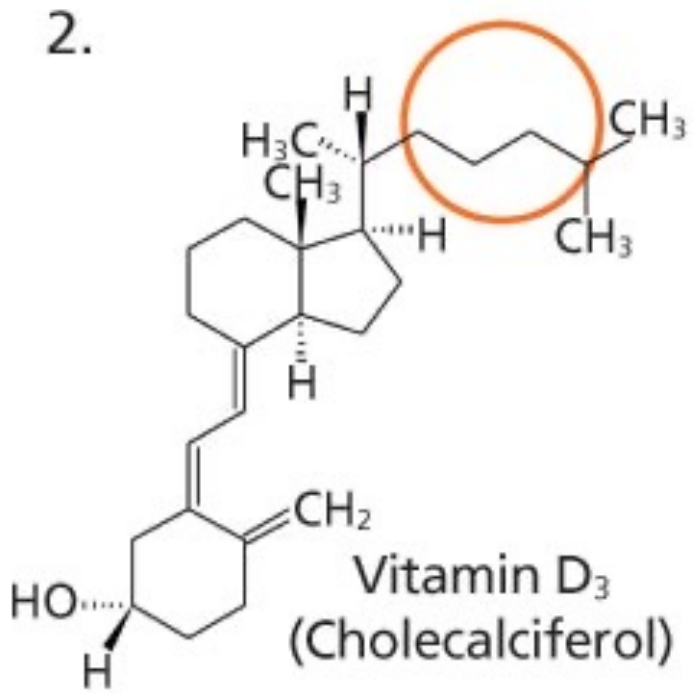
Sources of vitamin D

1.



Vitamin D_2
(Ergocalciferol)

2.



Vitamin D_3
(Cholecalciferol)

Ergocalciferol – derived from UV irradiation of plants

Cholecalciferol – derived from UV irradiation of skin (animals and humans) and certain foods (oily fish, egg yolks)

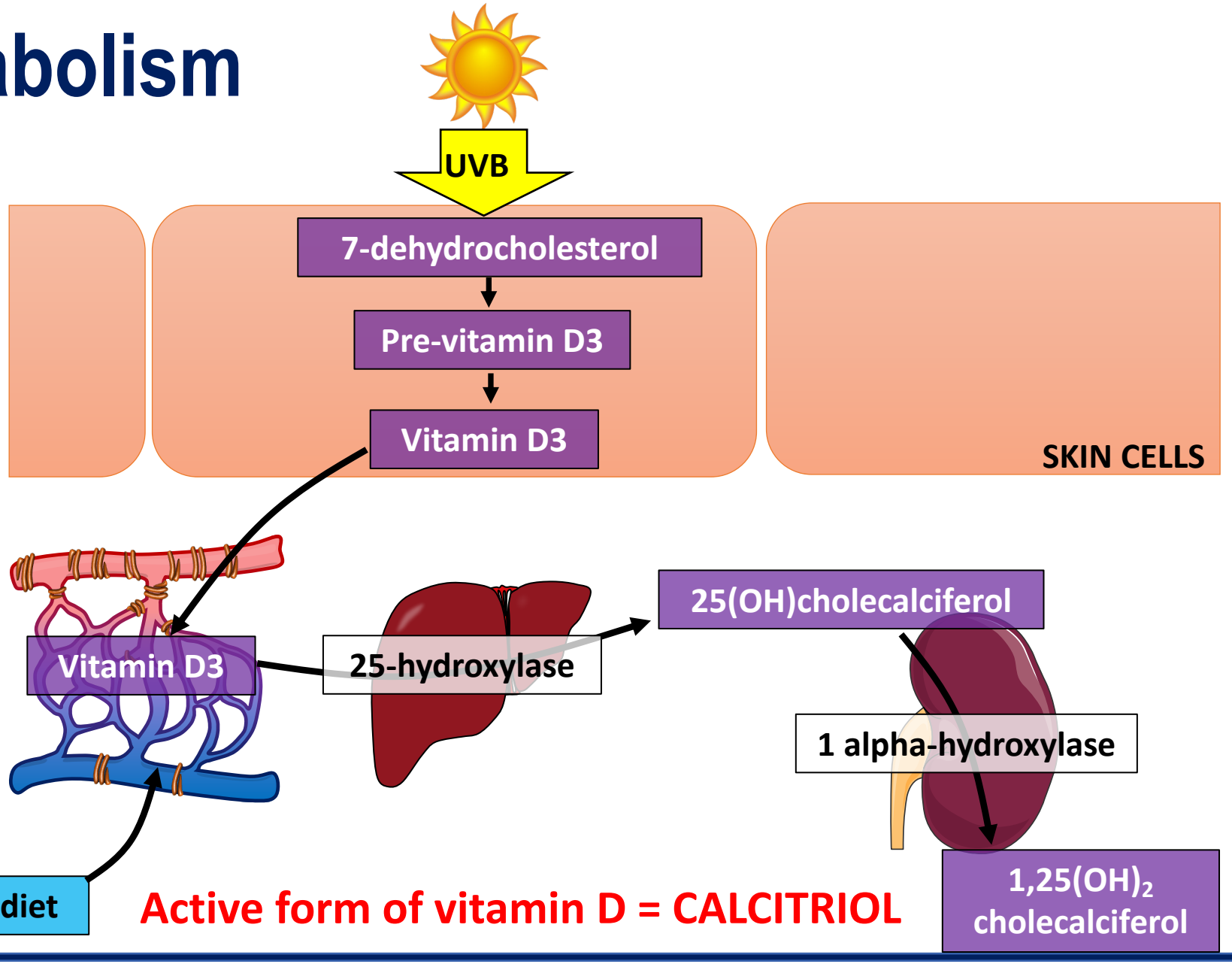
Calcium & phosphate: Outline calcium and phosphate homeostasis and the causes and effects of dysregulation.

Vitamin D metabolism

25-OH cholecalciferol

- biologically *inactive*

1,25$(OH)_2$ cholecalciferol (calcitriol) regulates its own synthesis by decreasing transcription of 1 alpha-hydroxylase

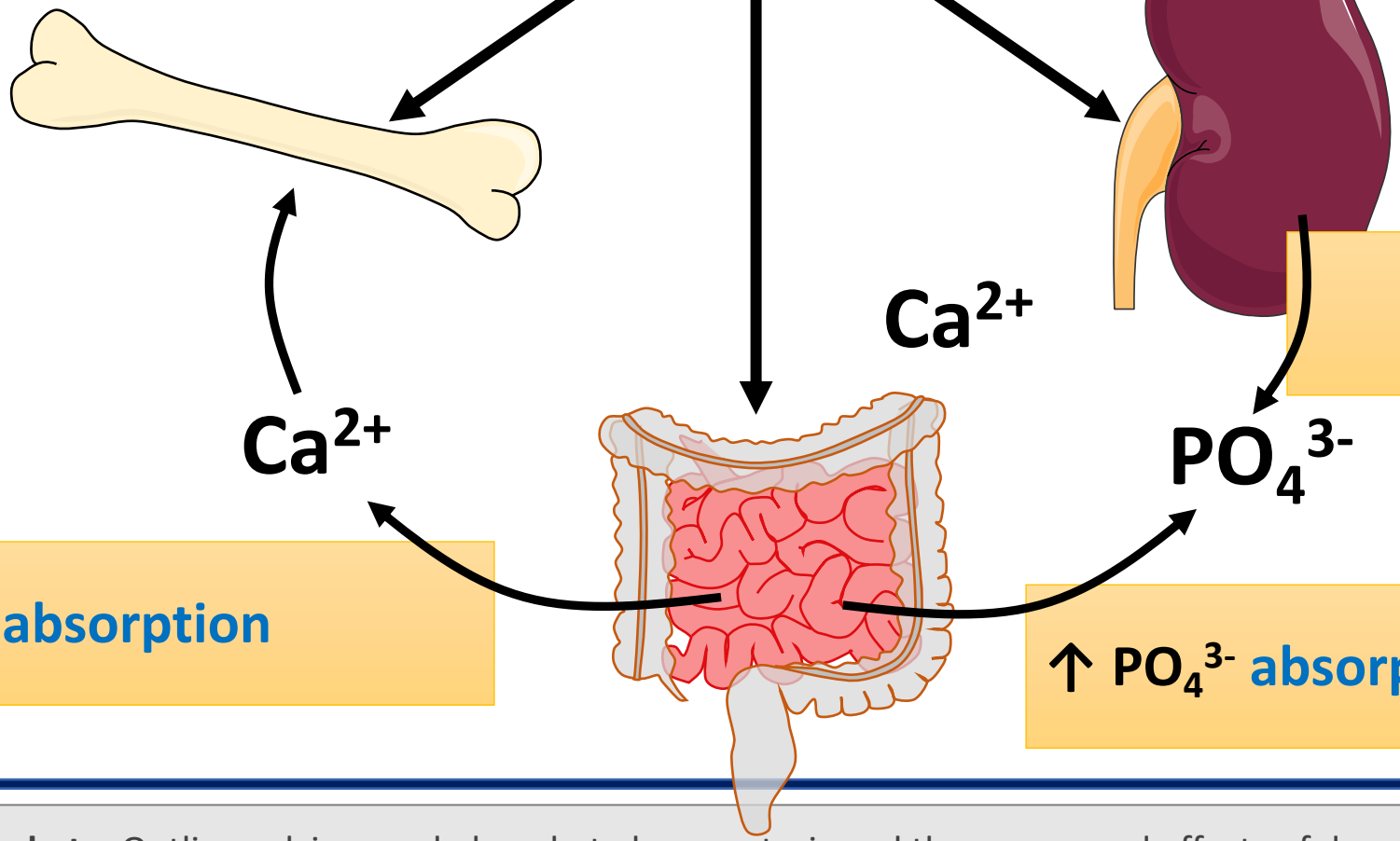


Calcium & phosphate: Outline calcium and phosphate homeostasis and the causes and effects of dysregulation.

Effects of calcitriol

MAJOR ROLE OF CALCITRIOL =
↑ Ca^{2+} and PO_4^{3-} reabsorption from the GUT
provides building blocks for bone

$1,25\ (OH)_2\ D_3$

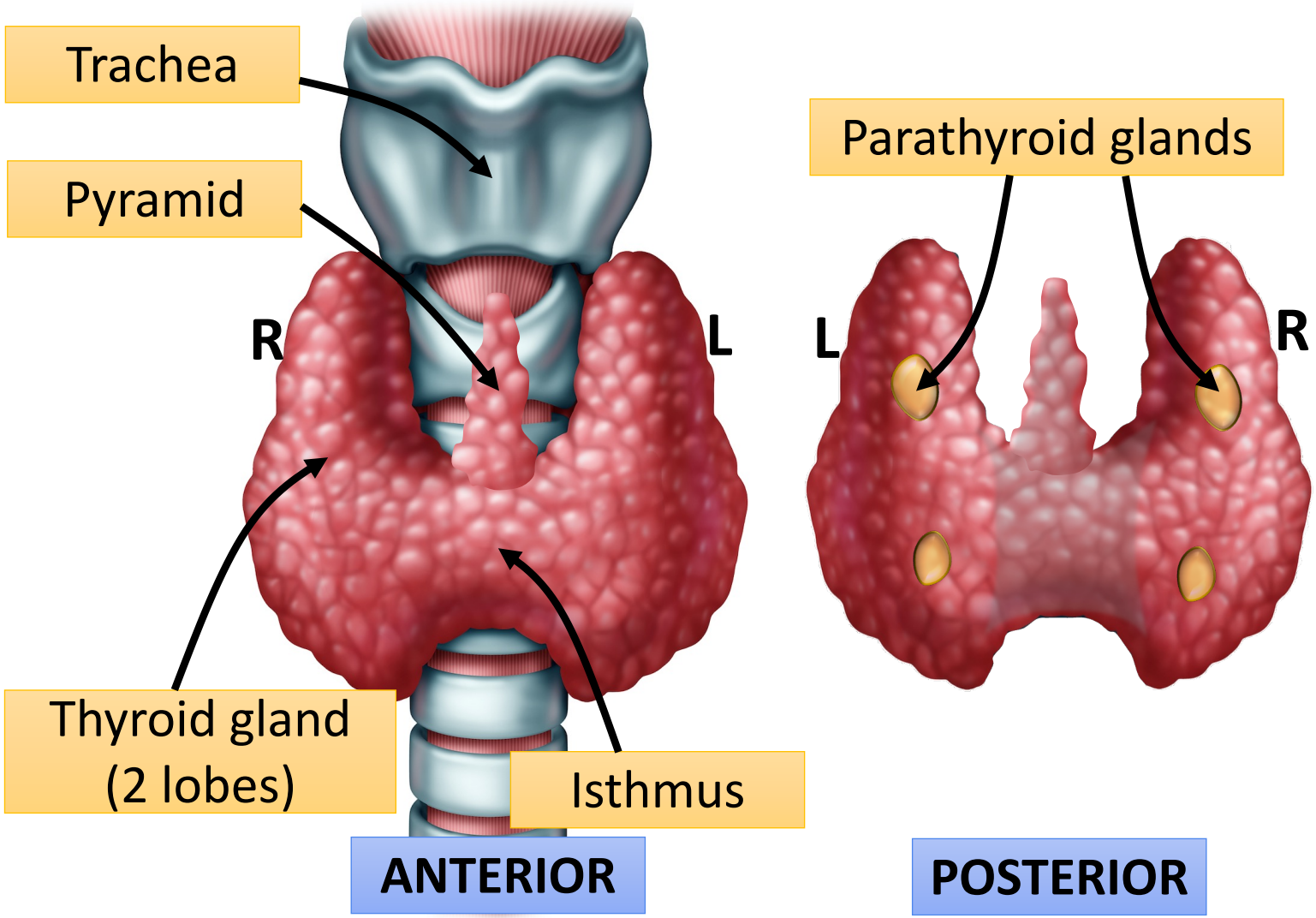


↑ Ca^{2+} and PO_4^{3-} reabsorption

↑Ca^{2+} absorption

↑ PO_4^{3-} absorption

Parathyroid hormone (PTH)



- **Chief cells** in parathyroid glands
- Secreted as a **large precursor** (pro-PTH) & cleaved to PTH
- **G-protein coupled calcium sensing receptor** on chief cells detects change in circulating calcium concentration
- PTH secretion **inversely proportional** to circulating calcium

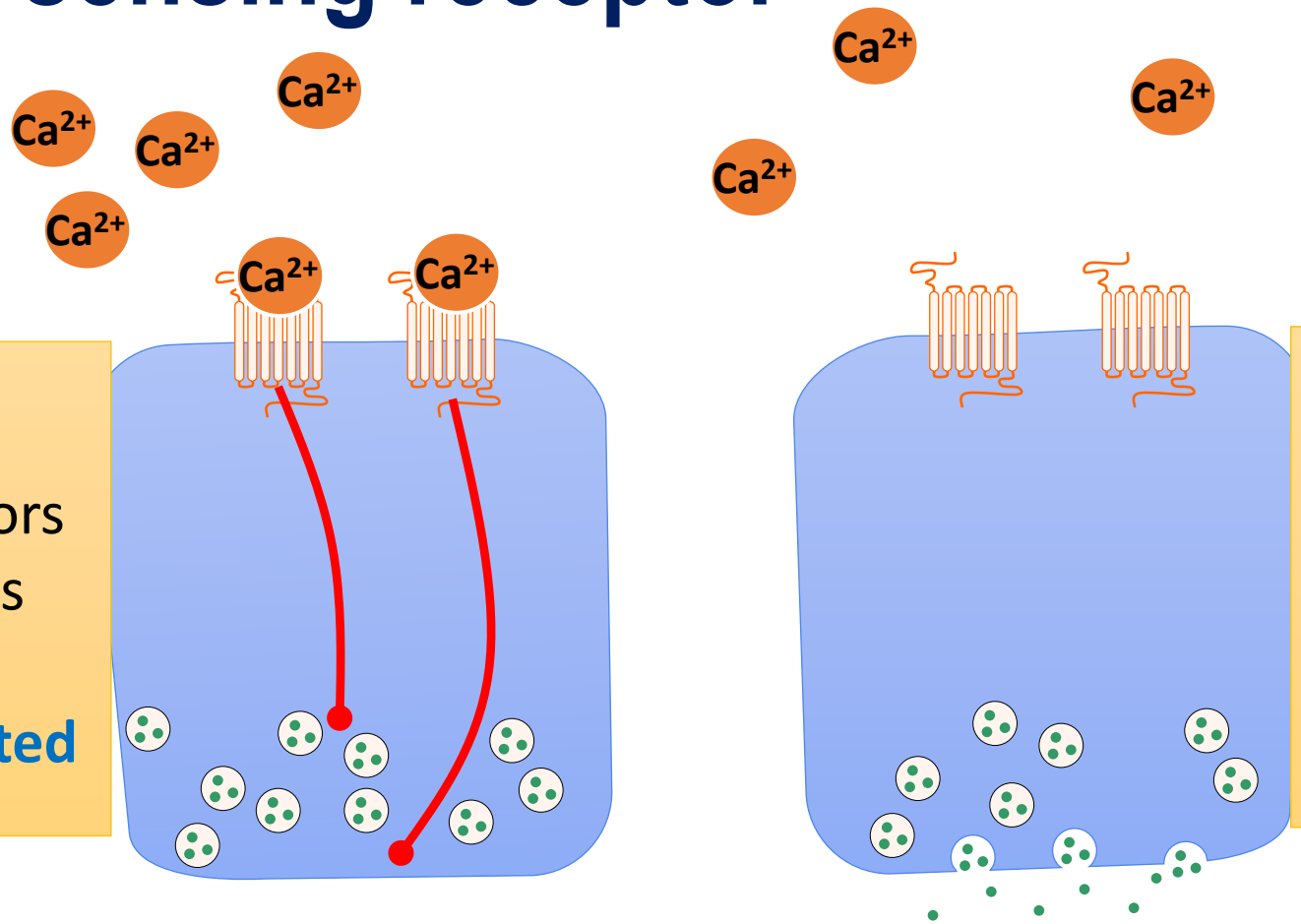
Calcium & phosphate: Outline calcium and phosphate homeostasis and the causes and effects of dysregulation.

Calcium sensing receptor

High [Ca^{2+}]

Ca^{2+} binds to receptors on parathyroid cells

PTH secretion inhibited



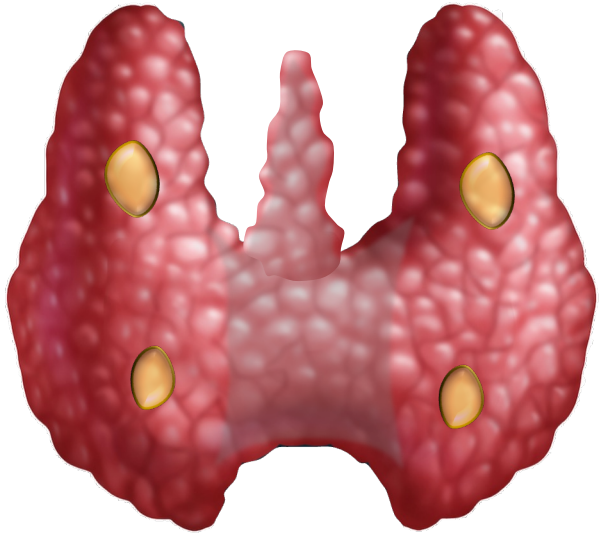
Low [Ca^{2+}]

Less Ca^{2+} binding to receptors on parathyroid cells

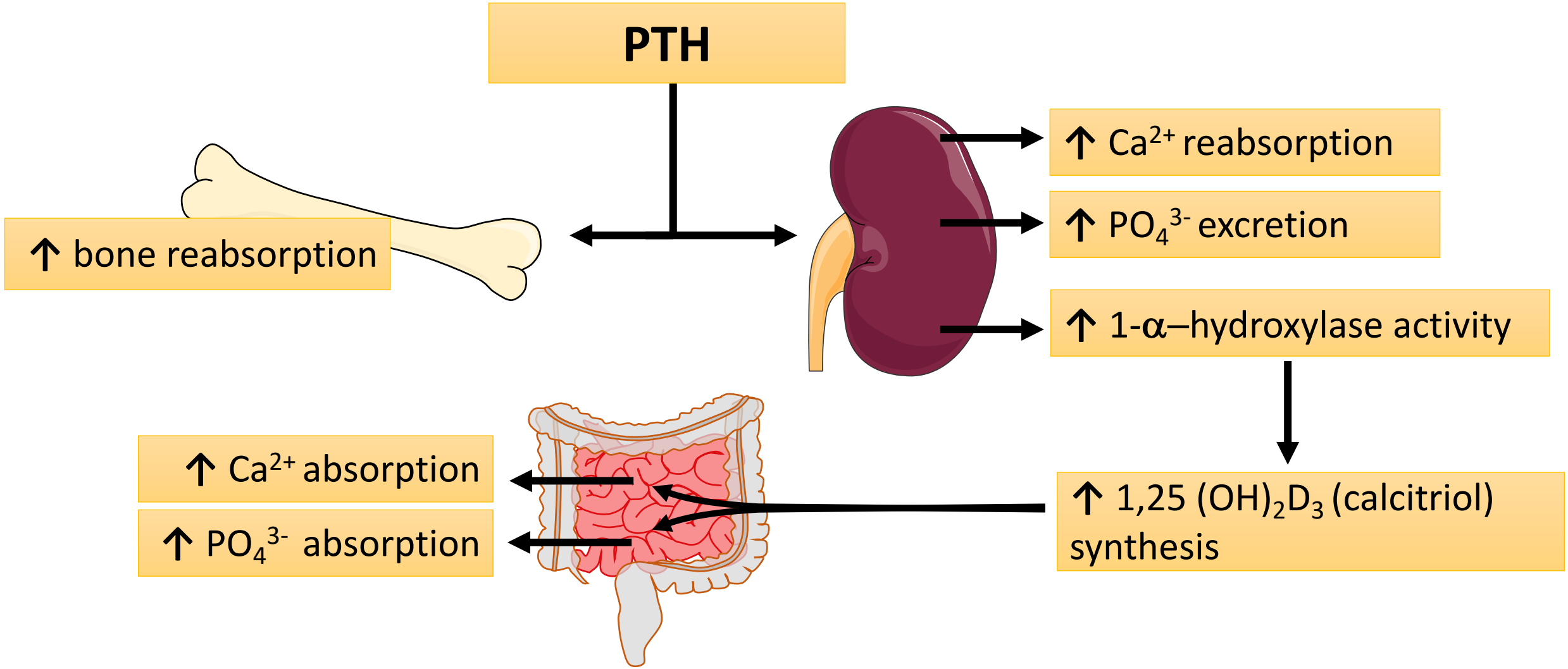
PTH secreted

MENTIMETER QUESTION

When calcium in the bloodstream (serum/plasma calcium) increases, what happens to parathyroid hormone (PTH)?

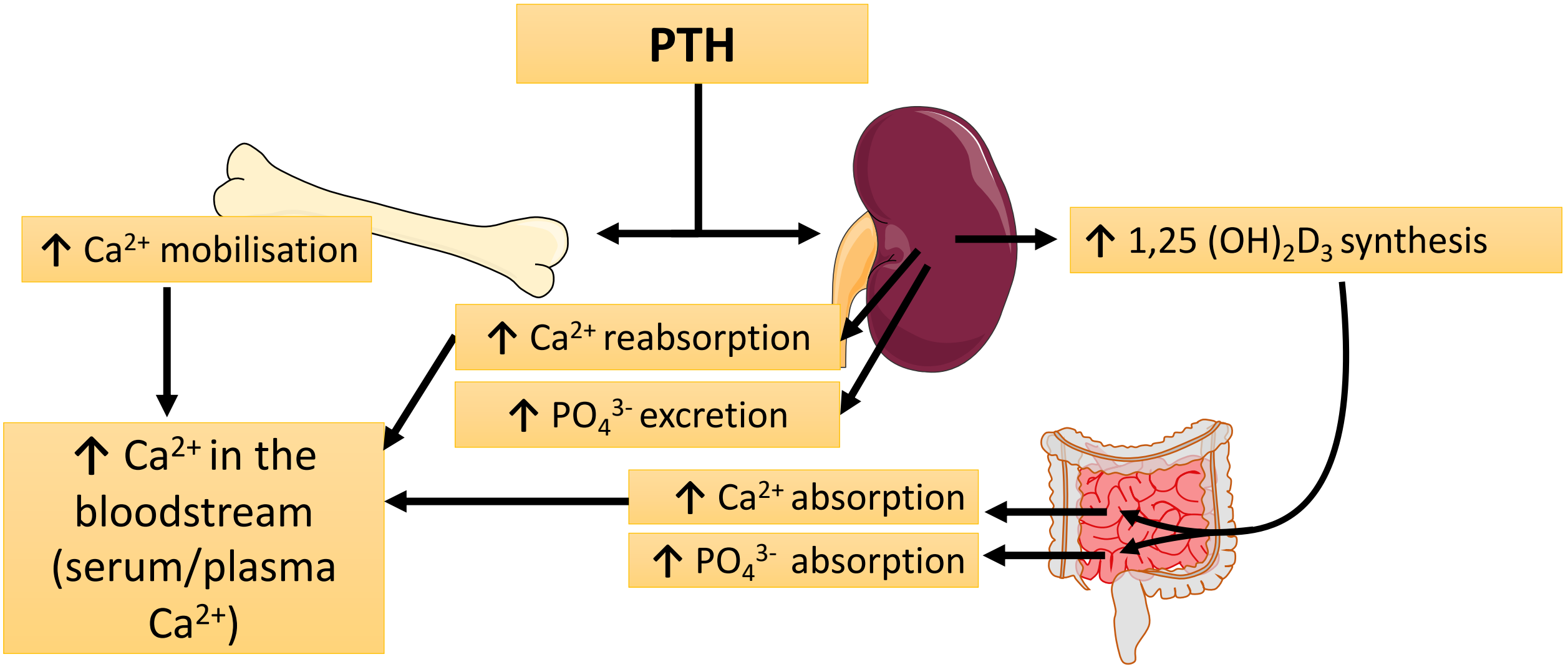


Actions of parathyroid hormone (PTH)



Calcium & phosphate: Outline calcium and phosphate homeostasis and the causes and effects of dysregulation.

Regulation of calcium & phosphate by PTH



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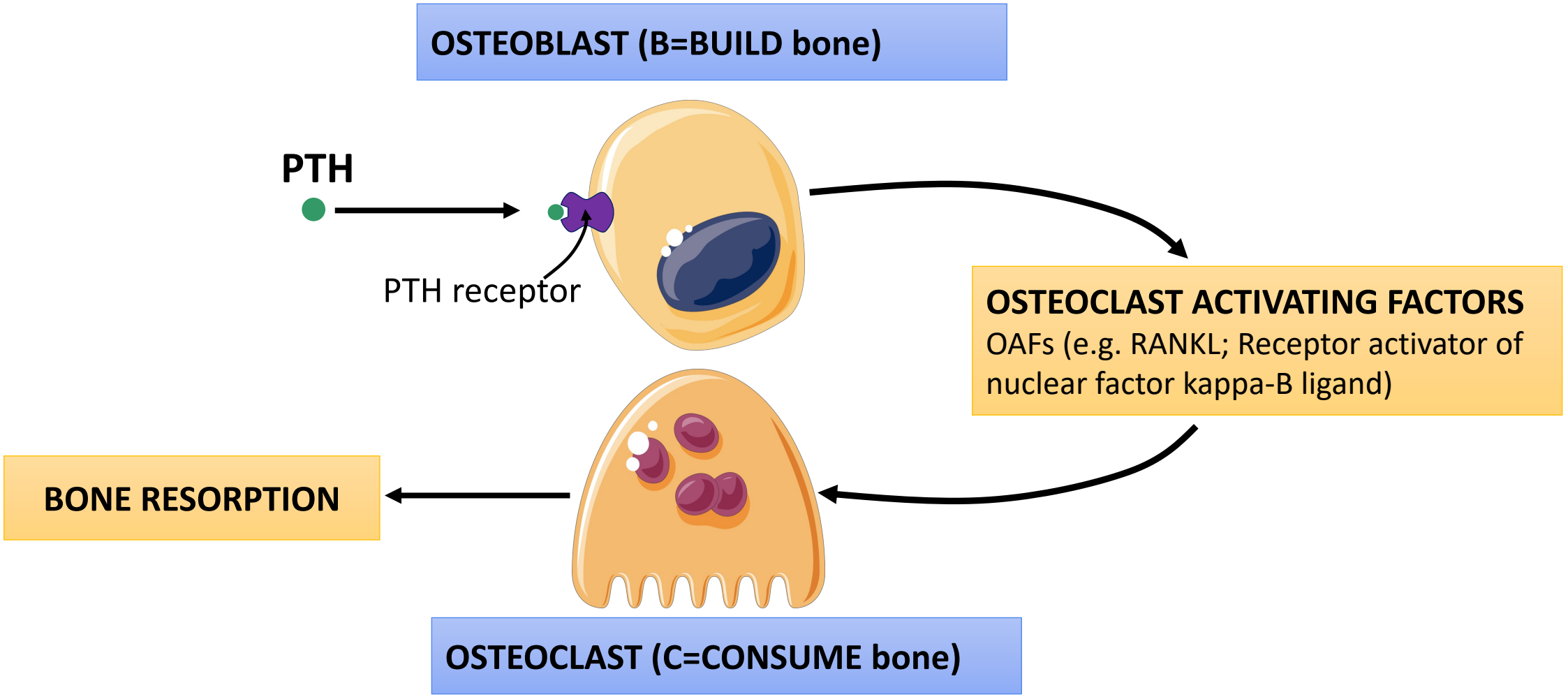
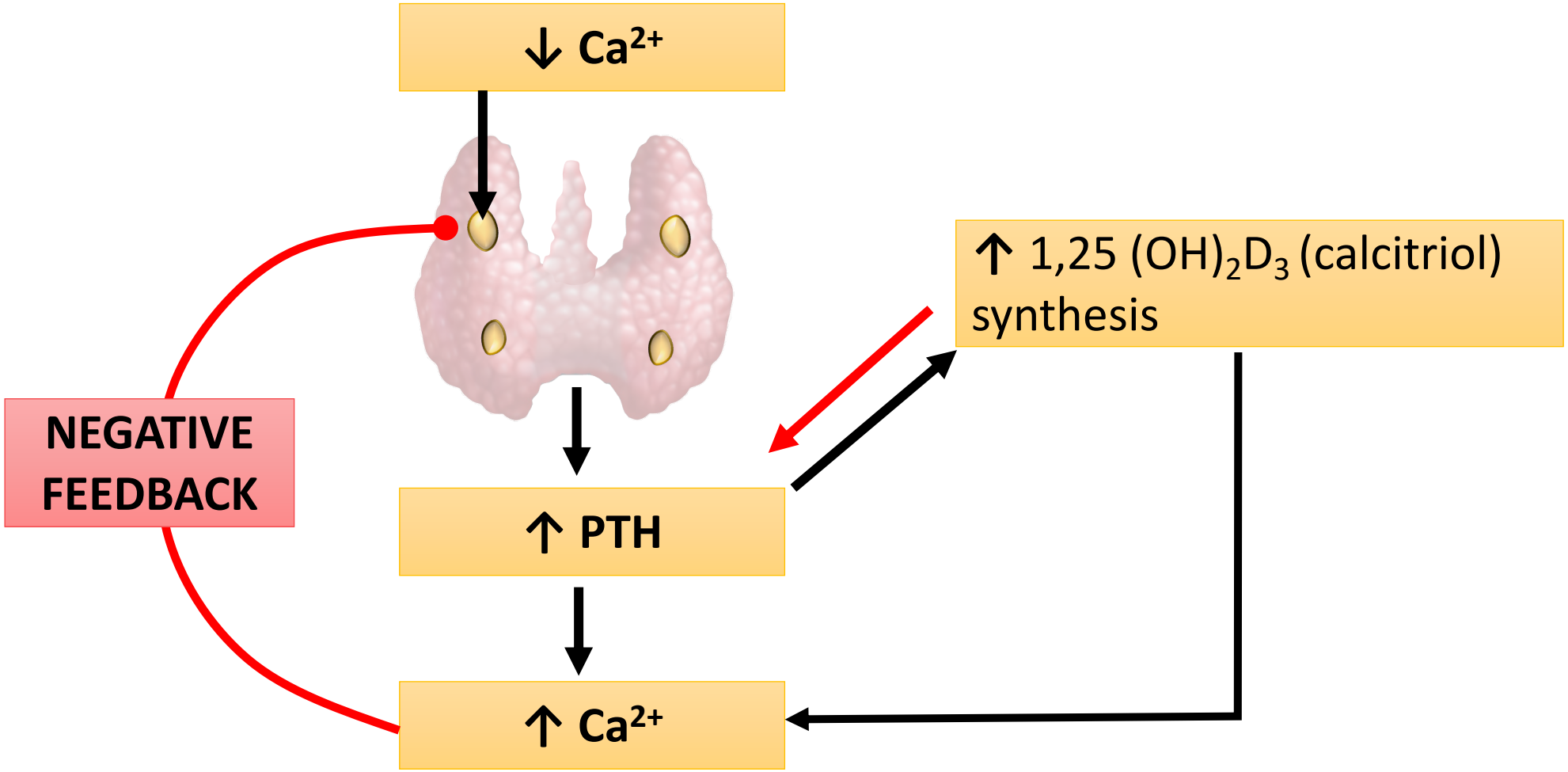
PTH action in bone



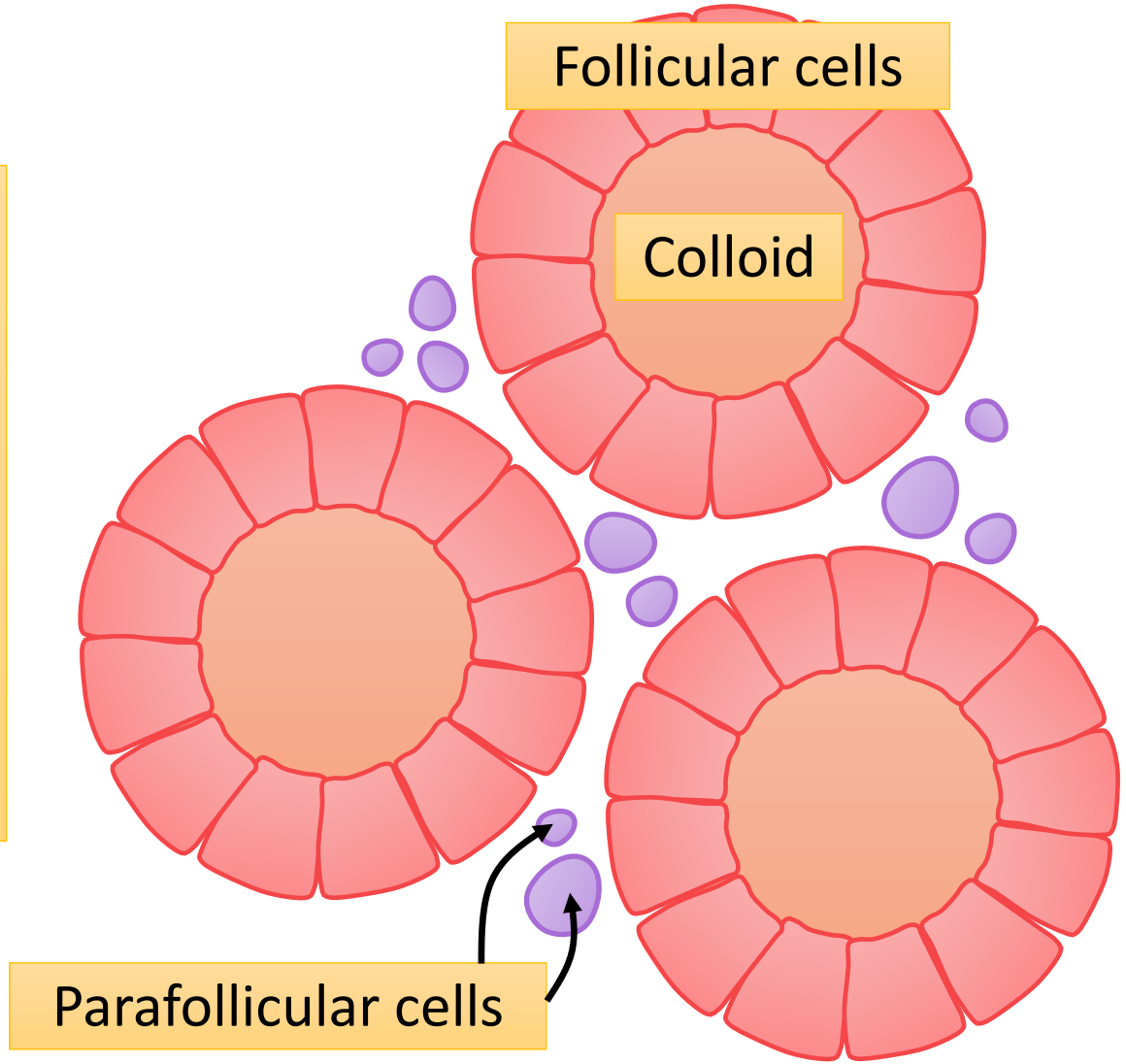
PTH regulation



Calcium & phosphate: Outline calcium and phosphate homeostasis and the causes and effects of dysregulation.

Calcitonin

- Secreted from **parafollicular (C) cells** of the thyroid gland
- Reduces serum calcium
- Physiological role in **calcium homeostasis in humans unclear**
- Removal of thyroid gland does not affect calcium levels in the bloodstream



Calcium & phosphate: Outline calcium and phosphate homeostasis and the causes and effects of dysregulation.

Abnormal calcium metabolism

HIGH serum calcium = **HYPERCALCAEMIA**
LOW serum calcium = **HYPOCALCAEMIA**

Action potential generation in nerves/skeletal muscle requires Na^+ influx across cell membrane

HIGH extracellular calcium (HYPERcalcaemia)

Ca^{2+} blocks Na^+ influx, so **LESS** membrane excitability

LOW extracellular calcium (HYPOcalcaemia)

enables GREATER Na^+ influx, so **MORE** membrane excitability

Hypocalcaemia

Sensitises excitable tissues; muscle cramps, tetany, tingling

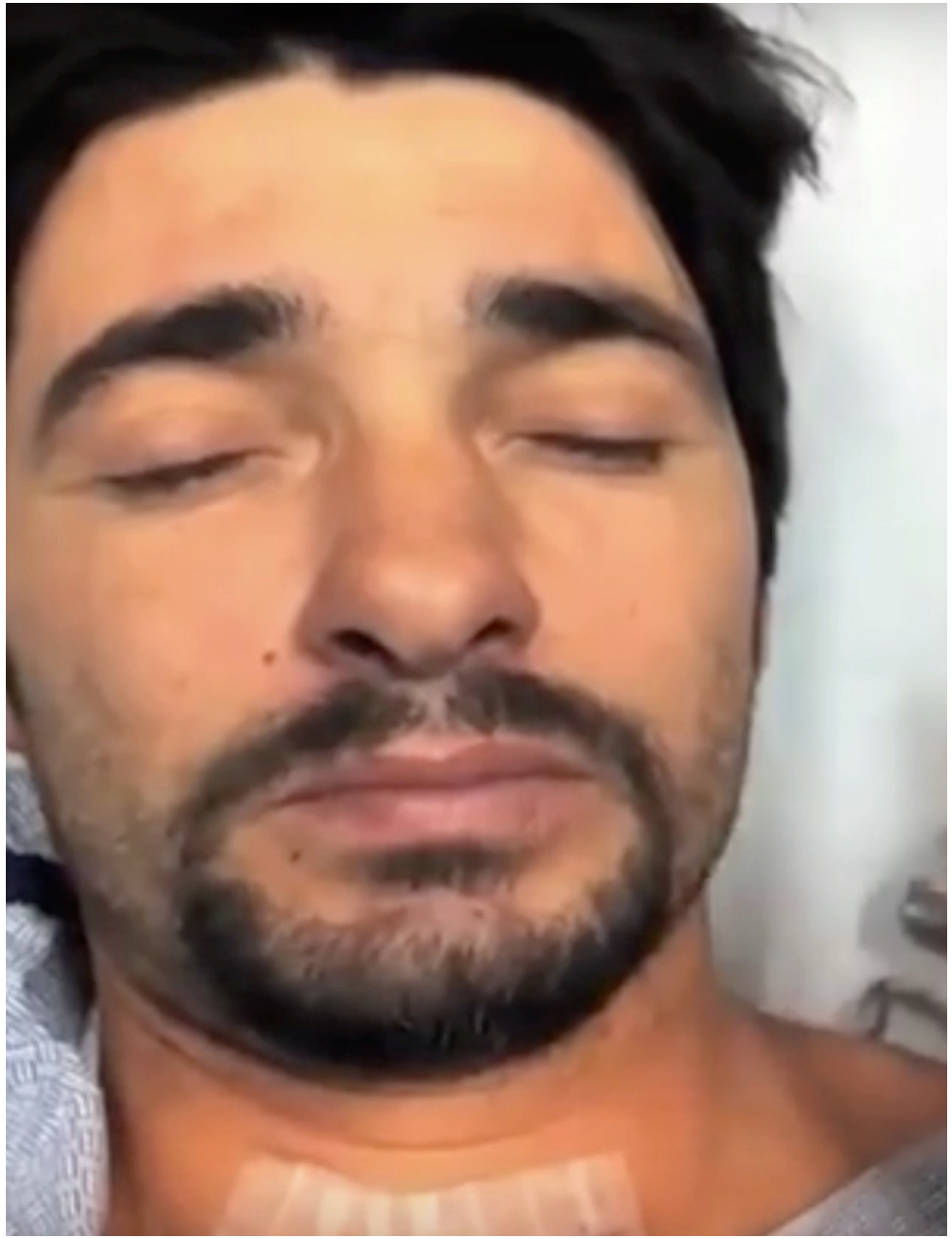
Signs & symptoms

- Paraesthesia (hands, mouth, feet , lips)
- Convulsions
- Arrhythmias
- Tetany

Mnemonic - [CATs go numb]

Chvostek's sign

Tap facial nerve just below zygomatic arch
Positive response = **twitching of facial muscles**
Indicates neuromuscular irritability due to **hypocalcaemia**



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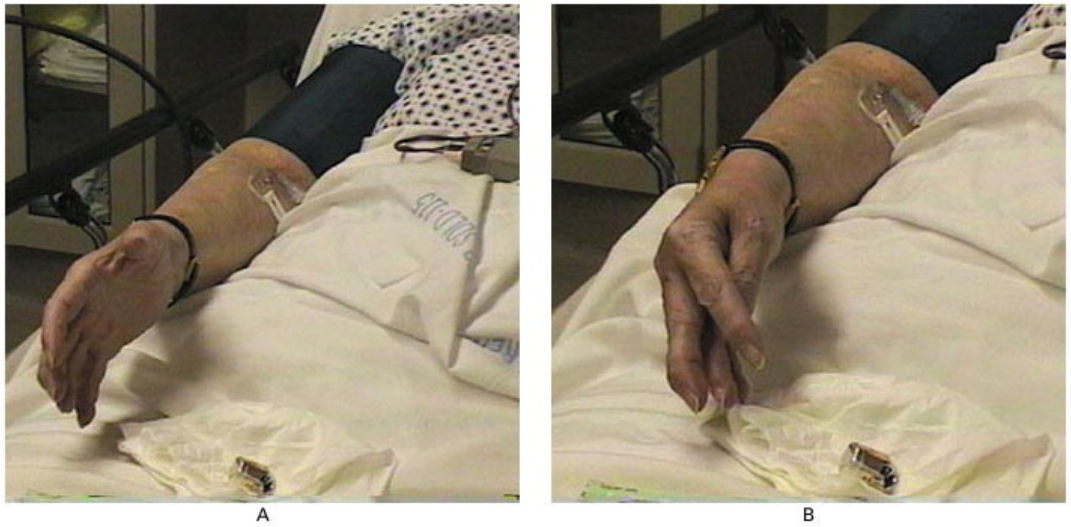
Trousseau's sign

Inflation of BP cuff for several minutes induces carpopedal spasm = **neuromuscular irritability due to hypocalcaemia**



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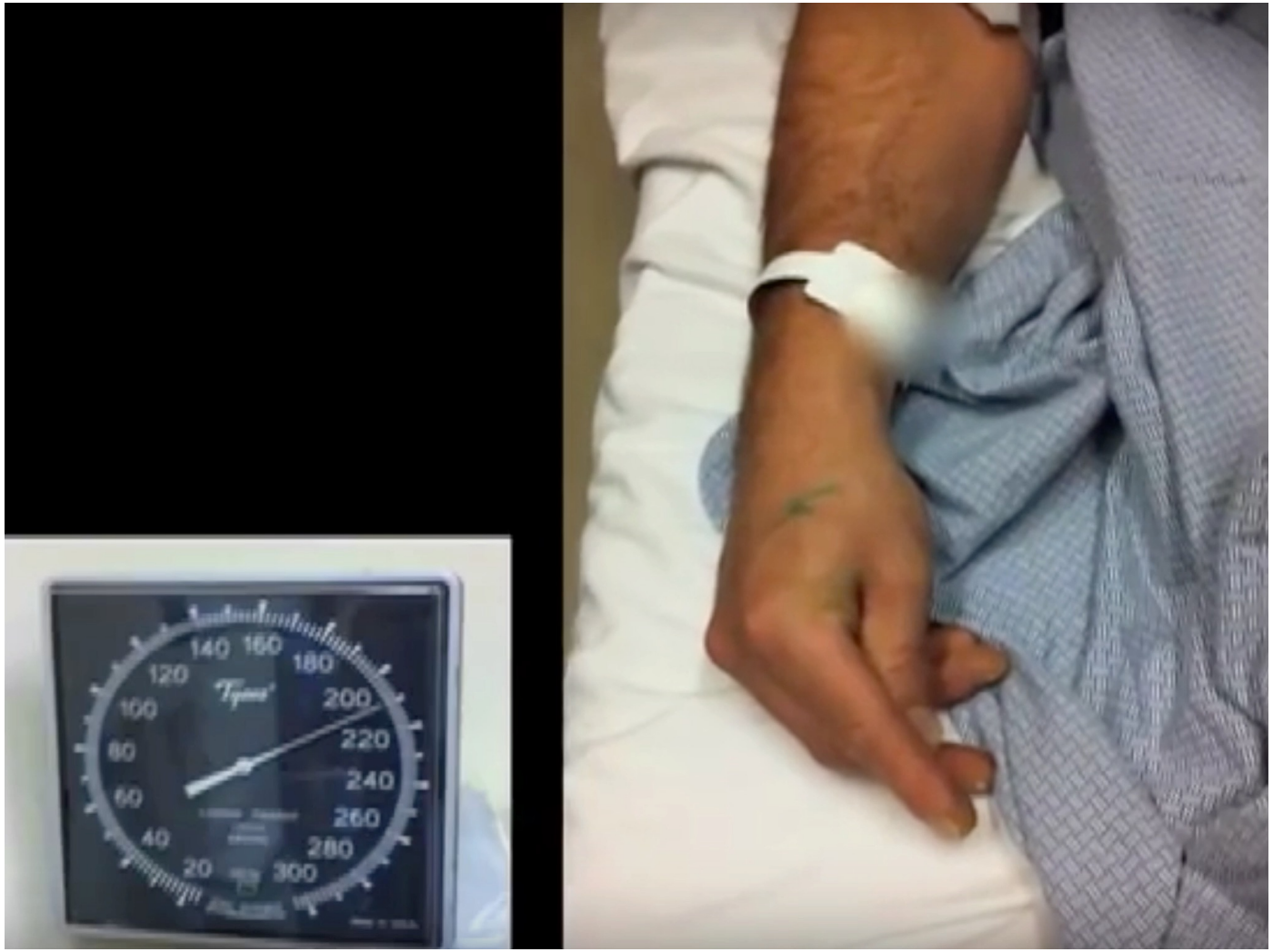
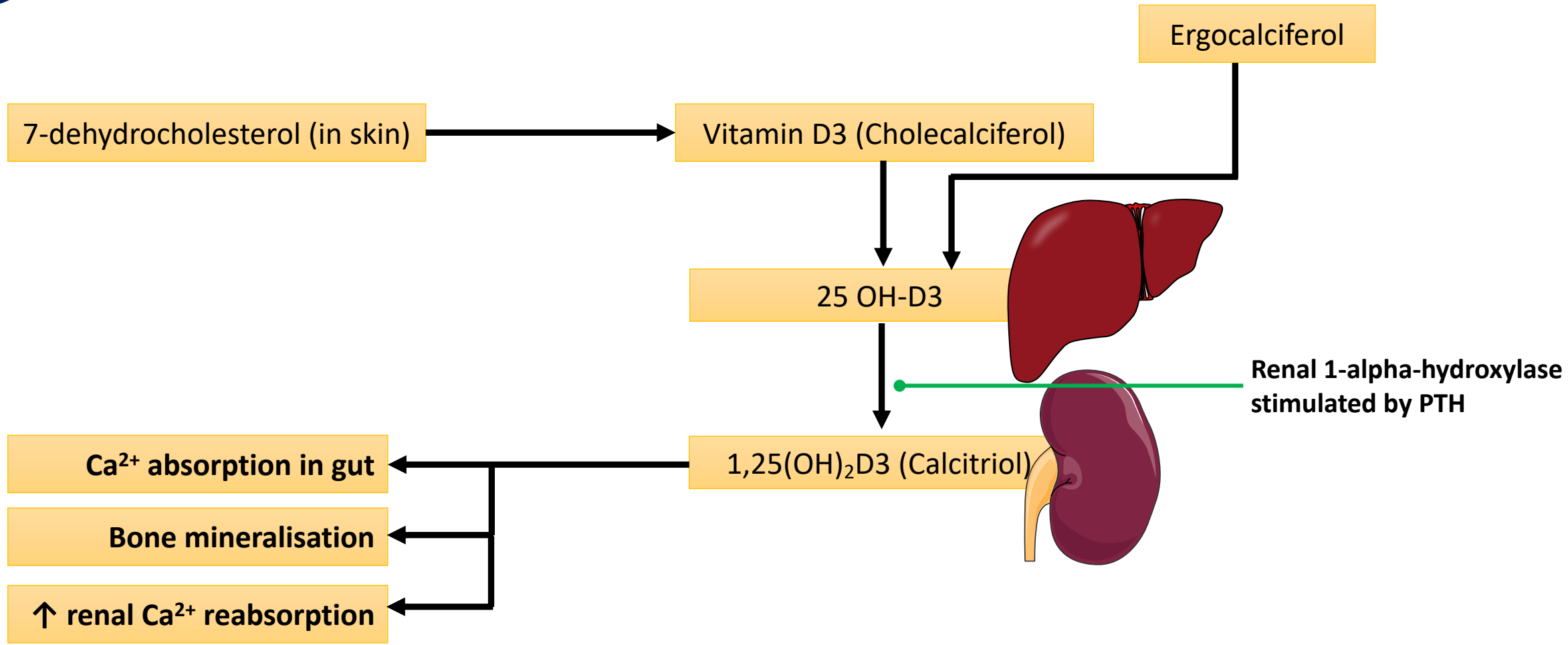


Causes of vitamin D deficiency



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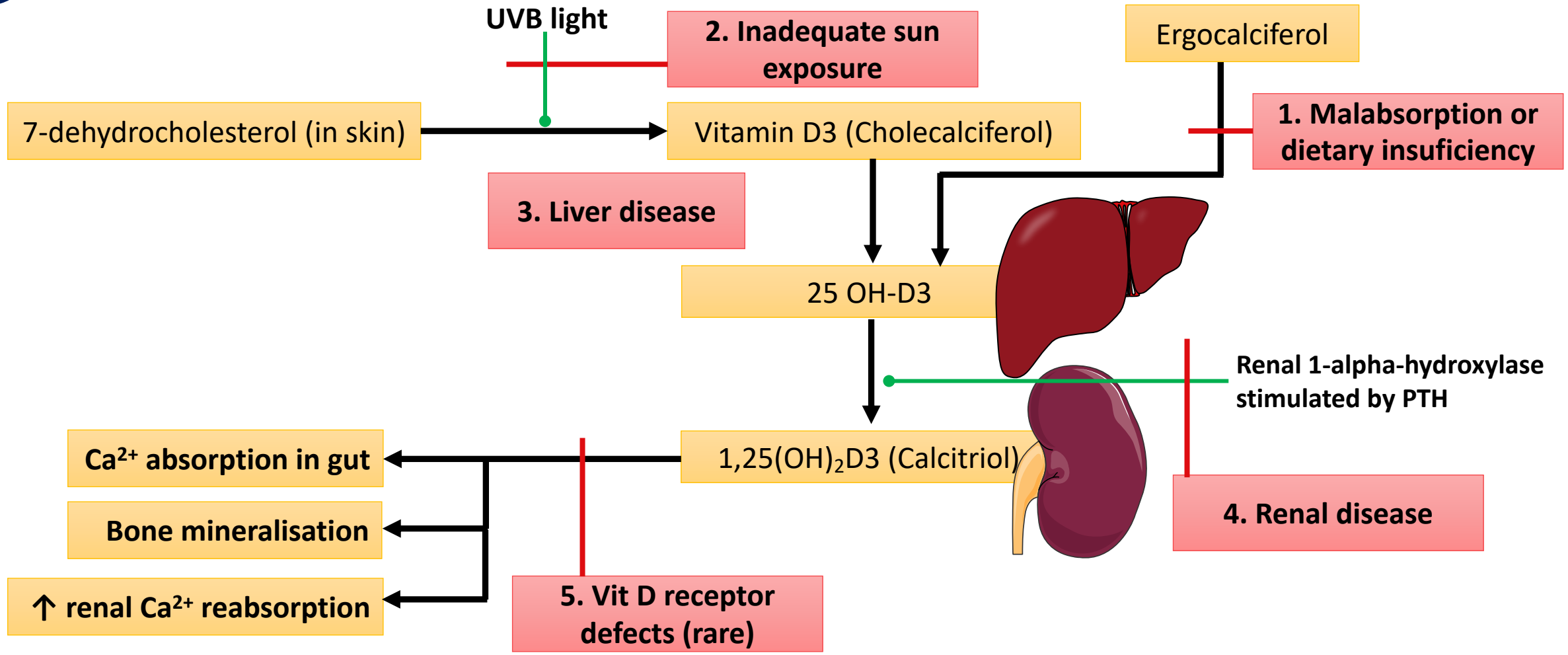

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Consequence of vitamin D deficiency

Lack of bone mineralisation = 'soft' bones

In children – rickets (bowing of bones)

In adults – osteomalacia (fractures, proximal myopathy)

Glasgow c. 1900

Hypercalcaemia

Signs & symptoms

'Stones, abdominal moans and psychic groans'

Reduced neuronal excitability – atonal muscles

Stones – renal effects

- Nephrocalcinosis – kidney stones, renal colic

Abdominal moans - GI effects

- Anorexia, nausea, dyspepsia, constipation, pancreatitis

Psychic groans - CNS effects

- Fatigue, depression, impaired concentration, altered mentation, coma (usually >3mmol/L)

Calcium & phosphate: Outline calcium and phosphate homeostasis and the causes and effects of dysregulation.

MENTIMETER QUESTION

Name a clinical feature of hypercalcaemia.

Session review

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Vitamin D deficiency

- Vitamin D synthesis
- Causes of vitamin D deficiency
- Clinical features of vitamin D deficiency

Hypercalcaemia and hypocalcaemia

- Clinical features of hypocalcaemia and hypercalcaemia