Clinical Chemistry

Trainee Council

PEARLS OF LAB MEDICINE

Parathyroid Hormone

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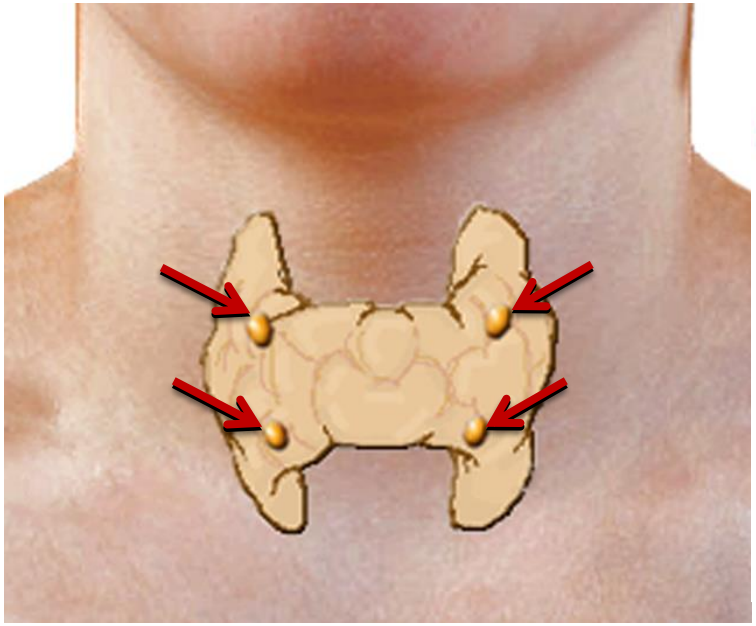
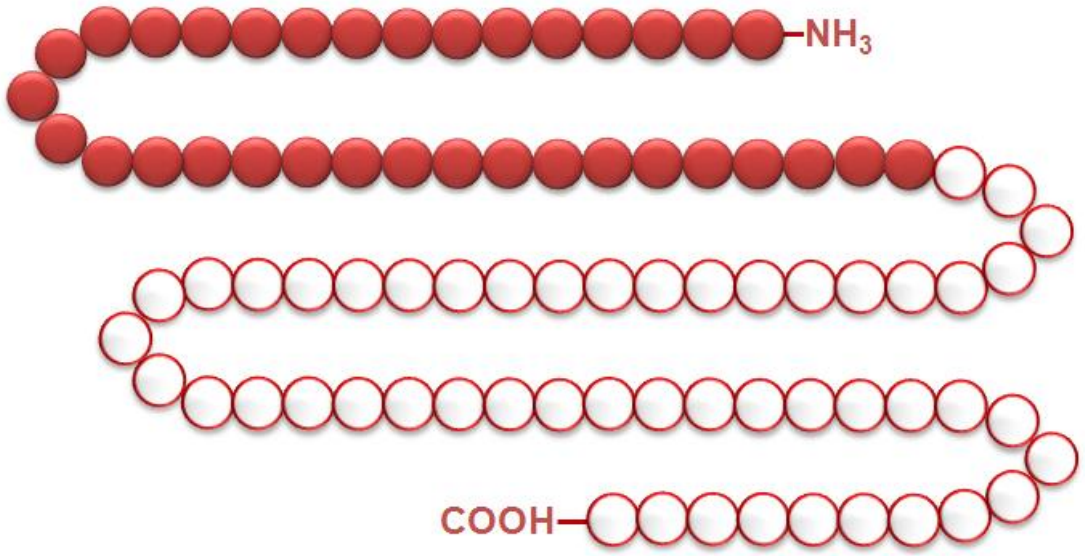
Parathyroid Hormone

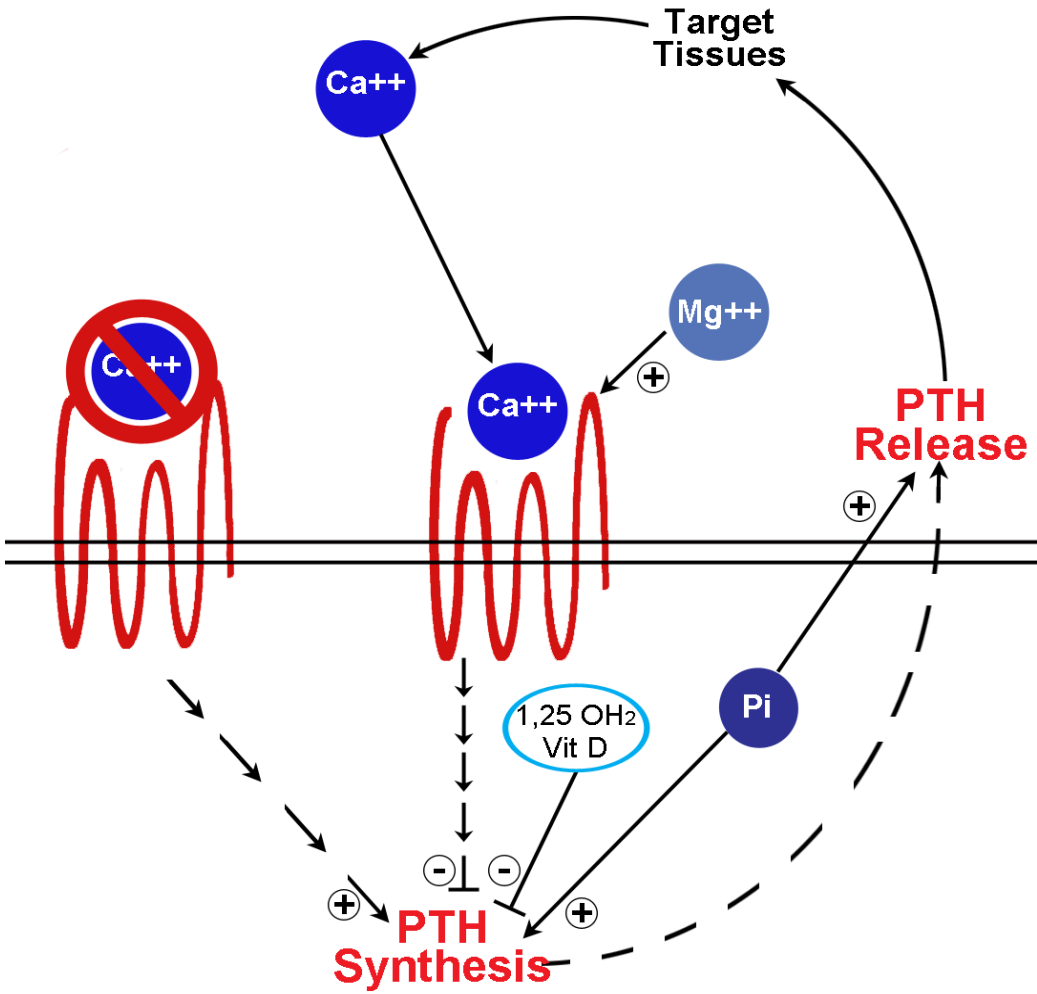
- 84 amino acid-long protein synthesized, stored, and secreted by chief cells of the parathyroid glands





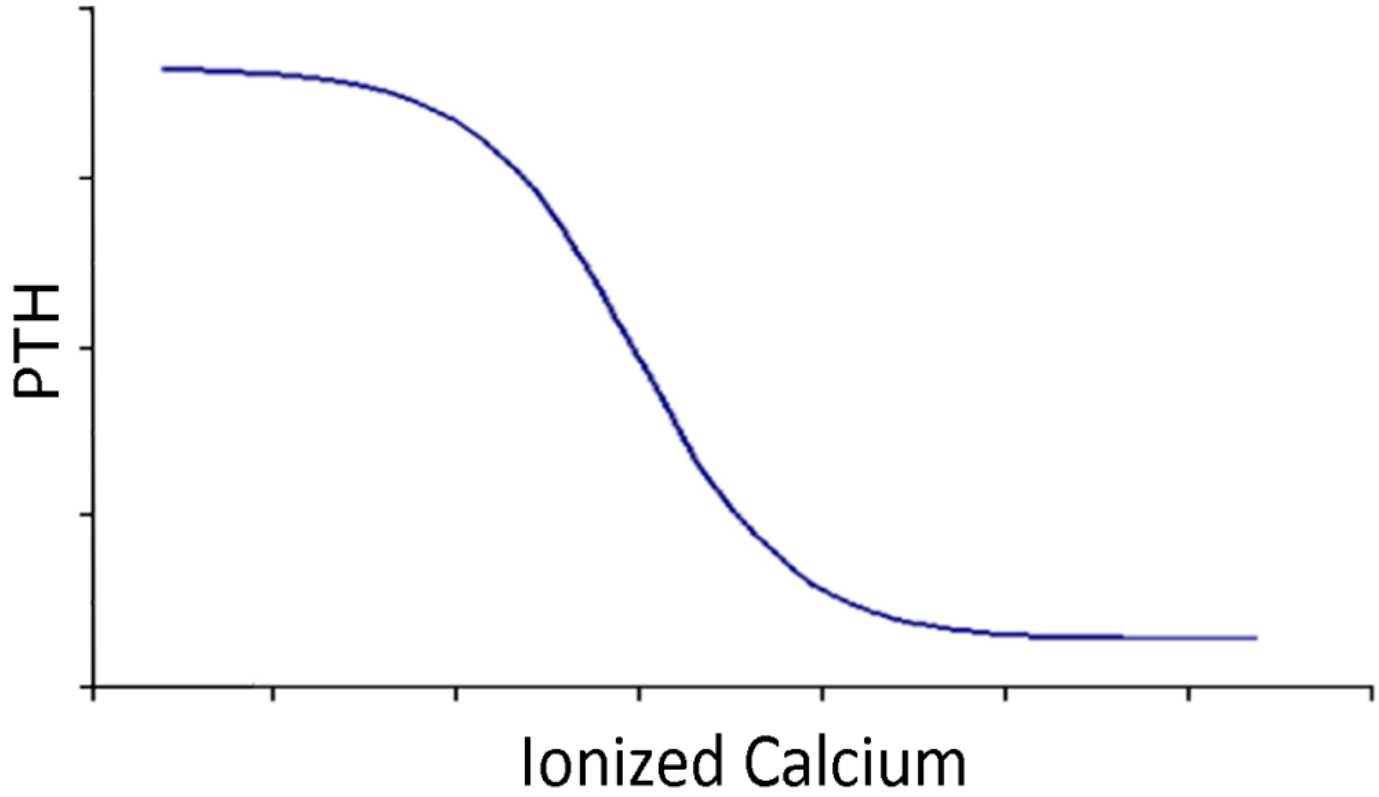
Parathyroid Hormone: Regulation

- Primarily regulated by free calcium concentration
  - Low free calcium increases PTH
  - Increased free calcium inhibits PTH release and increases it's degradation
- Minor regulation by vit D, magnesium, and phosphate



Parathyroid Hormone: Regulation

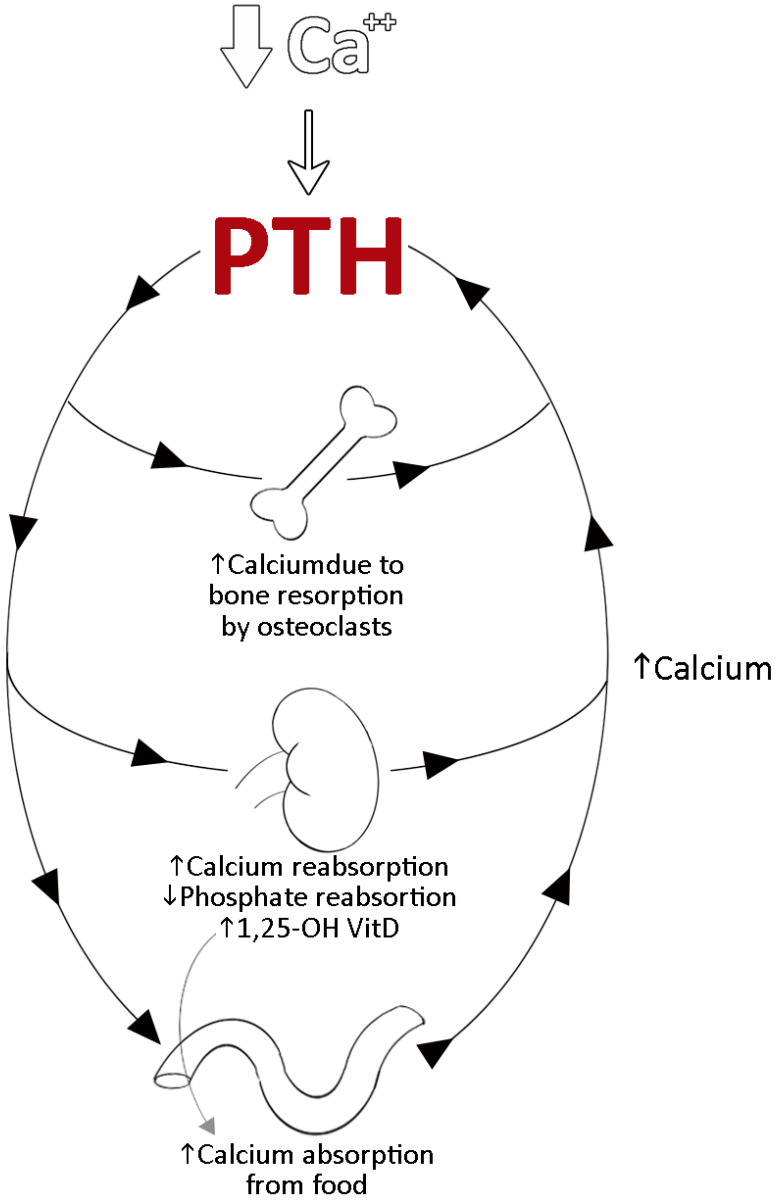
- PTH is inversely related to circulating calcium



Conlin PR, Fajtova VT, et al. JCEM. 1989; **69**: 593-599

Parathyroid Hormone: MoA

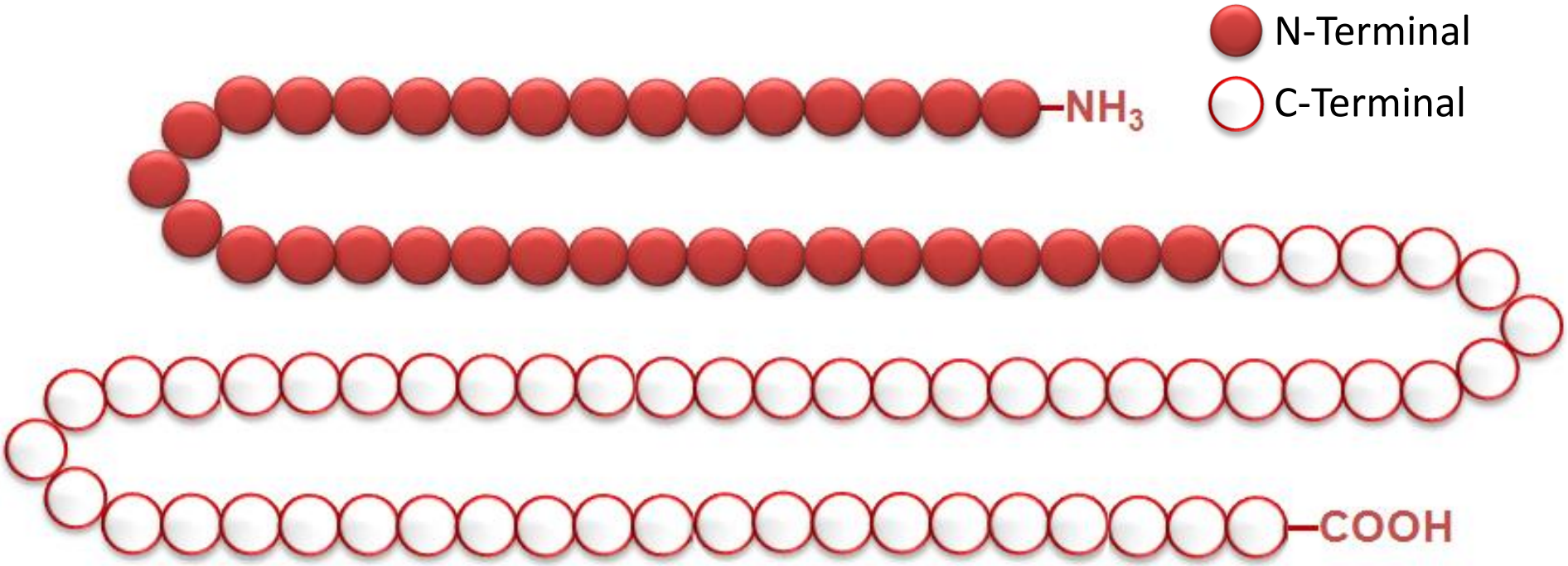
- PTH released in response to low free calcium
- Mechanism of Action: regulate bone and mineral metabolism
  - Activates osteoclasts to mobilize calcium and phosphate
  - Increases calcium reabsorption in distal convoluted tubule
  - Decreases phosphate reabsorption in proximal tubules
  - Induces 1,25$(OH)_2$-Vitamin D formation by kidney
    - Increases intestinal absorption of Calcium and Phosphate



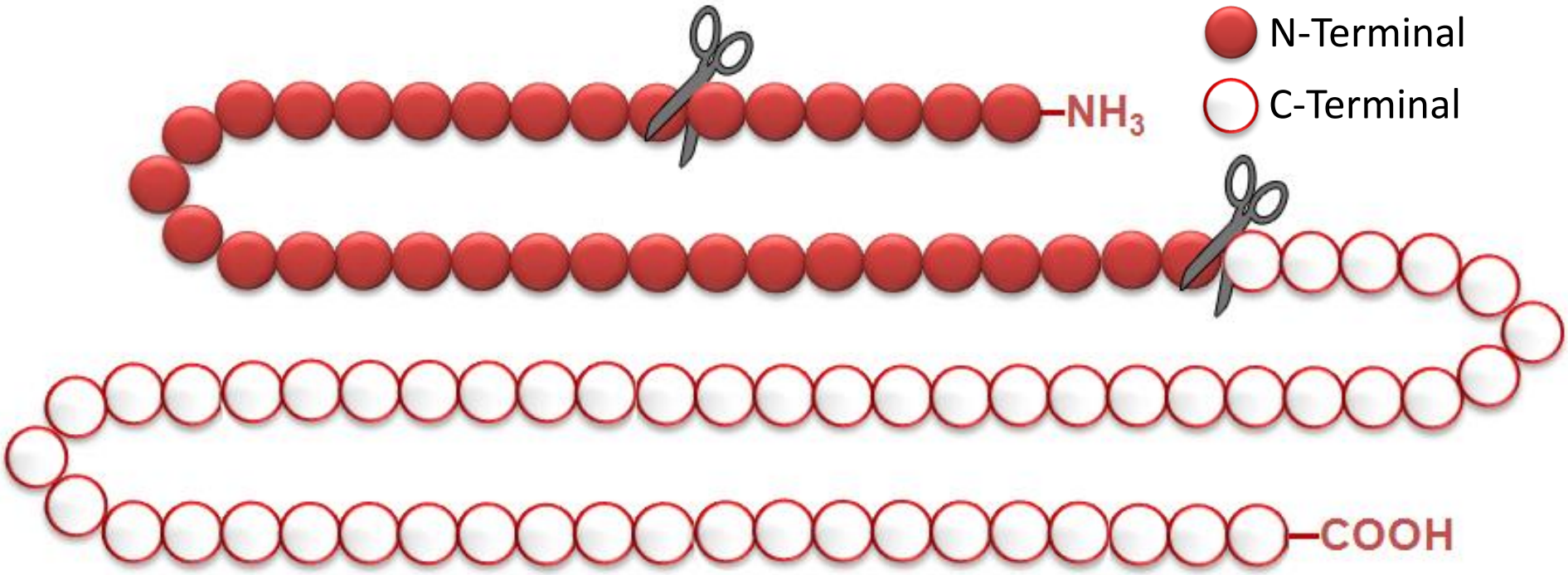
Hyperparathyroidism

- Hypersecretion of PTH → hypercalcemia
- Most patients are asymptomatic at the time of diagnosis
- "Stones, bones, abdominal groans, and psychiatric moans"
  - Bones: osteoporosis, osteomalacia, osteitis fibrosa cystica
  - Stones: kidney stones
  - Abdominal groans: constipation, nausea, indigestion
  - Psychiatric moans: lethargy, depression, psychosis, ataxia

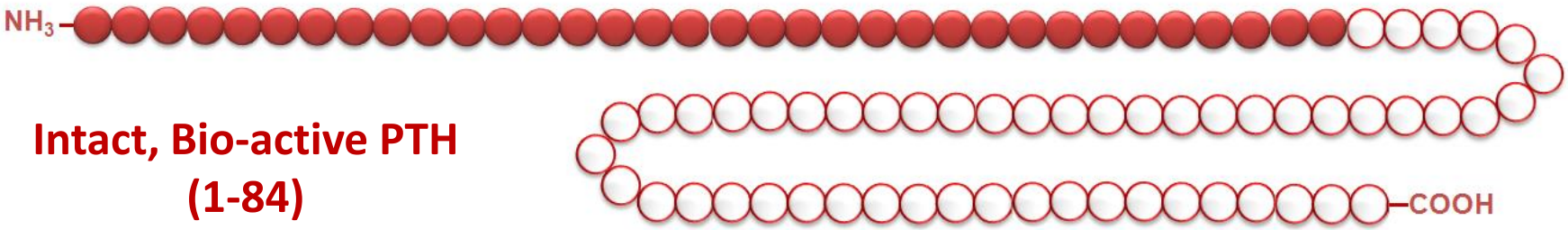
Circulating Forms of PTH



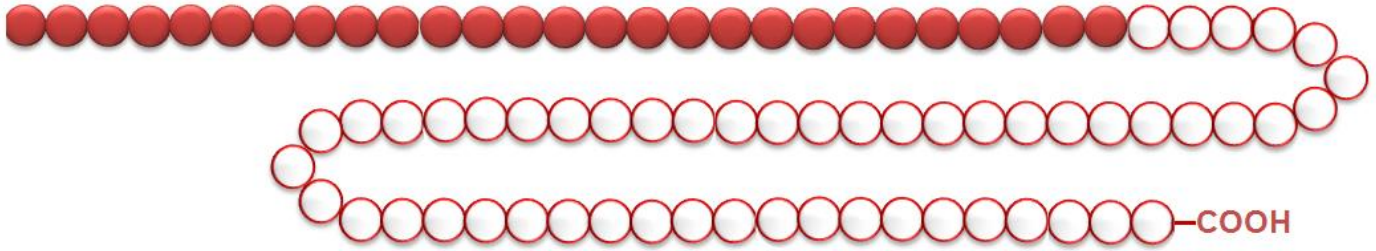
Circulating Forms of PTH



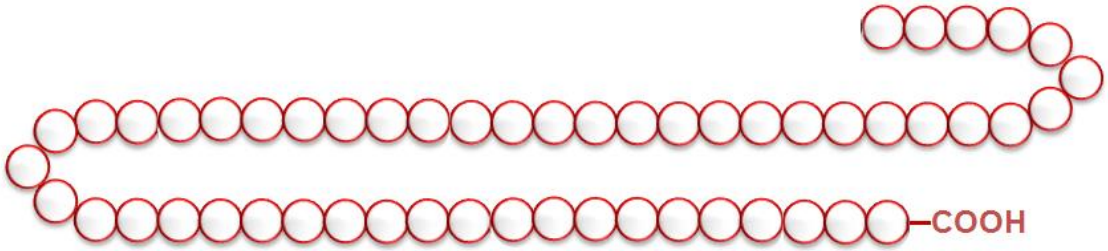
Circulating Forms of PTH



Intact, Bio-active PTH (1-84)

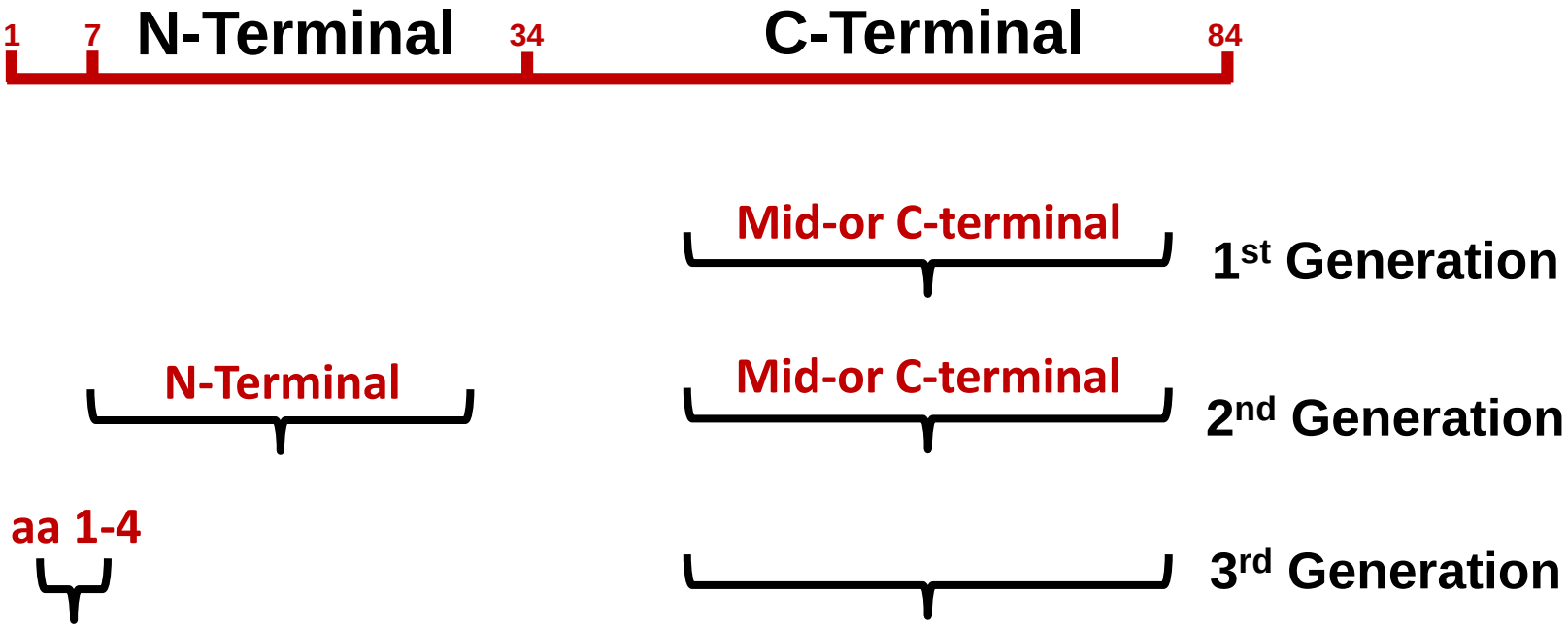


N-Trucated PTH (non 1-84)



C-Terminal Fragments

Parathyroid Hormone Assays

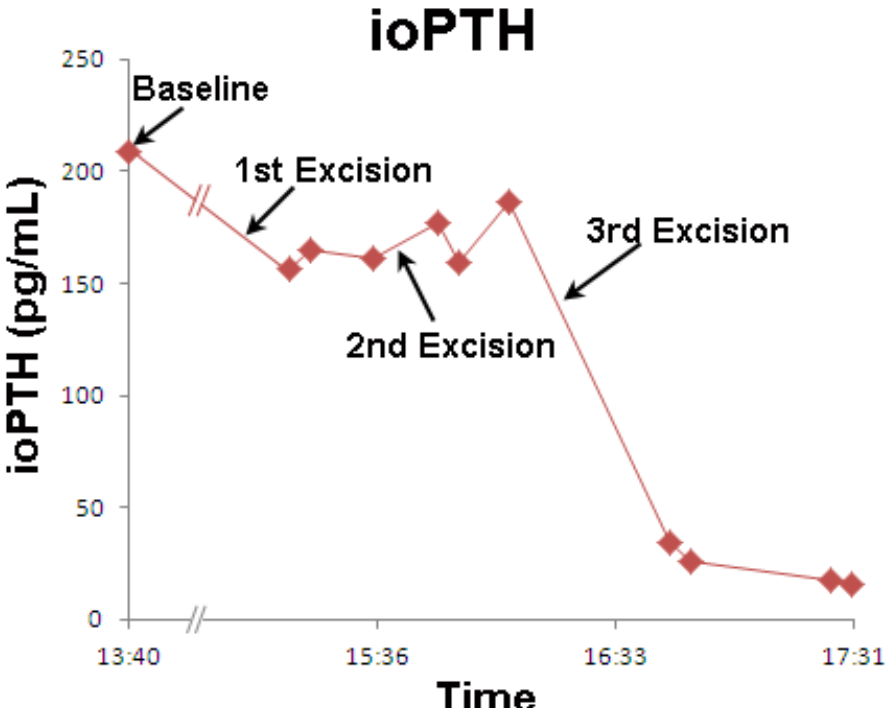


Reporting PTH

- Preferred sample types: serum and plasma
- Reference Intervals
  - 10-65 pg/mL
- May be reported along with calcium

Intra-Operative PTH

- Parathyroidectomies may be guided by the concentration of serum PTH
- A drop in PTH of 50% or more 10 minutes post-resection signals success in removing the abnormally secreting parathyroid tissue
- A rapid turn-around time is essential
  - Shortened incubation
    - Compromised sensitivity



PTH-Related Protein (PTHrP)

- Hypercalcemia is a fairly common finding in patients with cancer, and is often due to excretion of PTHrP
- PTHrP is distinct from PTH, but has some N-terminal homology, which is believed to interact with the PTH receptor, mimicking PTH activity
- PTH is usually suppressed in the face of elevated calcium
- PTHrP measured by immunoassay
- Normal range is <1-2 pmol/L
- Collect and process on ice + protease inhibitors

Summary

- PTH is made and released from the parathyroid glands in response to low ionized calcium
- Regulates bone & mineral metabolism, particularly Ca^{++}
- Primary hyperparathyroidism causes hypercalcemia and low bone mineral density
- PTH can be found in many lengths, depending on the state of degradation
- Immunoassays for PTH measure different constituents of the circulating PTH, depending on where the antibodies bind.

Summary (cont.)

- PTH interpreted with calcium result
- Intra-Operative PTH assays are shortened by decreasing incubation periods and enable surgeons to accurately identify and remove hyper-secreting parathyroid tissue
- PTHrP is a frequent cause of hypercalcemia of malignancy and should be considered in cases of hypercalcemia with suppressed PTH.

References

- Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, Fourth Edition ed: Elsevier Saunders, 2006.
- Conlin PR, Fajtova VT, et al. Hysteresis in the relationship between serum ionized calcium and intact PTH during recovery from induced hyper- and hypocalcemia in normal humans. JCEM. 1989; **69**: 593-599
- Henrich LM, Rogol AD, et al. Persistent hypercalcemia after parathyroidectomy in an adolescent and effect of treatment with cinacalcet HCl. Clin Chem. 2006; **52**(12): 2286-93.
- Inaba M, Nakatsuka K, et al. Technical and clinical characterization of the Bio-PTH (1-84) immunochemiluminometric assay and comparison with a second-generation assay for parathyroid hormone. Clin Chem. 2004; **50**(2): 385-90.
- Lusky K. Using rapid PTH in the OR: it's about time. CAP Today.