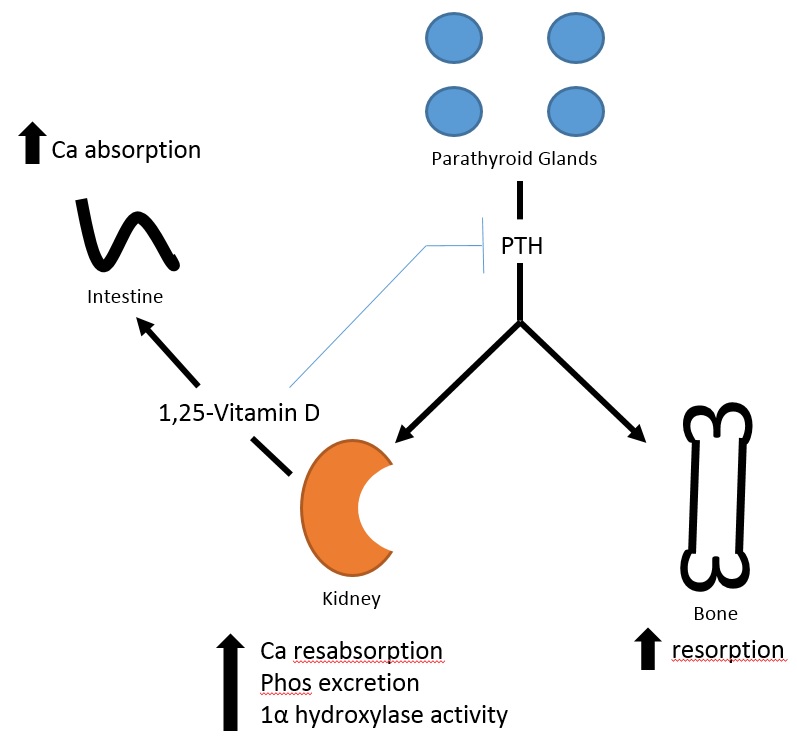
**Hypercalcemia in Pediatrics**

**Physiology of Calcium Homeostasis**

* Calcium (Ca) is maintained primarily by parathyroid hormone (PTH) and calcitriol (1,25 dihydroxyvitamin D) through actions on the bone, kidney, and GI tract
* PTH:
  + Secreted in response to low Ca (sensed by Calcium-sensing Receptor on parathyroid cells).
  + Actions:
    - Bone: PTH mobilizes Ca stores and promotes bone resorption by osteoclasts
    - Kidney: PTH increases Ca reabsorption in distal tubule, increases Phosphorus (Phos) excretion, and activates 1-alpha hydroxylase to convert 25-hydroxyvitamin D to 1,25-vitamin D
    - Net effect = Increased serum Ca, decreased serum Phos
* Calcitriol:
  + GI tract (primary source of calcium): calcitriol enhances intestinal Ca and Phos absorption
  + Net effect = Increase serum Ca and serum Phos



serum Ca and Phos

**Hypercalcemia**: Defined as [Ca] 2 standard deviations above mean (for age) adjusted for albumin

* Symptoms/Signs: “bones/stones” (nephrolithiasis, bone pain, polyuria), “groans” (abdominal pain, constipation), “psychic overtones” (fatigue, irritability, behavior change, depression, memory loss), failure to thrive, hypotonia, dehydration
* History**:** dietary assessment, medications (including OTC), family history of hypercalcemia
* Physical Exam: dysmorphic features, bony abnormalities
* Lab Evaluation: total Ca,albumin, ionized Ca, Phos, magnesium, PTH, 25-hydroxyvitamin D
  + Also consider: 1,25-hydroxyvitamin D, urine calcium/creatinine
* Differential diagnosis:
  + *PTH-Independent Hypercalcemia (more common)*
    - Milk-alkali syndrome
    - Hypervitaminosis D: Vitamin D toxicity, CYP24A1 mutation
    - Immobilization
    - Hypervitaminosis A
    - Granulomatous disorder: subcutaneous fat necrosis of the newborn, TB, sarcoid
    - Endocrinopathies: hyperthyroidism, adrenal insufficiency, pheochromocytoma, severe congenital hypothyroidism
    - Inborn errors of metabolism
    - Williams Syndrome: infantile hypercalcemia
    - Medications: thiazide
    - Phosphate depletion in neonates
    - Hypercalcemia of malignancy (uncommon): PTHrP-mediated, osteolysis, 1-25-mediated
  + *PTH-depending Hypercalcemia (less common)*
    - **Primary hyperparathyroidism**
      * Labs: high Ca, low Phos, high PTH
      * Evaluation: Sestamibi, thyroid US to localize enlarged gland(s)
      * Causes (neonatal): maternal hypocalcemia
      * Causes (children): genetic tumors/hyperplasia (MEN1, MEN2A, MEN3, MEN4, HPT-JT), non-syndromic (FIHP), PTH/PTHrP receptor activating mutations, carcinoma, lithium
    - Tertiary Hyperparathyroidism (from chronic renal disease or hypophosphatemic rickets)
    - **Familial hypocalciuric hypercalcemia**
      * Labs: high Ca, normal/high PTH, Ca/Cr clearance < 0.01
      * No symptoms of high PTH (no nephrolithiasis, bone loss)
      * No treatment needed
* Management:
  + Based on underlying etiology
  + If symptomatic:
    - IVF hydration (with NS)
    - Loop diuretics (enhance urinary Ca excretion but require caution given resulting volume contraction)
    - Calcitonin (short window of effectiveness due to tachyphylaxis)
    - IV bisphosphonates
  + If granulomatous disorder: glucocorticoids
  + If primary hyperparathyroidism: parathyroidectomy, cinacalcet

Available resources/References

1. Sperling, Mark A. Pediatric Endocrinology 4th Edition.