CKD: Bone Mineral Metabolism

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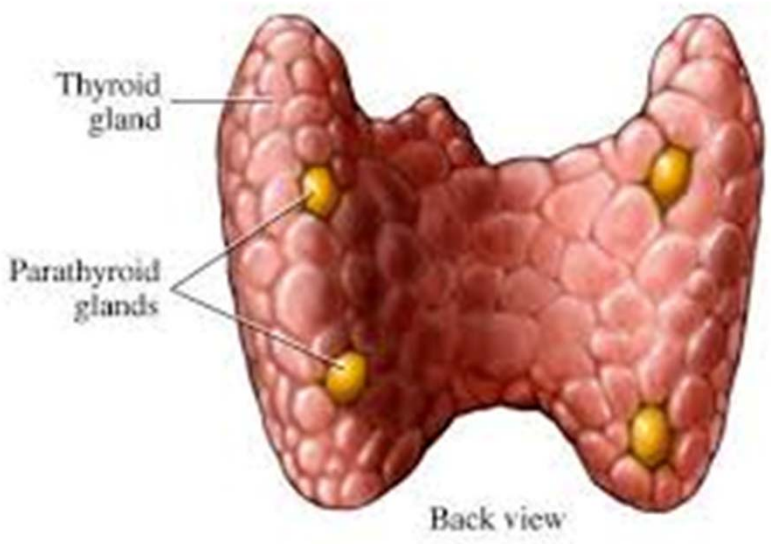
TUMS
ULTRA
1000
HAPPY NEW YEAR
I MADE YOU A SANDWICH

CKD - KDIGO

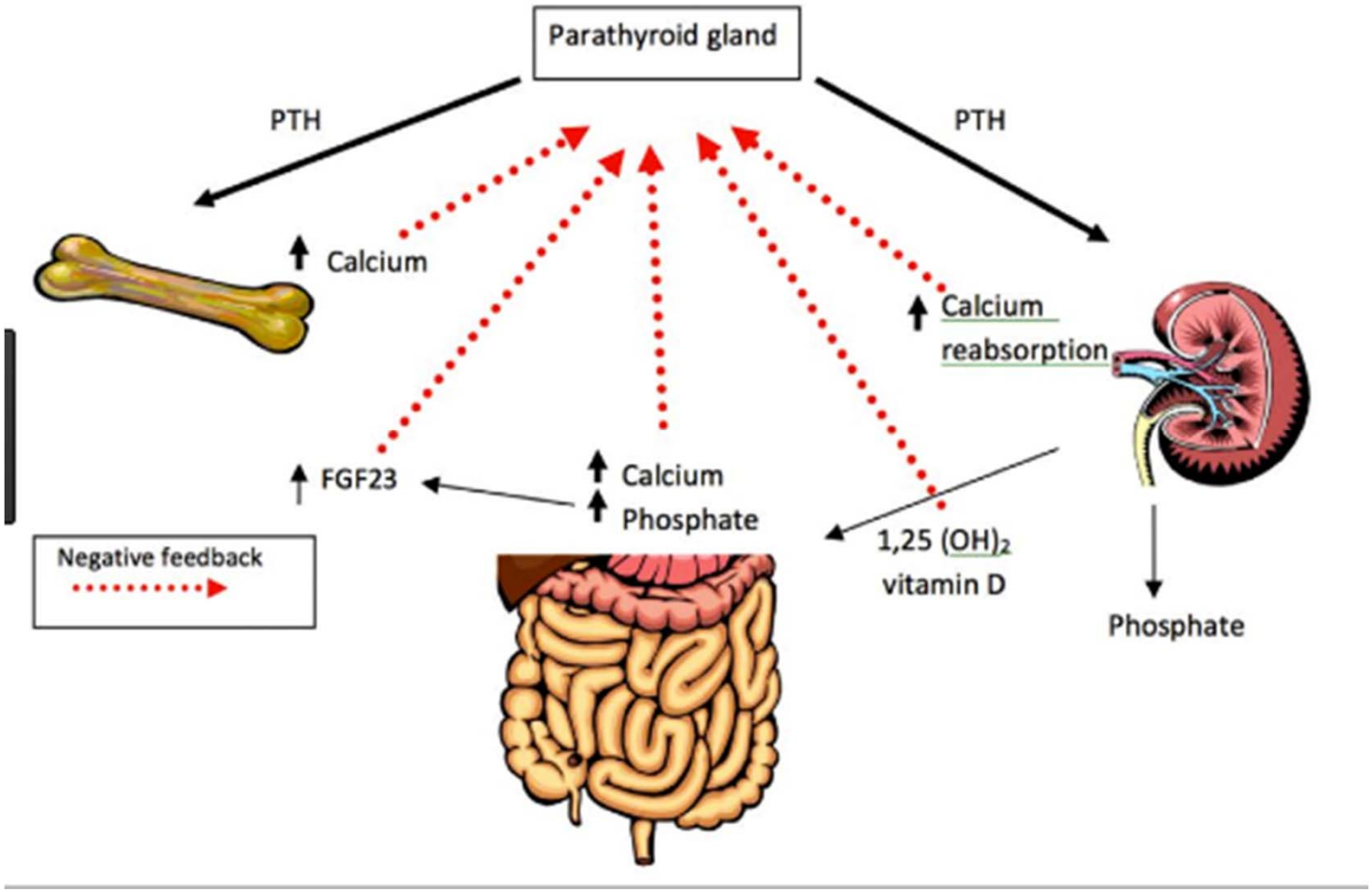
- Definition and Classification of CKD
  - CKD: abnormalities of kidney structure/function for > 3 months with health implications
    - ≥1 marker of kidney damage:
      - ACR ≥30 mg/g
      - Urine sediment abnormalities
      - Electrolyte and other abnormalities due to tubular disorders
      - Abnormalities detected by histology
      - Structural abnormalities (imaging)
      - History of kidney transplant
- OR GFR < 60

Parathyroid glands

- 4 glands behind thyroid in front of neck



Parathyroid physiology



Parathyroid hormone

- Normal circumstances PTH:
  - Increases calcium
  - Lowers PO4 (the renal excretion outweighs the bone release and gut absorption)
  - Increases Vitamin D

- Controlled by feedback
  - Low Ca and high PO4 increase PTH
  - High Ca and low PO4 decrease PTH

In renal disease: Gets all messed up!

- Decreased phosphate clearance: **High Po4**
- Low 1,25 OH vitamin D = **Low Ca**
- Phosphate binds calcium = **Low Ca**
- Low calcium, high phosphate, and low VitD all feedback to cause **more PTH release**

- This is referred to as **secondary hyperparathyroidism**
- Usually not seen until GFR < 45

Who cares

- Chronically high PTH
  - High bone turnover = **renal osteodystrophy**
    - Osteoporosis/fractures
    - Osteomalacia
    - Osteitis fibrosa cystica
- High phosphate
  - Associated with faster progression CKD
  - Associated with higher mortality
- Calcium-phosphate precipitation
  - Soft tissue, blood vessels (eg: coronary arteries)
- Low 1,25 OH-VitD
  - Immune status, cardiac health?

KDIGO

- KDIGO: Kidney Disease Improving Global Outcomes
- Most recent update regarding "Mineral and bone disorders" was 2017, previous guidelines were in 2009

So what can we do? KDIGO

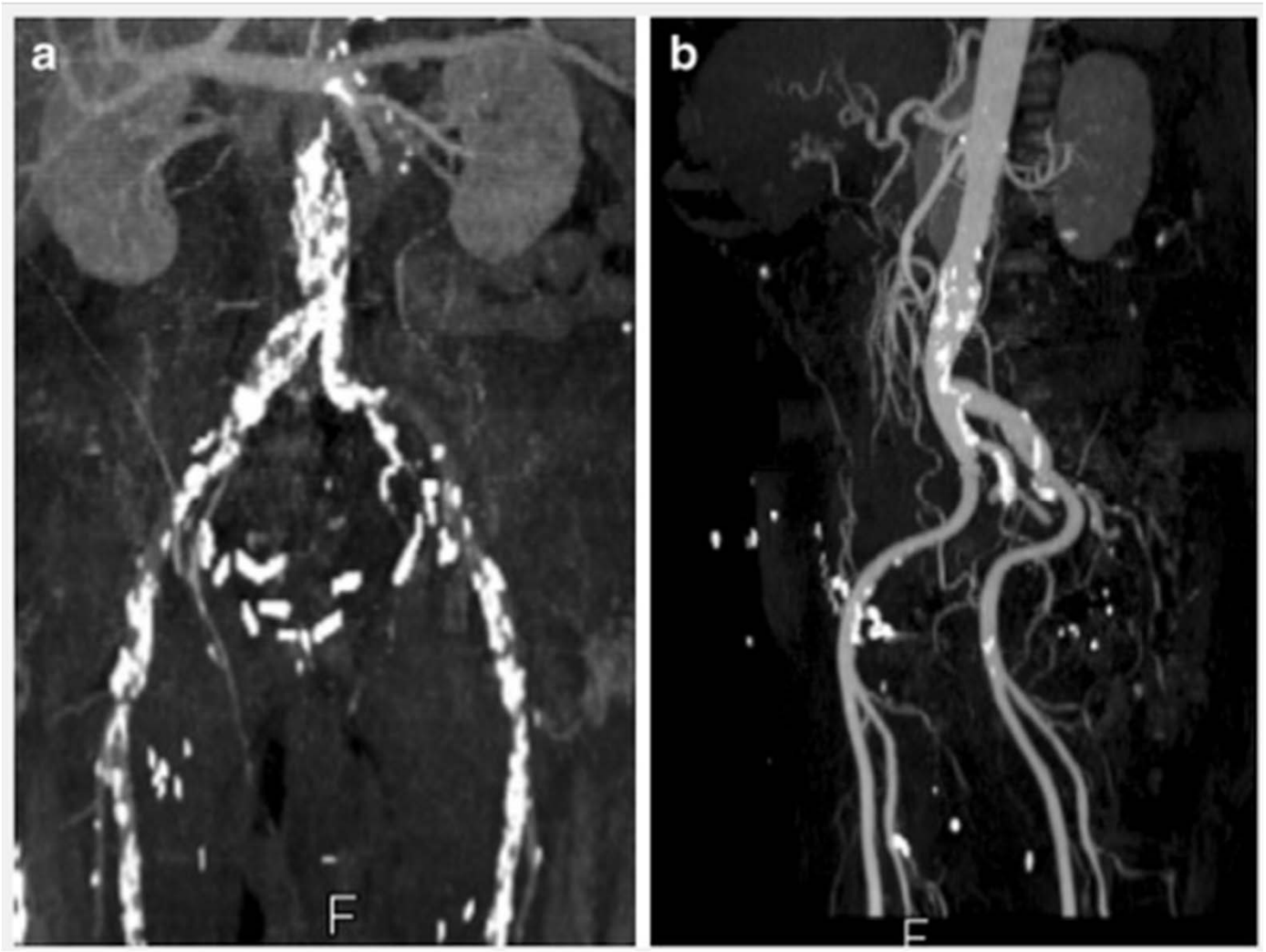
- Monitor serum Ca, PO4, PTH, ALP at least once once GFR < 60 (Stage 3a)
- Frequency of measurement depends on CKD stage (q1-6 months)

Phosphate

- KDIGO 2017: "Suggest lowering phosphate towards the normal range"
- Practically we tend to target PO4 level of 1.1 – 1.8 mmol/L in patients with very low GFR

Phosphate

- DIET!!!
- Phosphate binders
  - Calcium based 1st line (cheaper)
    - Calcium carbonate or Calcium acetate
    - Max 1.5 g/day elemental calcium
    - Acetate lower calcium load
  - Non-calcium based ($), 2nd line
    - Use when hypercalcemic or calcium load too high
    - Evidence of reduced coronary calcification
    - Sevelamer (renagel)
    - Lanthinum ?safety
    - KIDGO recommends avoiding aluminum containing binders



Rajiah P, Schoenhagen P - Insights Imaging (2013)

Calcium

- Guidelines basically suggest avoiding hypercalcemia
- Avoid high doses of calcium binders

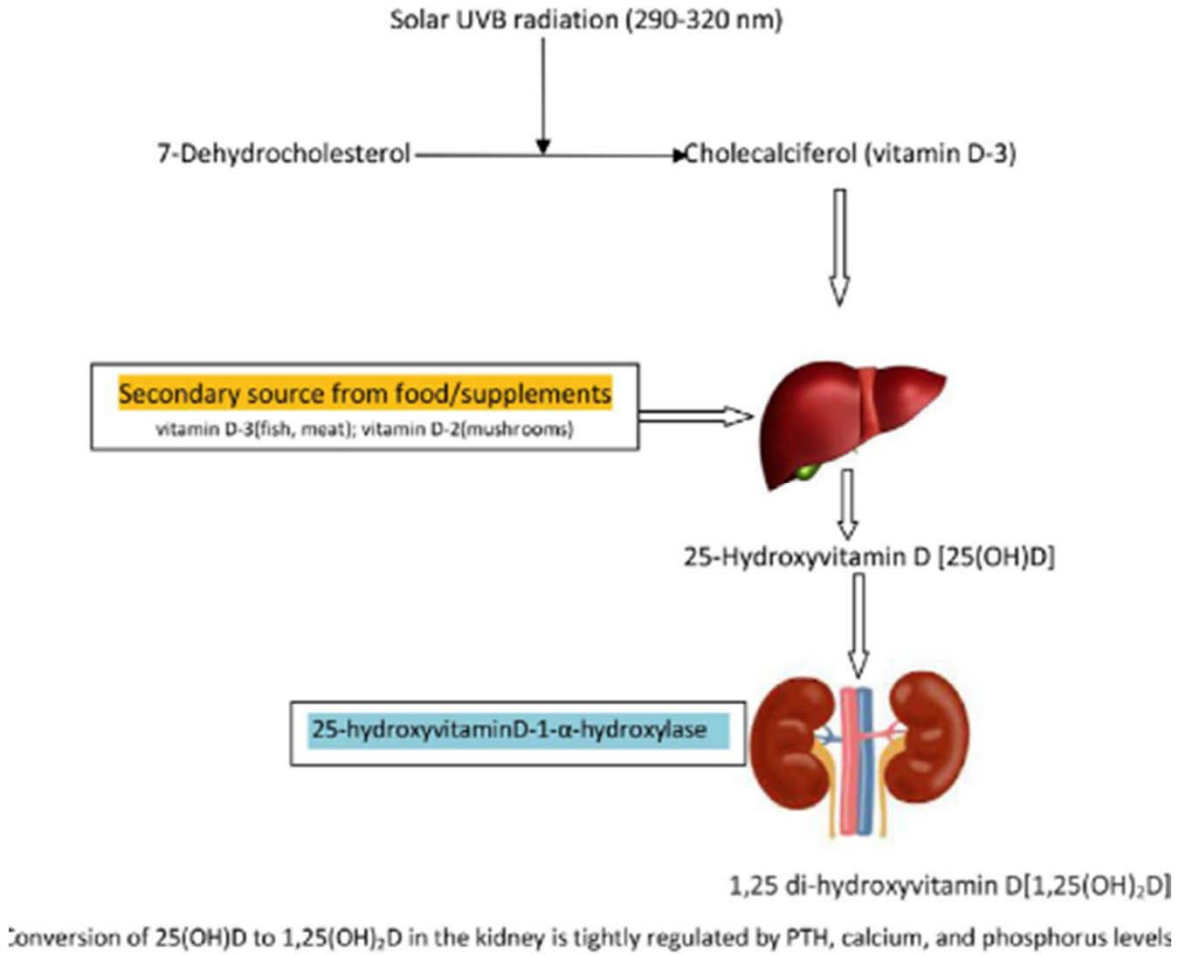
PTH

- The optimal level of PTH is not clear in CKD
- Treat reversible causes (low Ca, high PO4) in progressively rising PTH
- In CKD5 we generally target level 2-9x the upper limit of normal (Normal =8-9 pmol/L)
  - Based on CSN 2006 guidelines
- CKD patients should have a higher "expected PTH"
- Basically want to avoid having it too high or too low (both can cause problems)

PTH

- First line: Treatment of high PO4 and low Calcium
- If still high, add activated vitamin D
  - Alfacalcidol (one-alpha)
  - Calcitriol (if liver failure)
- Can use cinacalcet or parathyroidectomy in difficult to control disease (this typically occurs in end stage renal disease)

Vitamin D



Conversion of 25(OH)D to $1,25(OH)_2D$ in the kidney is tightly regulated by PTH, calcium, and phosphorus levels

Vitamin D in Children's Health

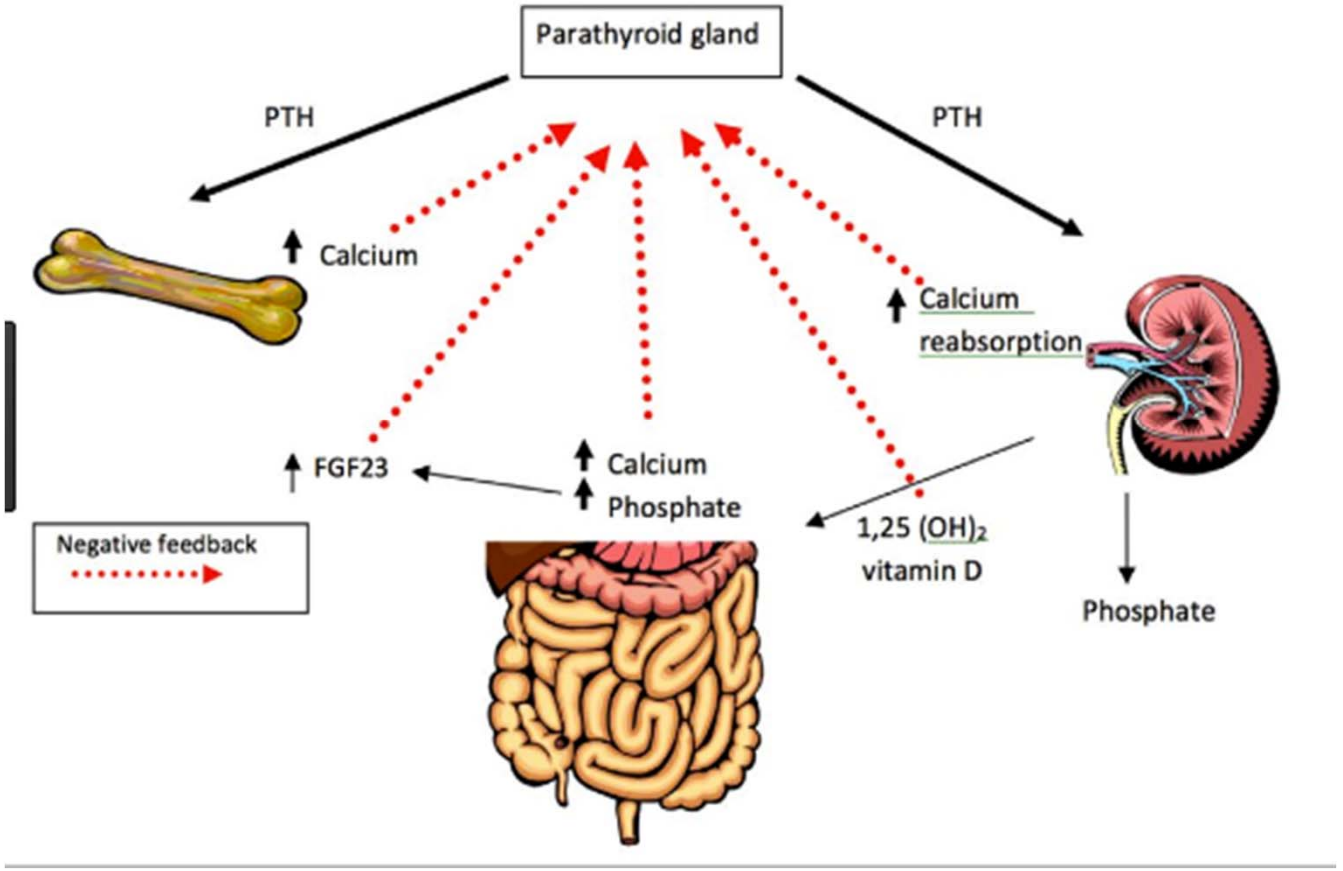
Full-text available · Article · Sep 2014 · Children

Joy A. Weydert

Some other tidbits

Primary hyperparathyroidism

- Parathyroid adenoma or hyperplasia



Primary hyperparathyroidism

- Parathyroid adenoma causes excess PTH secretion
- Not responsive to negative feedback
- **High PTH, High Calcium, Low phosphate**
- Different from secondary in renal failure where you get high phosphate and low calcium
- Requires surgical intervention

Primary hyperparathyroidism

- We do see this this in our CKD patients and catching it is important
- Some clues: PTH higher than expected for level of GFR, calcium high, phosphate low

Tertiary hyperparathyroidism

- In the setting of renal failure and prolonged secondary hyperparathyroidism
- Chronic stimulation of parathyroid gland leads to hyperplasia, and autologous PTH secretion
- **+++ PTH, High Ca, High PO4**
- Severe bone disease
- Needs surgery
- Sometimes can be medically managed (cinacalcet)

Questions??