Making Bones Strong and More: Vitamin D, Calcium, and Phosphorus

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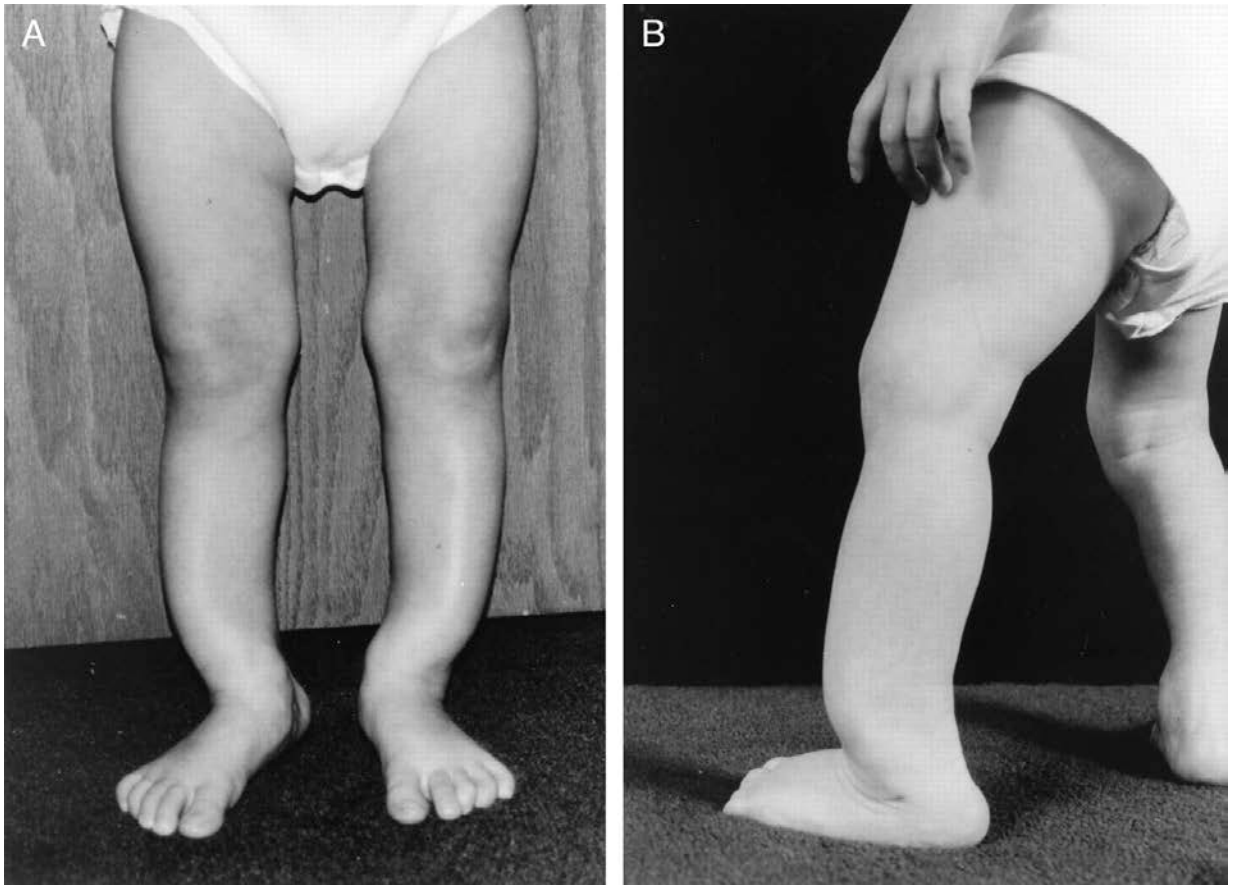
Disclosure

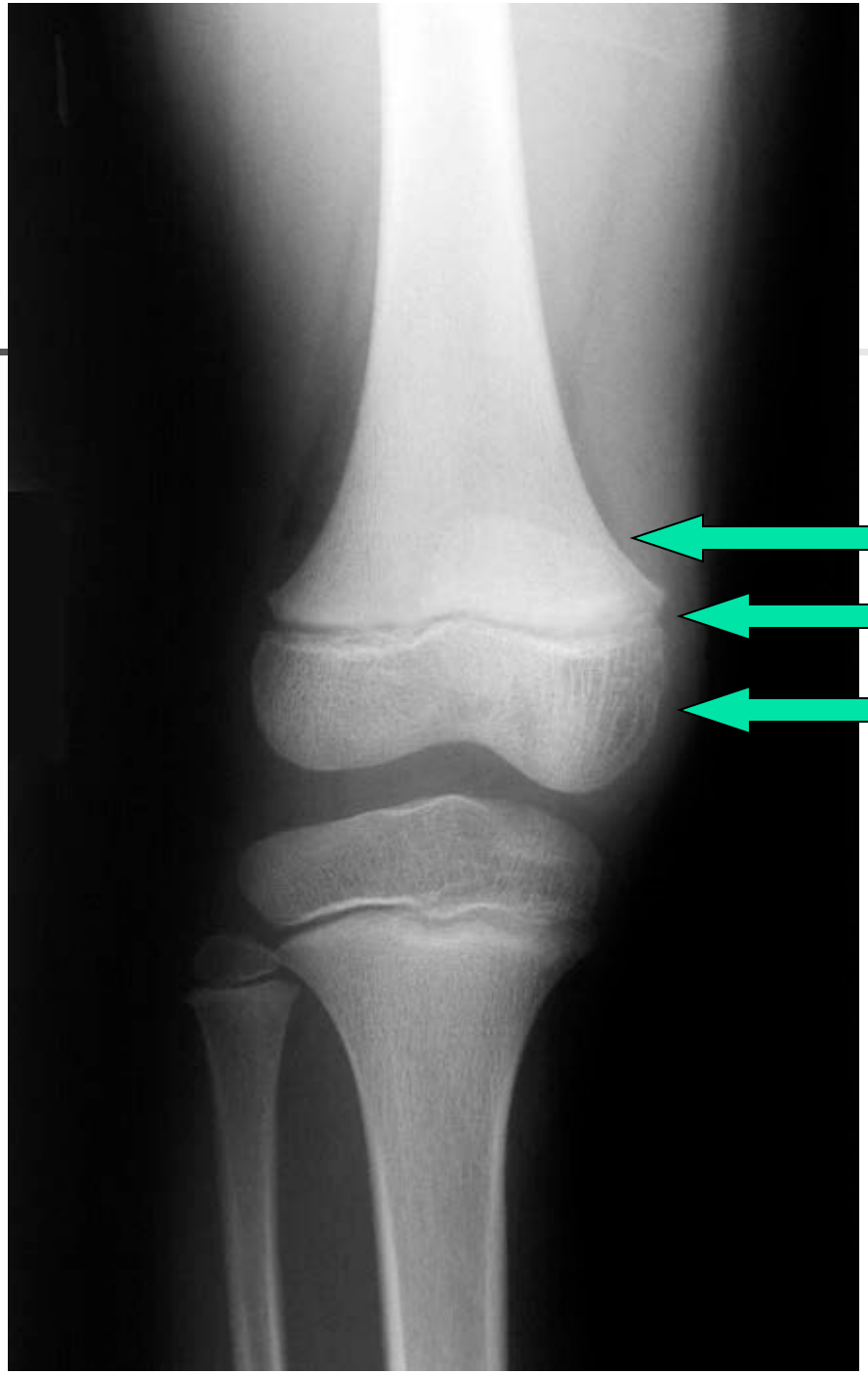
- Support from Abbott Laboratories for clinical studies of Calcijex and Zemplar
- Consultant for Abbott Laboratories

Objectives

- Identify risk factors for nutritional vitamin D deficiency.
- Explain the difference between a nutritional vitamin D supplement and active vitamin D.
- Plan the treatment of a patient with an elevated serum phosphorus level.
- List 2 potential complications of treatment with calcium supplements.

Rickets



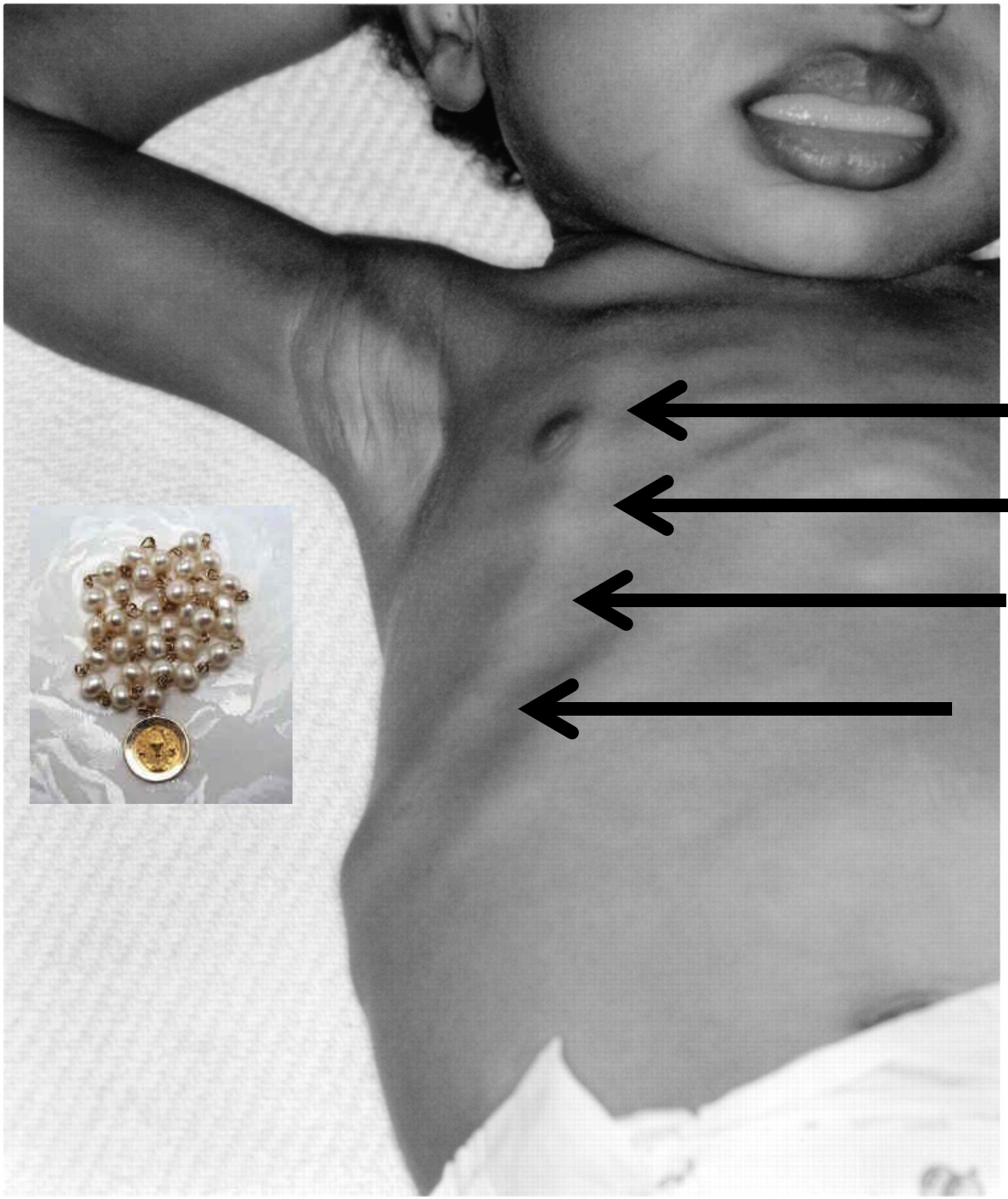

Metaphysis
Growth plate
Epiphysis

Rickets?

- Does it occur in 2013?
- What are the 2 most common groups in the United States?
  - Breast fed infants (African American)
  - Chronic kidney disease patients

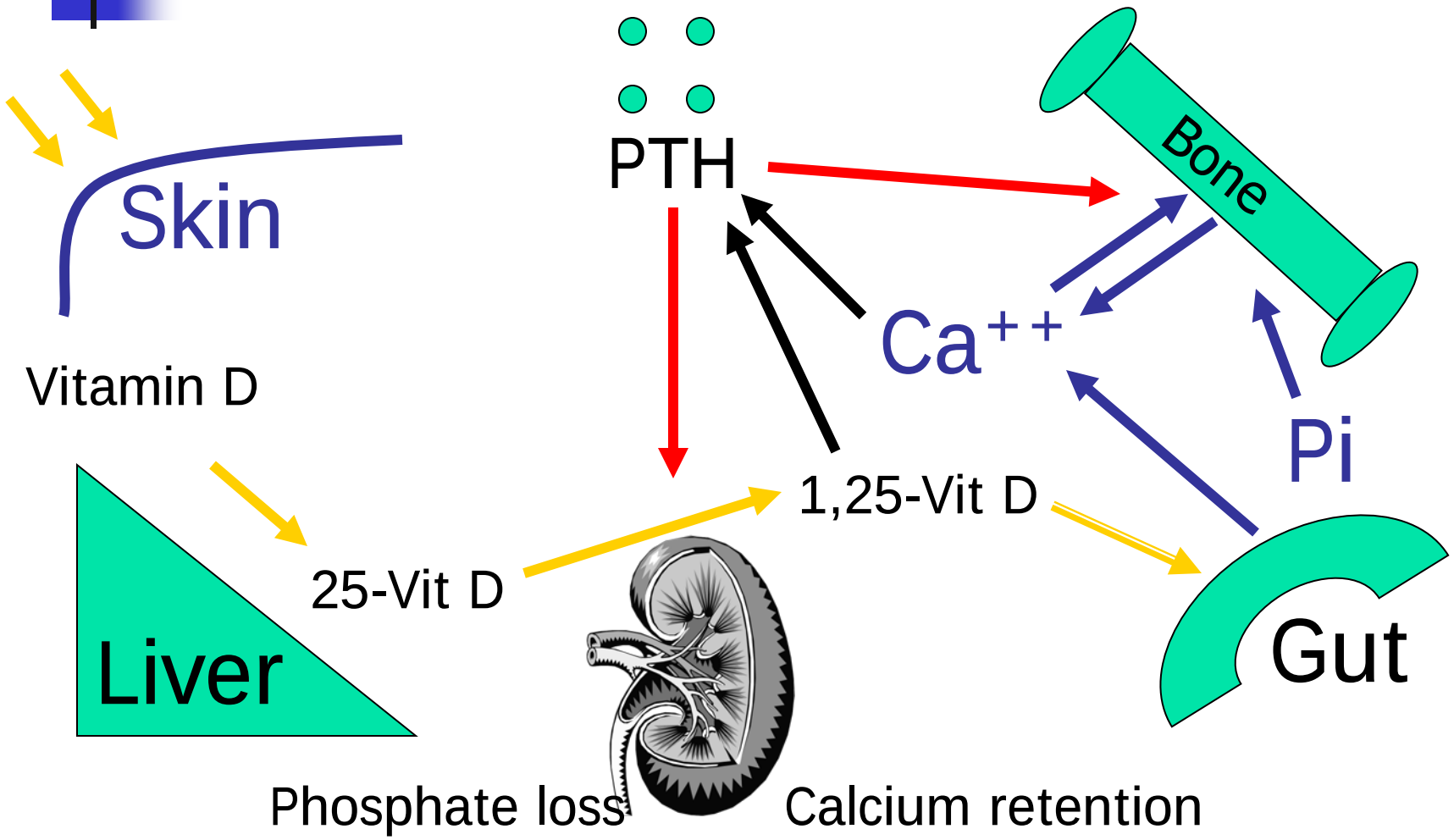
Rickets: Clinical Features

- Frontal bossing
- Delayed dentition and carries
- Rachitic rosary
- Enlargement of wrists and ankles
- Valgus or varus deformities
- Fractures
- Respiratory infections and pulmonary atelectasis

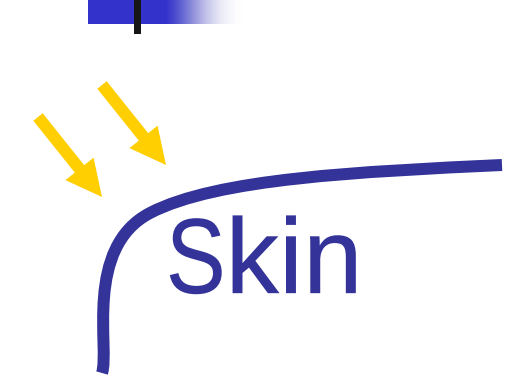


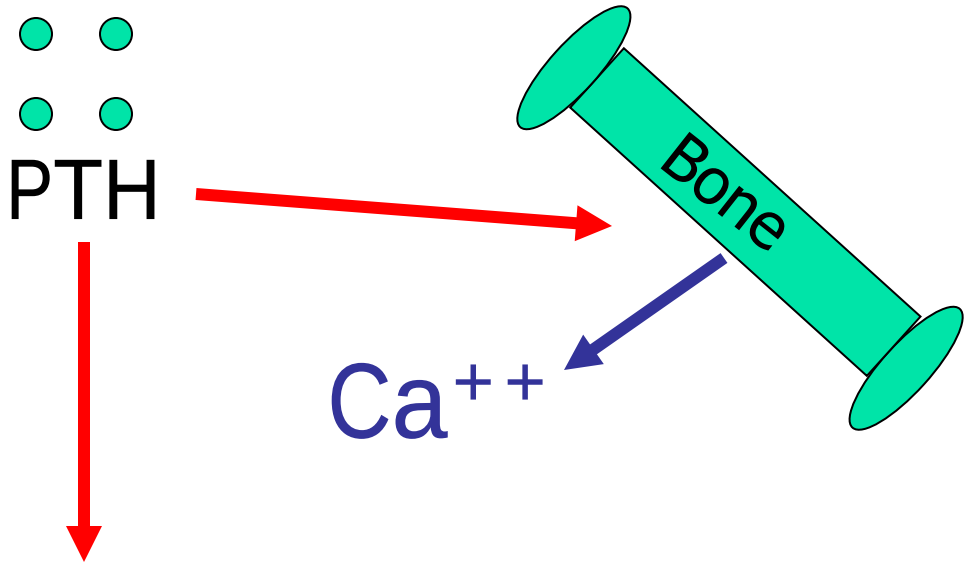
Windswept Deformity

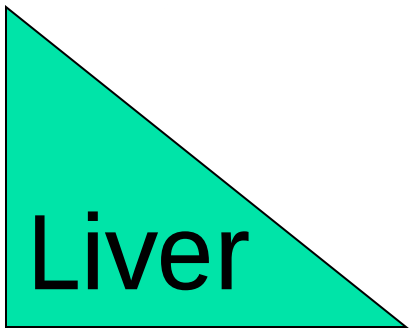
Calcium and Phosphate Metabolism

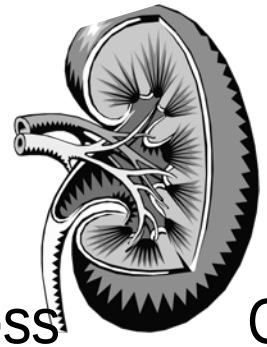


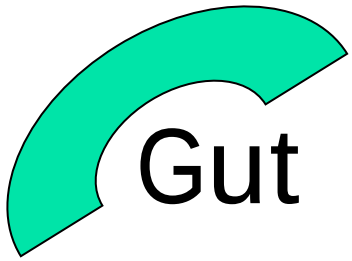
Vitamin D Deficiency











Phosphate loss

Calcium retention

Vitamin D From Sunlight

7-dehydrocholesterol

Cholecalciferol

(Vitamin D_3)

A Lack of Sunshine

- Exposure to sun
  - Less time outside
  - Latitude/season
  - Sunscreen
- Skin
  - Melanin slows vitamin D synthesis
  - Uremia decreases

Vitamin D From Diet

- Food sources limited
- Vitamin D added to milk/breakfast cereal
- Formula: 400 IU/L Vitamin D
- Human milk (12-60 IU/L)

Nutritional Vitamin D Deficiency

- Common
- Increased in CKD patients
- Other risk factors
  - African Americans
  - Decreased sun exposure
  - Poor intake

Nutritional Vitamin D Deficiency

- Definitions
  - Severe deficiency: <5 ng/mL
  - Mild deficiency: 5-15 ng/mL
  - Insufficiency: 16-30 ng/mL
- Common

Why Treat Nutritional Vitamin D Deficiency?

- Hyperparathyroidism
- Beyond bone
  - Local synthesis of 1,25-Vitamin D (including vascular smooth muscle and endothelial cells)
  - Receptors: vascular smooth muscle, myocytes, lymphocytes, osteoblasts
  - Fractures, autoimmune disease, CHF, hypertension, diabetes, inflammation, arterial calcification, atherosclerosis, cancer

Treatment

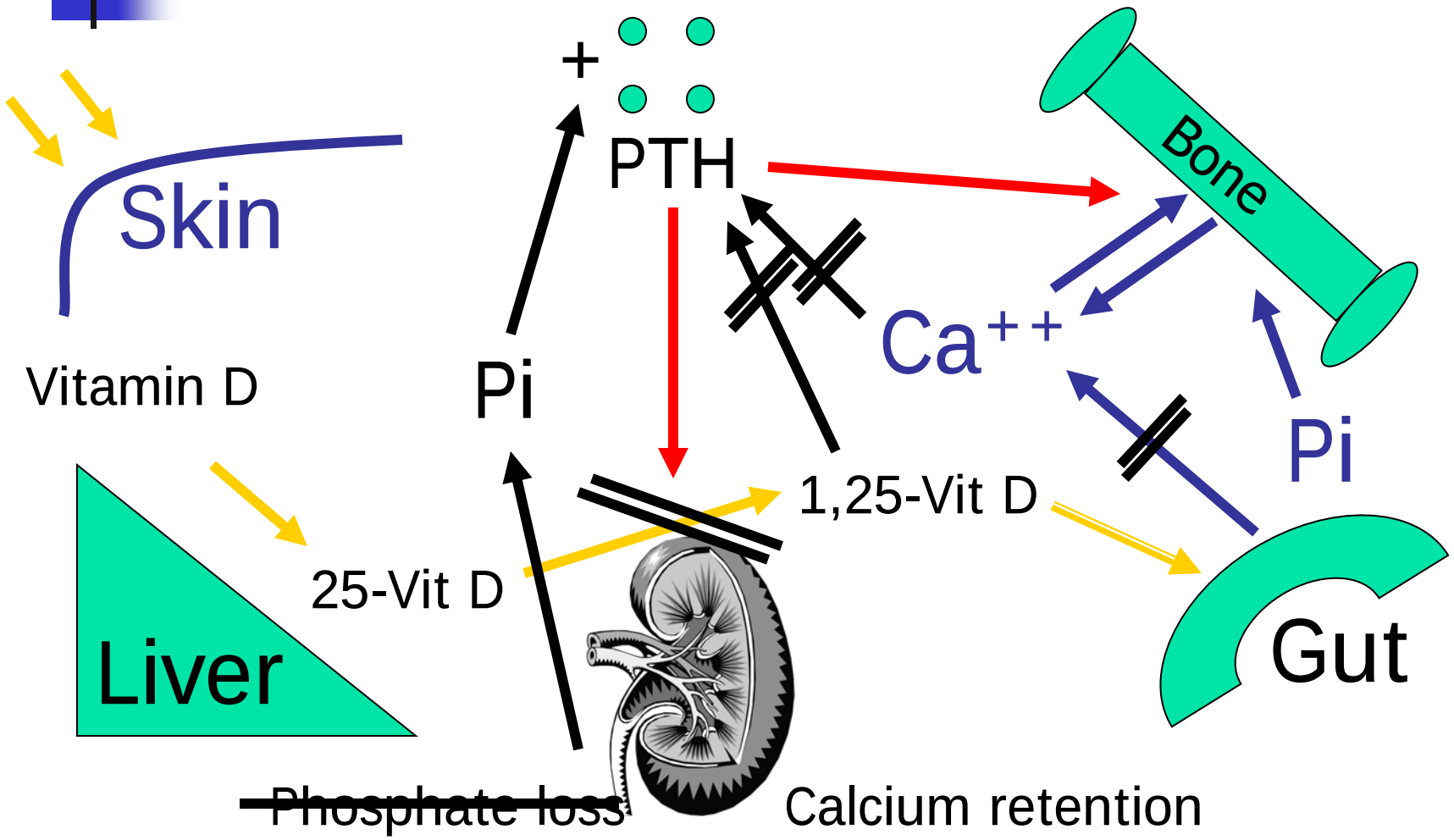
Level	Dose
<5	8,000/d x 4 wks or 50,000/wk x 4 weeks; then 4,000/d or 50,000 2x/month x 2 months
5-15	4,000/d or 50,000 q 2 weeks x 12 wks
16-30	2,000/d or 50,000 q 4 weeks x 12 weeks

- Preparations: 10,000 units/ml or 50,000 unit capsules
- Recheck level in 3 months

Unanswered Questions

- Measurement
  - Elevated PTH?
  - Repeat?
- Suppresses PTH?
- Maintenance dosing?
- Nephrotic syndrome?

Chronic Kidney Disease

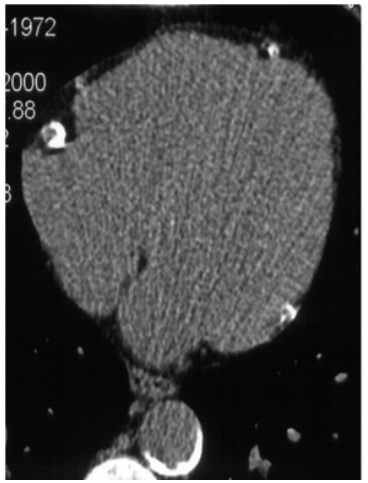


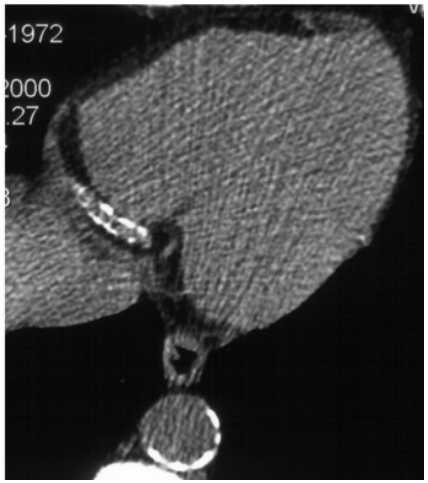
Metabolic Bone Disease: Goals

Healthy Bones

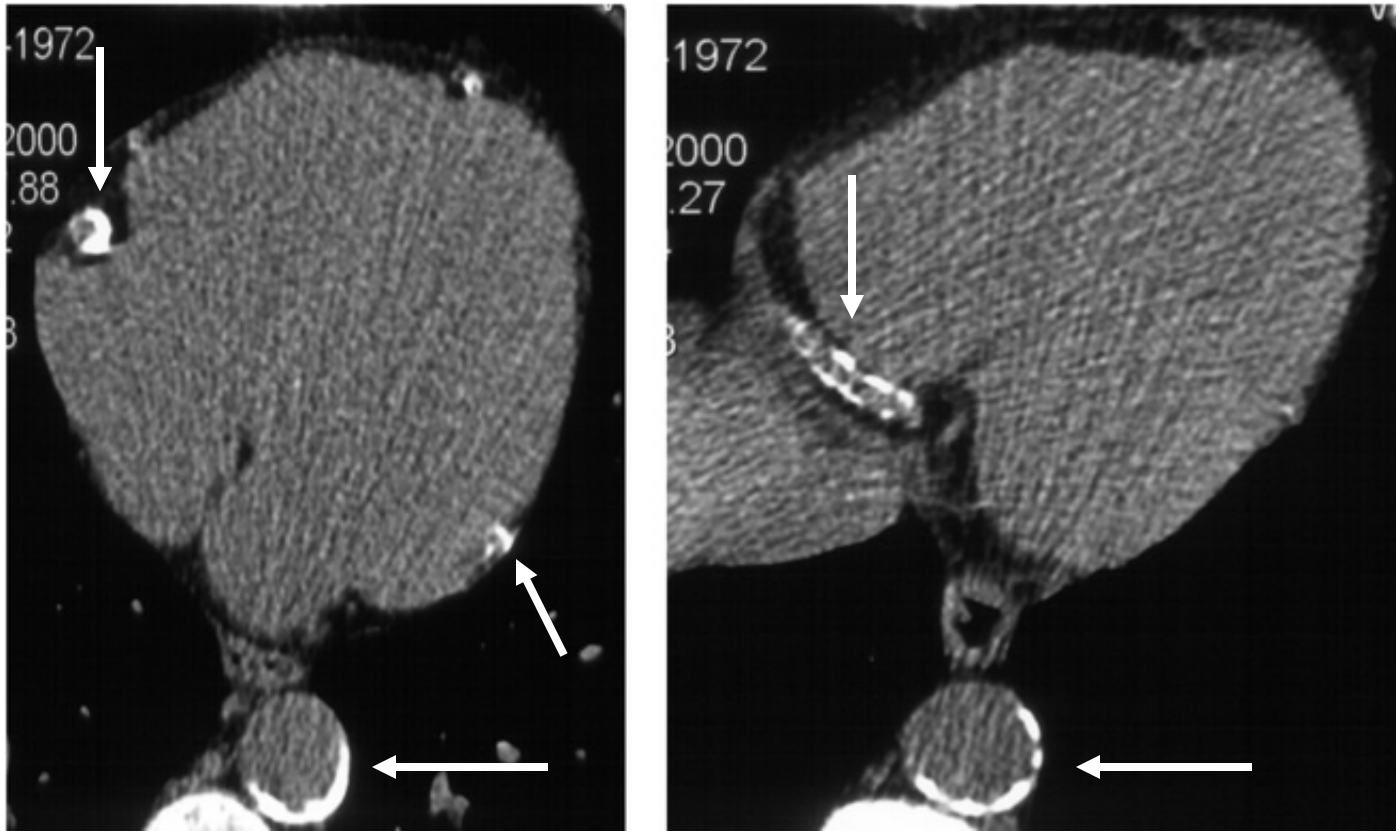
Optimize Growth

Avoid Vascular Calcifications





Vascular Calcifications: Electron-Beam CT



27-year-old male hemodialysis patient with extensive calcification in all 3 coronary arteries and aorta.

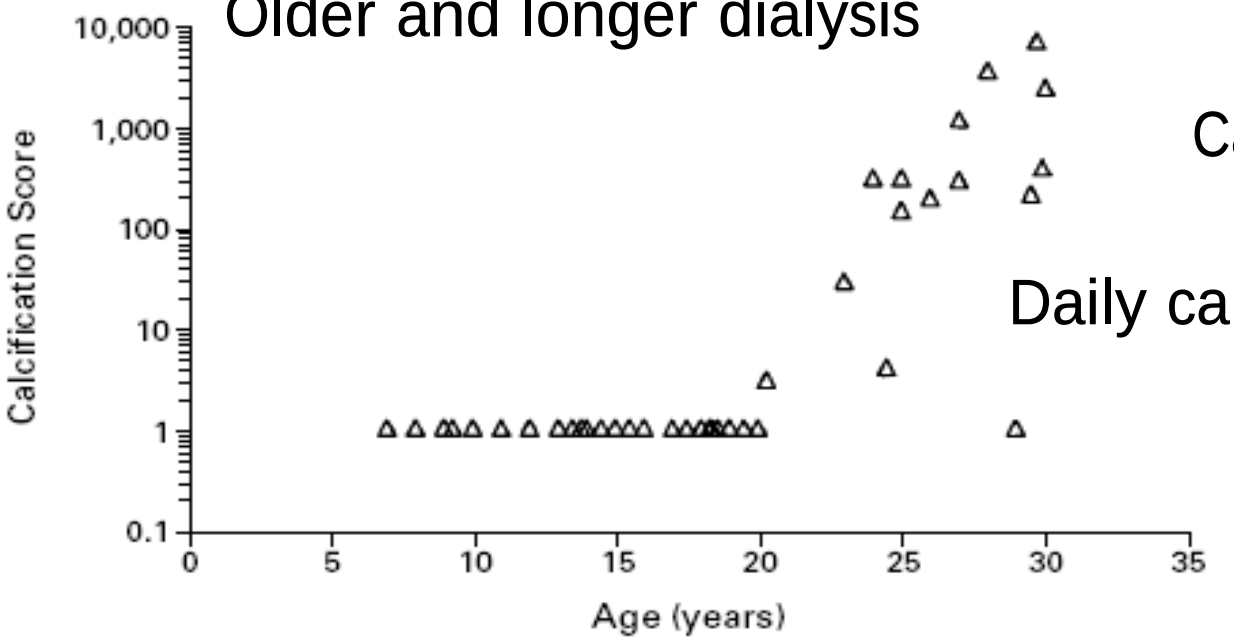
Coronary Artery Calcifications

Older and longer dialysis

Phosphorus

Ca x Pi

Daily calcium intake



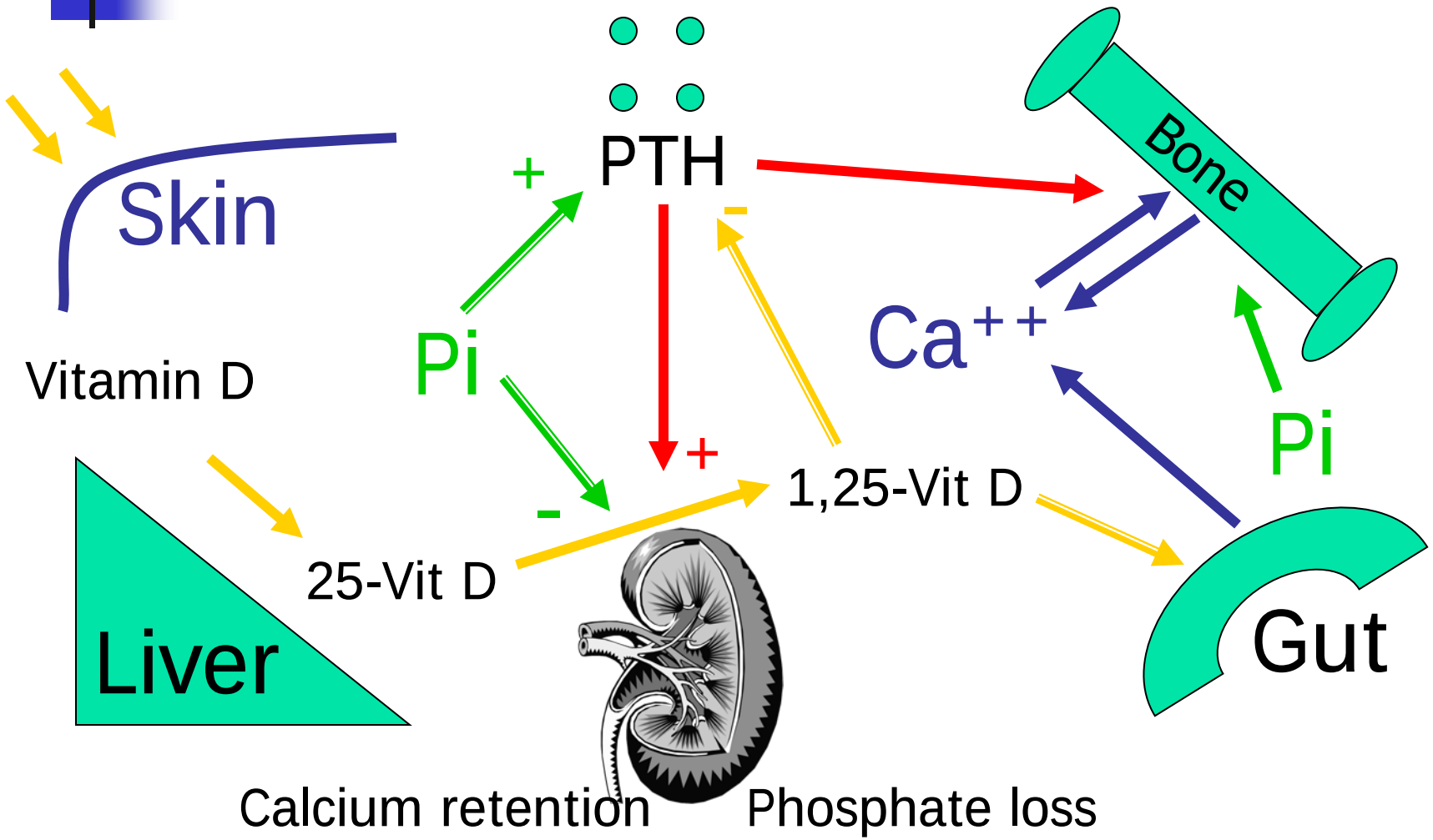
Why Vascular Calcifications?

- Disordered mineral metabolism
- Treatment
  - Calcium-containing binders
  - Active vitamin D
  - Suppression of PTH below recommended targets
  - Calcium transfer during dialysis

Management of Metabolic Bone Disease

Abnormality	Approach
Phosphorus	1. Diet 2. Binders
Calcium	1. Active vitamin D 2. Calcium
PTH	1. Lower phosphorus 2. Correct nutritional vitamin D deficiency 3. Active vitamin D 4. Correct hypocalcemia 5. Cinacalcet (Sensipar) 6. Parathyroidectomy

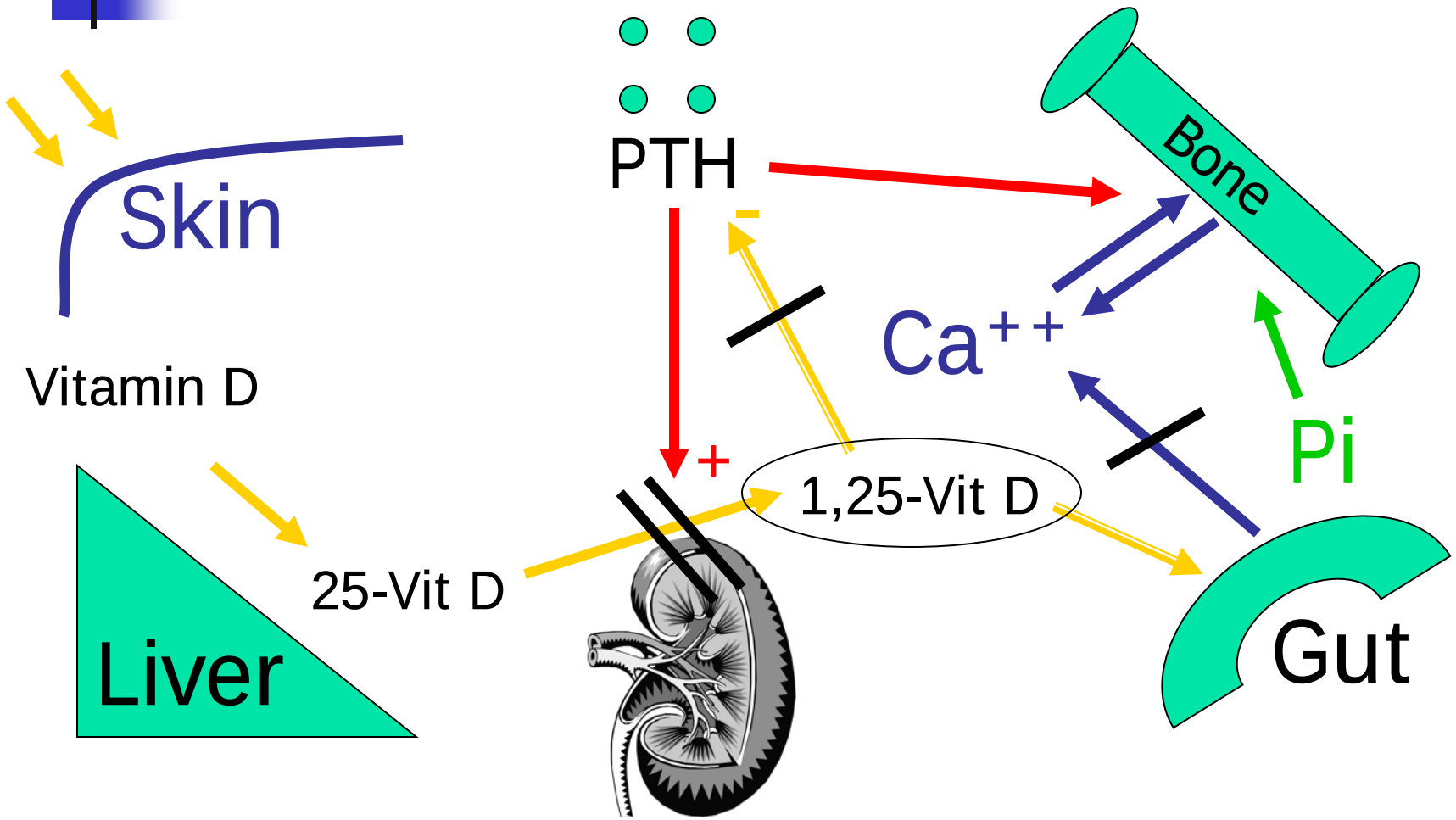
Phosphorus


Skin
Vitamin D
Liver
25-Vit D
Pi
+
PTH
-
+
-
1,25-Vit D
Bone
Ca++
Pi
Gut
Calcium retention
Phosphate loss

Hyperphosphatemia: Treatment

- Diet
  - PTH increased: dietary reference intake (DRI)
  - PTH increased and phosphorus increased: 80% DRI
- Binders
  - Calcium (avoid > 2x DRI or >2500 mg/day)
  - Non-calcium
    - Sevelamer hydrochloride (Renagel)
    - Sevelamer carbonate (Renvela)
    - Lanthanum (Fosrenol)
  - Aluminum (short-term; avoid citrate)
- Dialysis

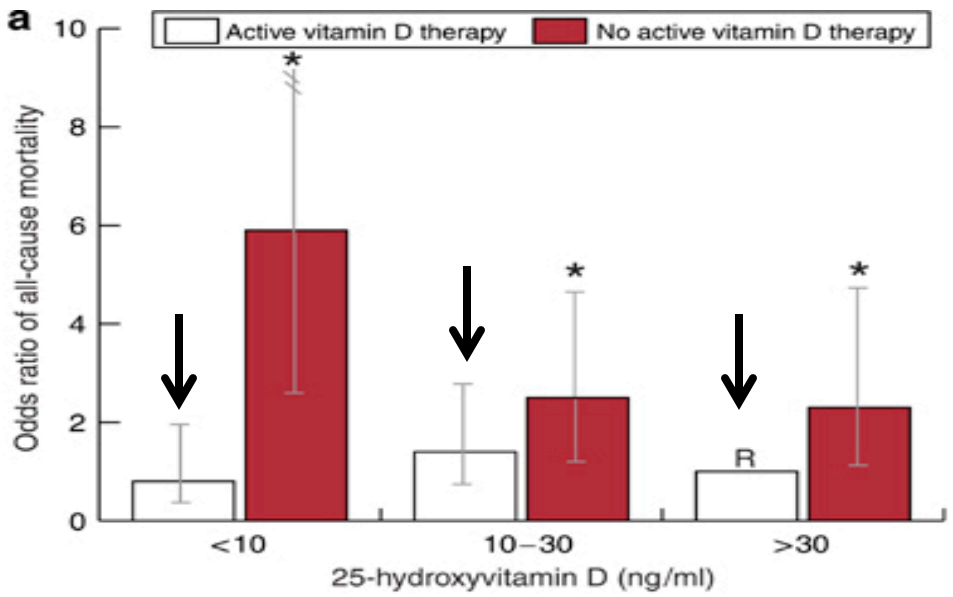
Active Vitamin D



Active Vitamin D

Compound	Preparations
Calcitriol (Rocaltrol and others)	IV (Calcijex) Capsules (0.25 and 0.5 mcg) Liquid (1 mcg/ml)
Paricalcitol (Zemplar)	IV Capsules (1, 2, and 4 mcg)
Doxercalciferol (Hectorol)	IV Capsules (0.5, 1, 2.5 mcg)

Vitamin D and Mortality



Wolf et al KI 72 1004 2007

Calcium: Treatment

- Target: normal level (corrected for albumin)
- High calcium
  - Stop calcium-containing binders
  - Stop active vitamin D
  - Decrease dialysate calcium
- Low calcium
  - Calcium
  - Active vitamin D

Objectives

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