Vitamin D and Pediatric Chronic Kidney Disease

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3rd Annual ASPN Multi-Disciplinary Symposium

October 2nd 2015

Objectives

1. Describe vitamin D metabolism and deficiency.
2. Understand disturbances in vitamin D metabolism in Chronic Kidney Disease (CKD).
3. Examine pediatric data.
4. Summarize the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines for vitamin D in children with CKD.

Outline

- **Overview of Vitamin D**
- **Vitamin D and Chronic Kidney Disease**
- **KDOQI Clinical Practice Guideline**
  - Bone mineral and vitamin D requirements

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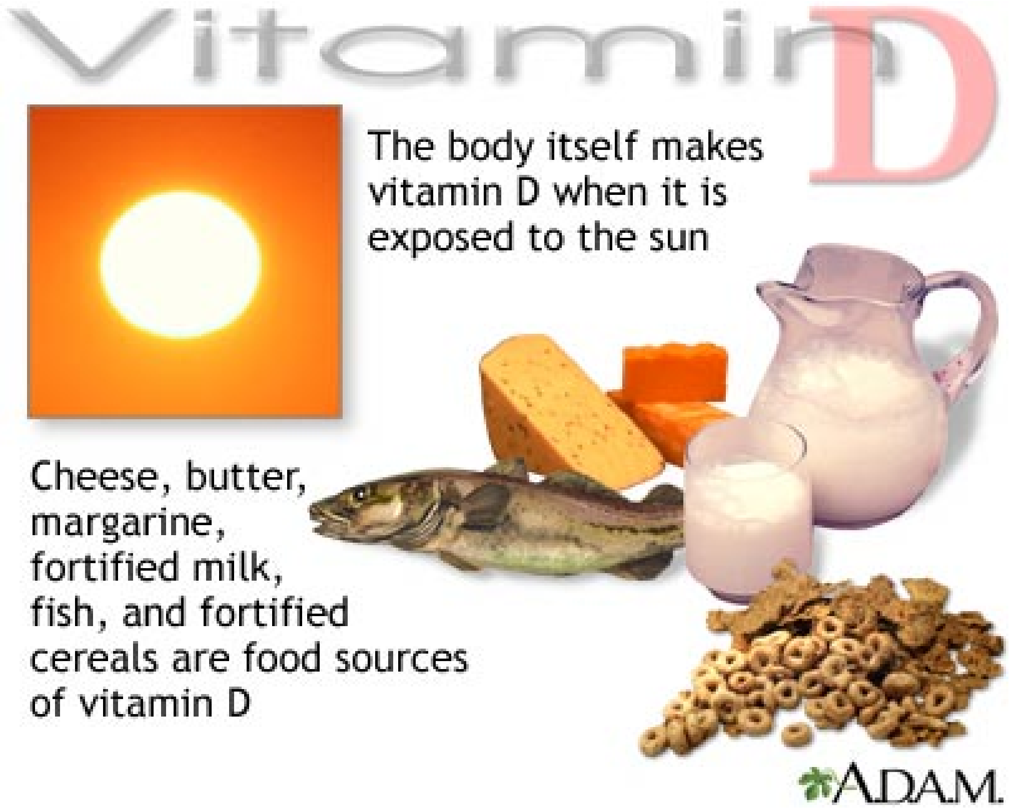
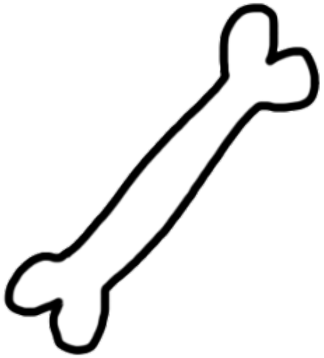
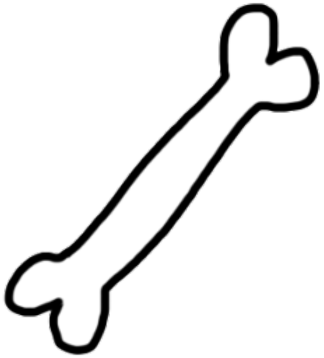
What is vitamin D ?



Why do we need vitamin D ?

- **Building & keeping strong bones**
- **Controlling calcium & phosphorus levels**
- **May have other benefits**
  - Increasing immunity
  - Preventing heart disease & cancer





National Institutes of Health 2014

Recommended Dietary Allowances (RDAs) for Vitamin D

Age	Male	Female
0–12 months	400 IU (10 mcg)	400 IU (10 mcg)
1–13 years	600 IU (15 mcg)	600 IU (15 mcg)
14–18 years	600 IU (15 mcg)	600 IU (15 mcg)
19–50 years	600 IU (15 mcg)	600 IU (15 mcg)
51–70 years	600 IU (15 mcg)	600 IU (15 mcg)
>70 years	800 IU (20 mcg)	800 IU (20 mcg)

National Institutes of Health 2014

Selected Food Sources of Vitamin D

Food	IUs per serving	Percent DV
Cod liver oil, 1 tablespoon	1,360	340
Swordfish, cooked, 3 ounces	566	142
Salmon (sockeye), cooked, 3 ounces	447	112
Tuna fish, canned in water, drained, 3 ounces	154	39
Orange juice fortified with vitamin D, 1 cup (check product labels, as amount of added vitamin D varies)	137	34
Milk, nonfat, reduced fat, and whole, vitamin D-fortified, 1 cup	115-124	29-31
Yogurt, fortified with 20% of the DV for vitamin D, 6 ounces (more heavily fortified yogurts provide more of the DV)	80	20
Margarine, fortified, 1 tablespoon	60	15
Sardines, canned in oil, drained, 2 sardines	46	12
Liver, beef, cooked, 3 ounces	42	11
Egg, 1 large (vitamin D is found in yolk)	41	10
Ready-to-eat cereal, fortified with 10% of the DV for vitamin D, 0.75-1 cup (more heavily fortified cereals might provide more of the DV)	40	10
Cheese, Swiss, 1 ounce	6	2

National Institutes of Health 2014

Sun Exposure

- **Recommendations for sufficient vitamin D synthesis**
  - Approximately 5–30 minutes
  - Between 10 AM and 3 PM
  - At least twice a week
  - To the face, arms, legs, or back without sunscreen

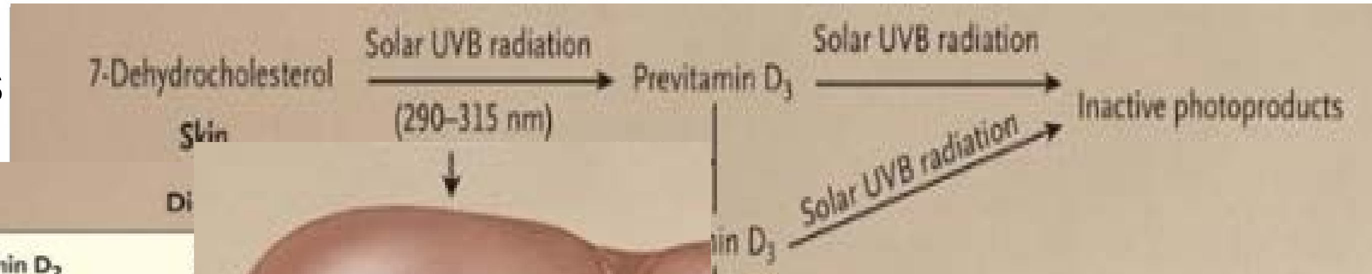
Synthesis and Metabolism of Vitamin D

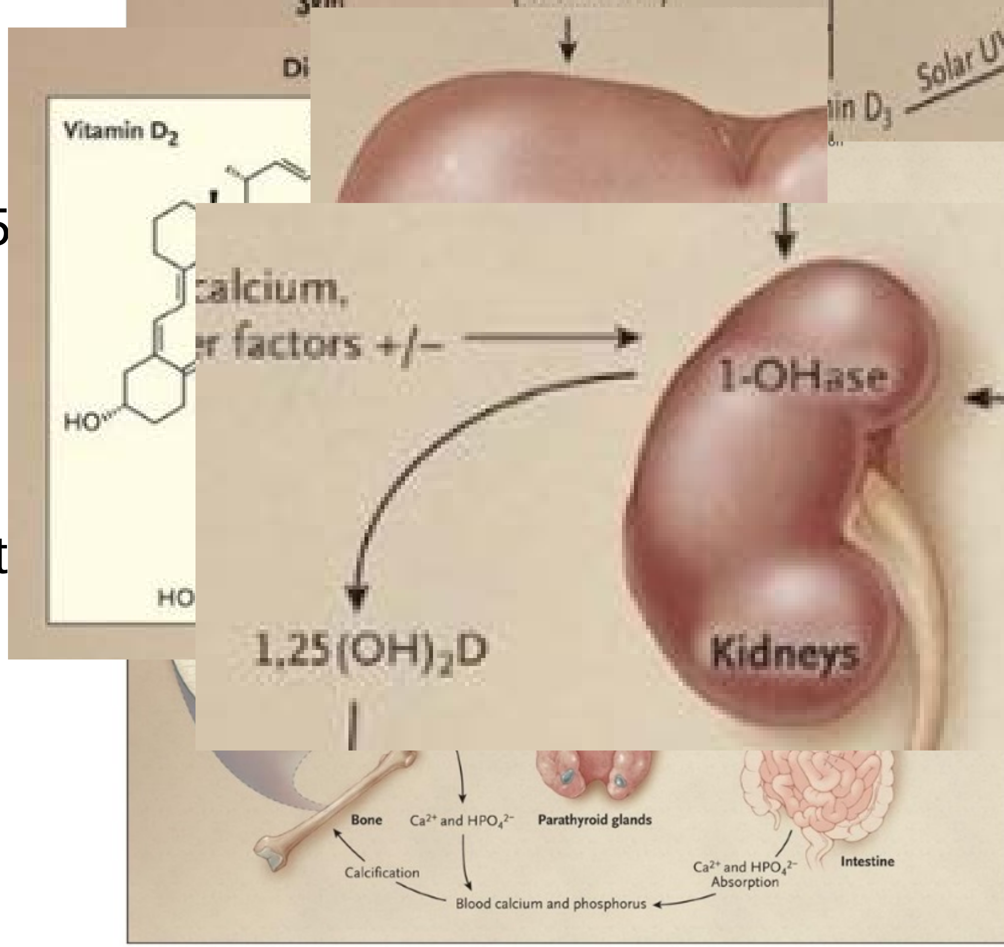
(1) Dermal Synthesis

(2) Nutrition

(5) **Liver:**
Vit D → Vit D-25 hydroxylase → 25(OH)D

(6) Determine St





(4) DBP Transport

(7) **Kidney:**
25(OH)D → (1α-OHase) → $1,25(OH)_2D$ (active)

Majority of circulating 1,25

Holick, M. NEJM 2007

Vitamin D Binding Protein

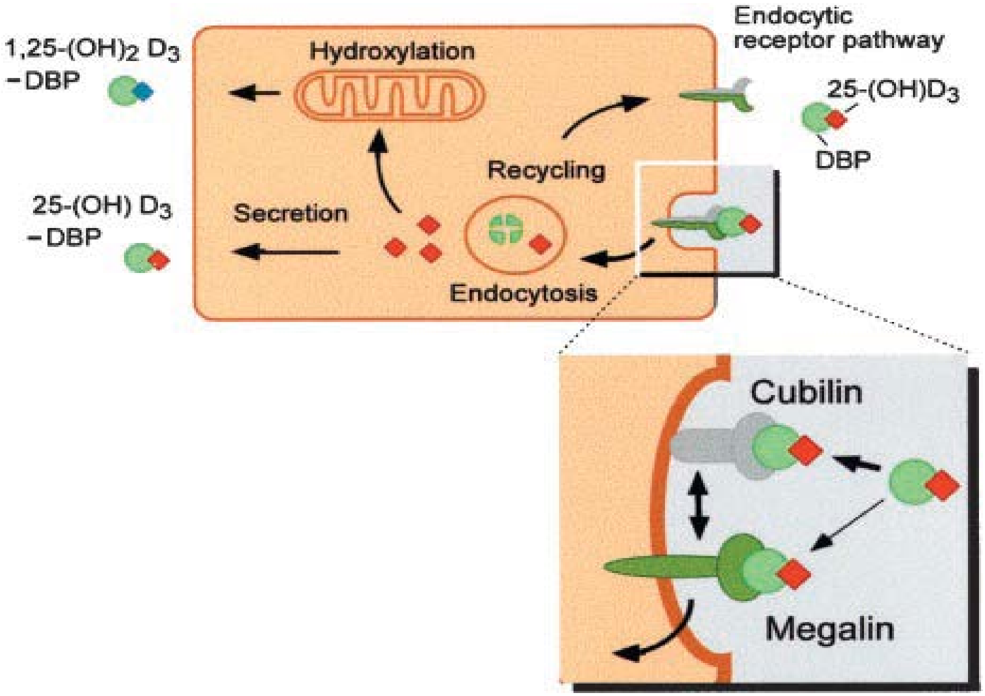
- >99% of circulating 25(OH)D and $1{,}25(OH)_2D$ are bound
- Proteinuric patients have urinary loss of vitamin D binding protein (DBP) and albumin
- Total serum 25(OH)D levels, the conventional index of vitamin D status, may not reflect free or bioavailable vitamin D in the setting of ↓ serum DBP and albumin

$$\text{Free } 25(\text{OH})\text{D} = \frac{\text{total } 25(\text{OH})\text{D}}{1 + (6 \times 10^3 \times \text{albumin}) + (7 \times 10^8 \times \text{DBP})}$$

Bikle et al. J Clin Endocrinol Metab 1986

Vitamin D Binding Protein

- **VitD-DBP complexes are <u>freely filtered</u> by the glomerulus**
- **VitD-DBP complexes are reabsorbed via megalin/cubilin-mediated endocytosis in the proximal tubule**
  - along with numerous other ligands



Other ligands:
Albumin
PTH
Retinol binding protein
B_2-microglobulin
α1-microglobulin

Nykjaer et al. Proc Natl Acad Sci U S A 2001

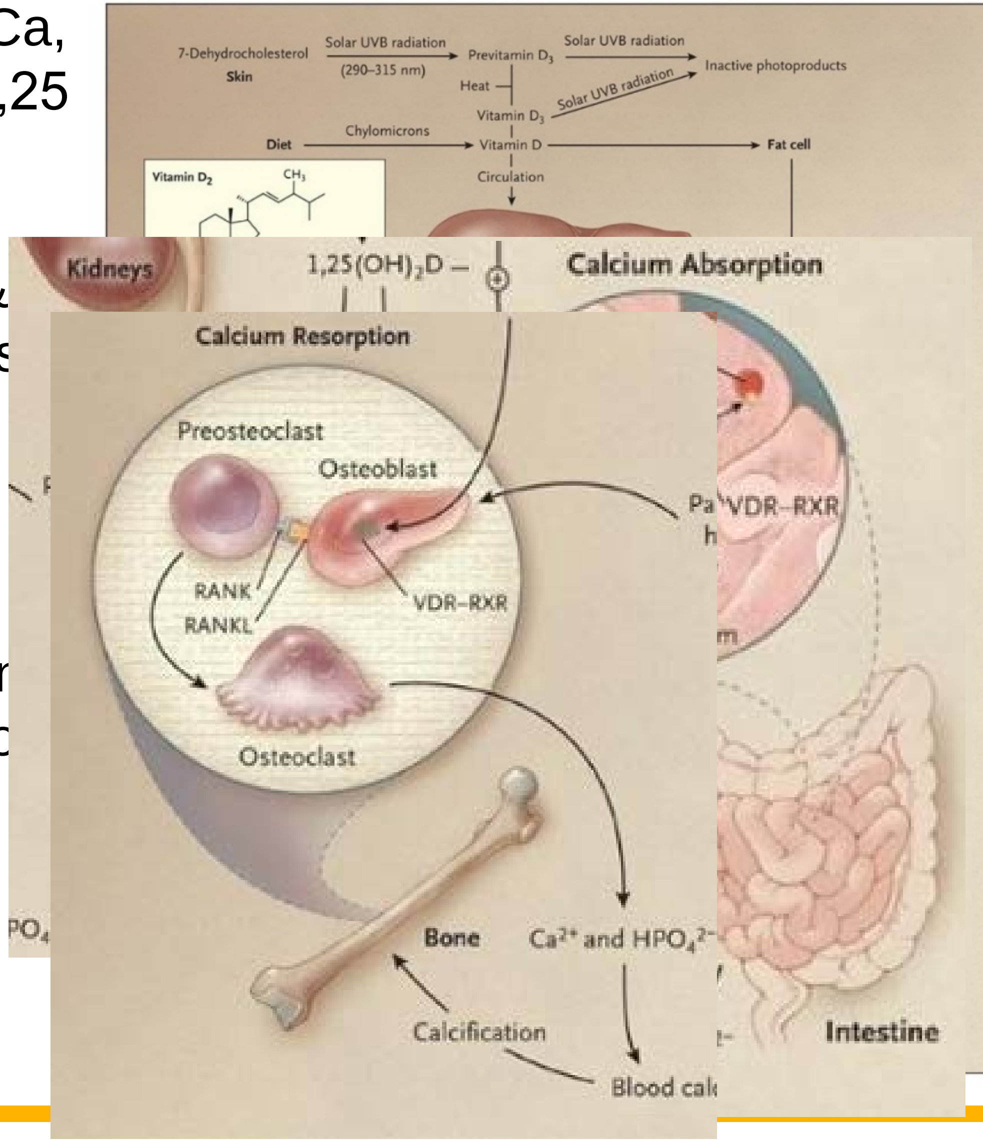
Synthesis and Metabolism of Vitamin D

Kidney: Phos, Ca, FGF-23 ↓ or ↑ 1,25

Bone:
1,25 anabolic & catabolic actions

catabolic → osteoclasts remove Ca & Phos to maintain serum Ca & Pho

adequate Ca & Phos promote skeletal mineralization



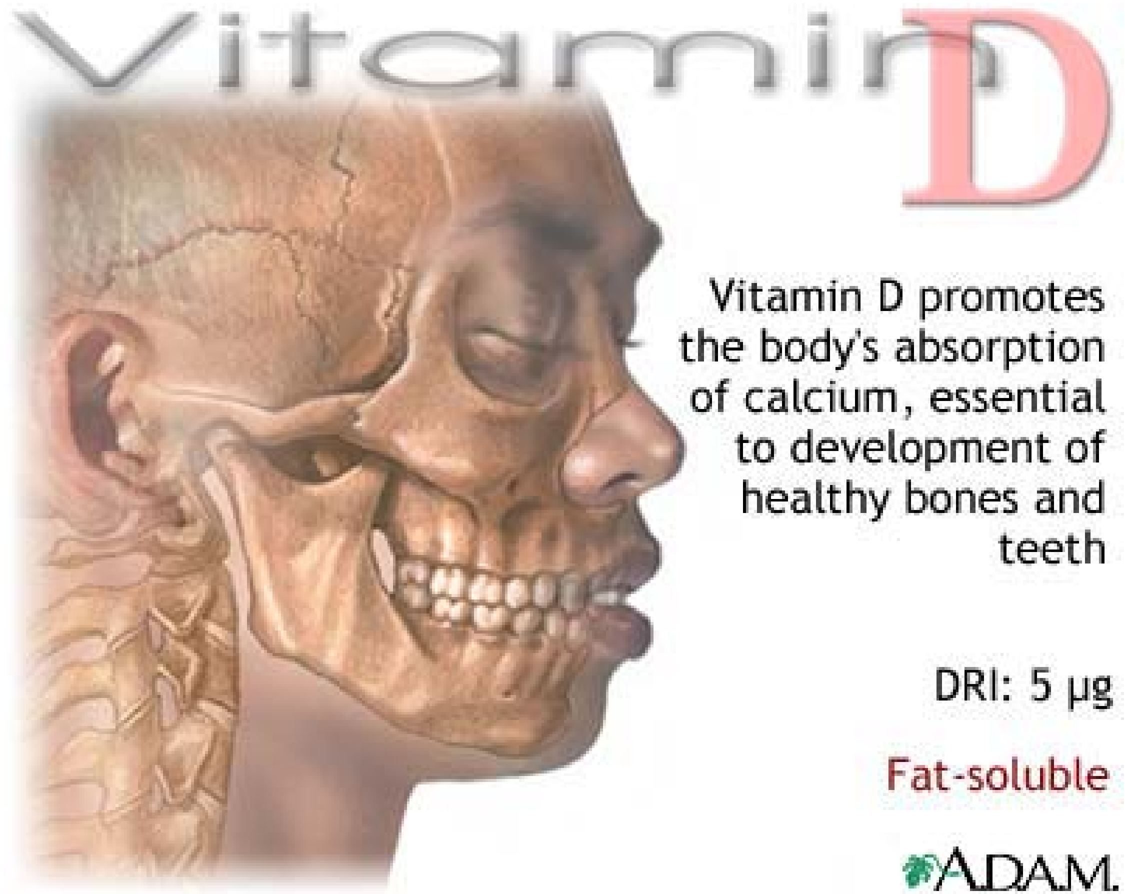
Parathyroid: PTH stimulates 25 → 1,25 & inhibits 24-OHase

Negative feedback: ↑1,25 →↓PTH & stimulates 24-OHase to catabolize 1,25 → calcitroic acid

Intestine: Ca absorption by interaction with VDR-RXR → ↑ TRPV6 (Ca Channel) & CaBP

Holick, M. NEJM 2007

Skeletal Actions of Vitamin D



Extra Skeletal Actions of Vitamin D

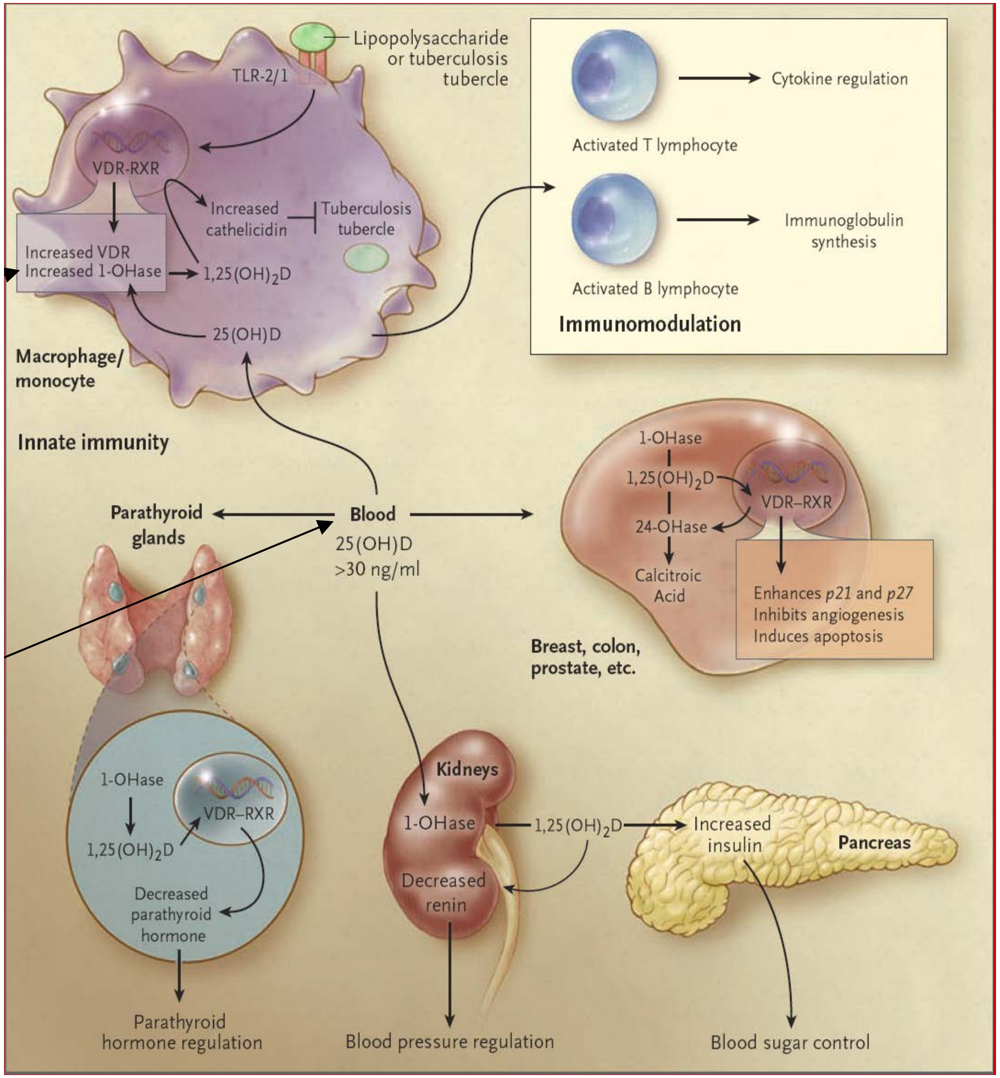
- **Extra skeletal actions of vitamin D**
  - Many cells have the VDR and the 1α-OHase
    - Breast, colon, pancreas, prostate
    - Immune cells (monocyte, macrophage, lymphocyte)
      - ✓ *Innate and acquired immunity*
      - ✓ *Autoimmune disease (MS, IBD, Type 1 diabetes)*
- **Locally produced 1,25$(OH)_2$ vitamin D**
  - Does not enter the circulation
  - Is not regulated by PTH
  - Does not affect calcium metabolism
  - Local and intracellular levels may exceed 100-1000 times circulating levels

Holick, M. NEJM 2007

Extra Skeletal Actions of Vitamin D

1,25 $(OH)_2D$ does not enter the circulation

Required for local synthesis of 1,25 $(OH)_2D$



Holick, M. NEJM 2007, Liu et al. Science 2006, Adams et al. J Immunol 2009

Burden of Vitamin D Deficiency

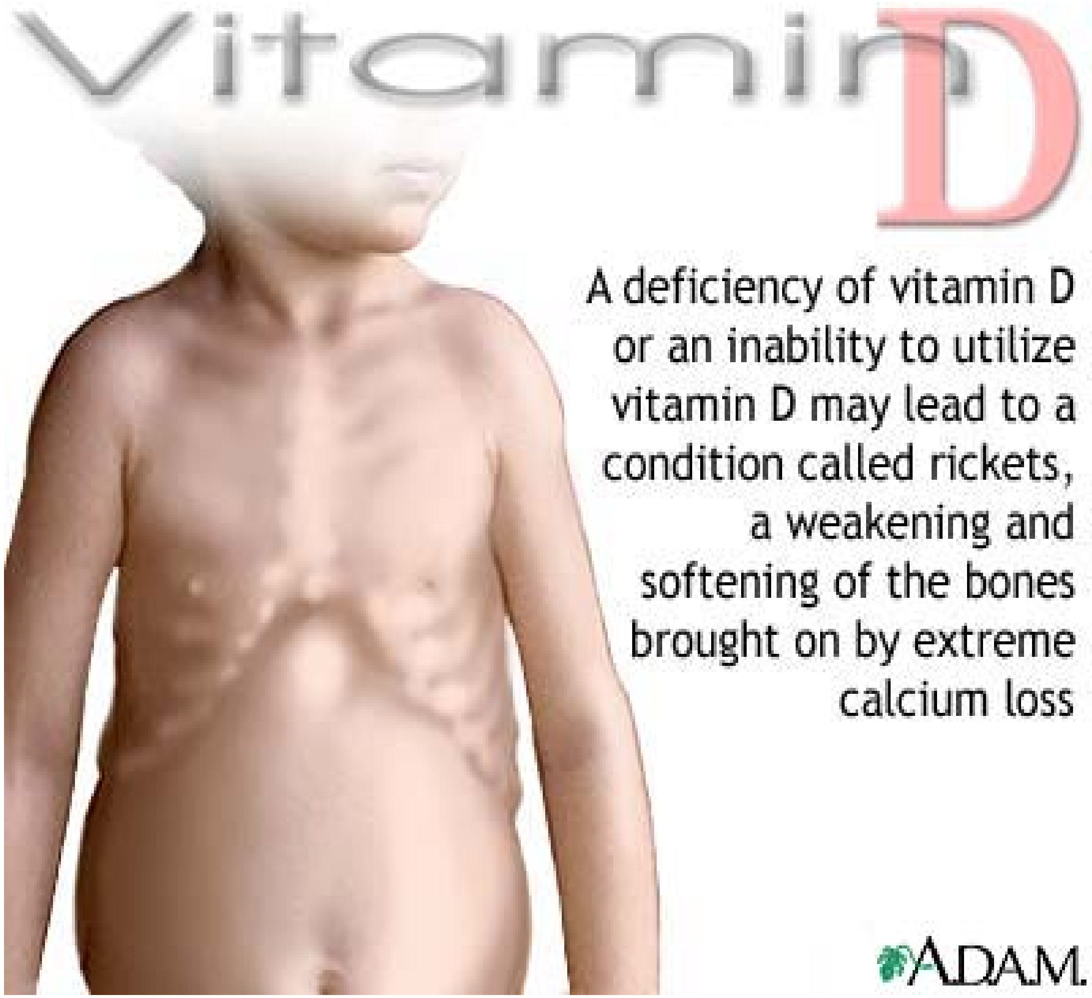
- **25(OH)D of 20 ng/ml**
  - Meets the requirements of ≥ 97.5% of the population

- **Based solely on classical skeletal actions**

- **Stressed that further research is needed to define the requirements for other facets of health**

Institute of Medicine Report 2011

Vitamin D Deficiency



Nutritional Rickets

- 1^{st} clinical description 350 years ago by Francis Glisson
- Rachitis derived from Greek for spine
- Old English “wrickken” – to twist
- 200 years later cod liver oil and sunlight shown to prevent → 1928 Nobel Prize to Adolf Windaus

Nutritional Rickets

- **Development of rickets depends on:**
  - Duration and severity of vitamin D deficiency
  - Growth rate
  - Dietary Calcium intake

- **Biochemical Findings:**
  - Normal Serum Calcium
  - ↓ Serum Phosphorus
  - Normal or ↑ $1,25(OH)_2D$

Rickets

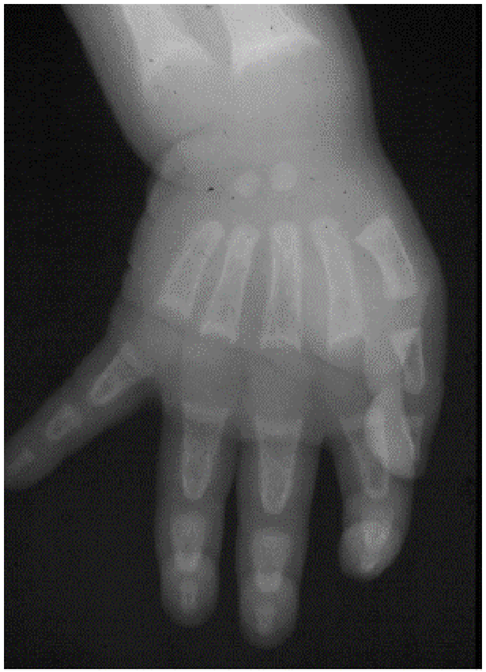


Figure 1: **Radiograph of wrist showing rickets**
Classic features of rickets include cupping, fraying, and splaying of the metaphysis. The ulna (which grows more quickly at its distal end) is more severely affected. Widening of the growth plates is not shown because the secondary ossification centres of the radius and ulna are not yet apparent.

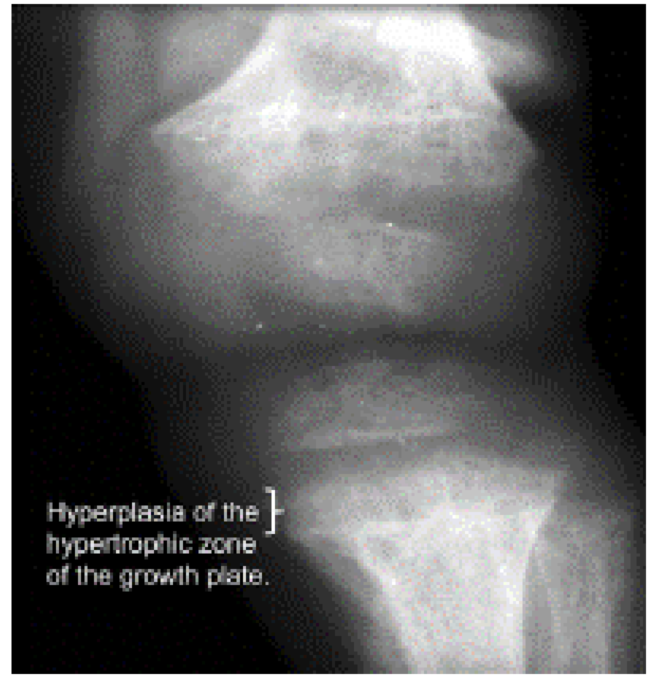


Fig. 1 Severe rachitic bone changes in a child with vitamin D receptor defect (vitamin D-dependent rickets type 2). The wide calcified lower hypertrophic zone of the growth plate is clearly evident. This is due to the defective apoptosis of the terminal hypertrophic chondrocyte due to hypophosphatemia

Wharton and Bishop.Lancet 2003

Tiosano and Hochberg. J Bone Miner Metab 2009

Burden of Vitamin D Deficiency

- **Highly prevalent in children and adults worldwide**
- **Adverse effects are now known to extend far beyond bone and mineral metabolism:**
  - Mortality
  - Cardiovascular disease
  - Insulin resistance
  - Autoimmune disease
  - Infection
  - Inflammation

Outline

- Overview of Vitamin D
- **Vitamin D and Chronic Kidney Disease**
- KDOQI Clinical Practice Guideline
  - Bone mineral and vitamin D requirements

CKD MBD

- **CKD –Mineral and Bone Disorder (MBD)**
  - A systemic disorder of mineral and bone metabolism caused by CKD and manifested by either one or a combination of:
    - Abnormalities of Ca, Phos, PTH, or **Vit D metabolism**
    - Abnormalities of bone turn over, mineralization, volume, linear growth, or strength
    - Vascular or soft tissue calcification
- **Renal Osteodystrophy**
  - An alteration of bone morphology in patients with CKD
  - It is one measurement of the skeletal component of the systemic disorder of CKD-MBD that is quantifiable by histomorphometry of bone biopsy

Moe. Kidney International 2006

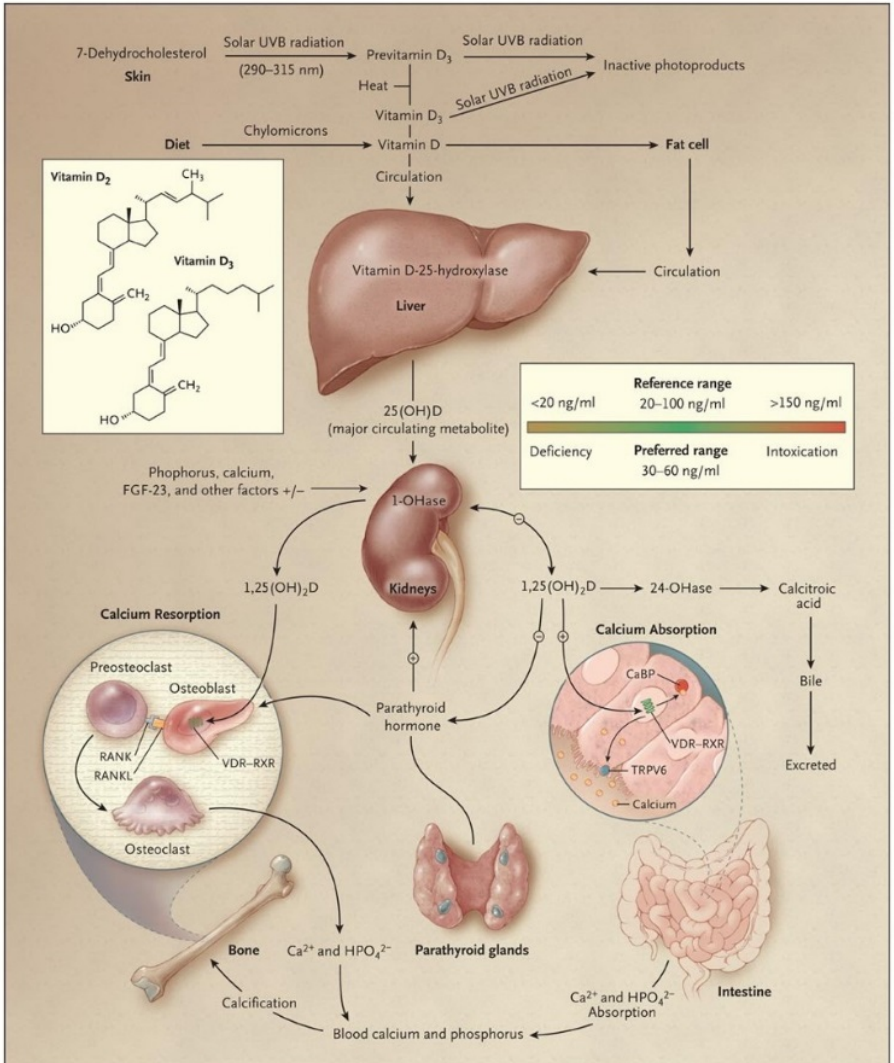
CKD MBD & Vitamin D

(1) ↓ Dermal Synthesis

(2) Nutritional D Deficiency

(3) ↓ Activation of 25(OH)D → $1,25(OH)_2D$

(7) ↑ FGF23



(4) ↑ Phos

(5) ↓ Ca Absorption

(6) ↑ PTH due to (4) and (5)

Holick, M. NEJM 2007

CKD Risk Factors

- **Risk Factors for lower 25(OH)D**
  - Decreased sunlight exposure
  - Less efficient dermal synthesis of Vitamin D_3
  - Dietary restrictions
  - Proteinuria – urinary losses of DBP & albumin

- **Risk Factors for lower 1,25(OH)$_2$D**
  - Lower substrate
  - Proximal tubal injury in the kidney
  - Increased FGF 23

Fibroblast growth factor 23 (FGF23)

- **Inhibits 1-α-OHase activity**
  - Needed to convert 25(OH)D → 1,25$(OH)_2$D

- **Induces 24-OHase activity**
  - Responsible for catabolism of 25(OH)D and 1,25$(OH)_2$D

$\uparrow$ FGF 23 = $\downarrow$ 1-α-OHase activity $\uparrow$ 24-OHase activity

Burden of Vitamin D Deficiency in CKD

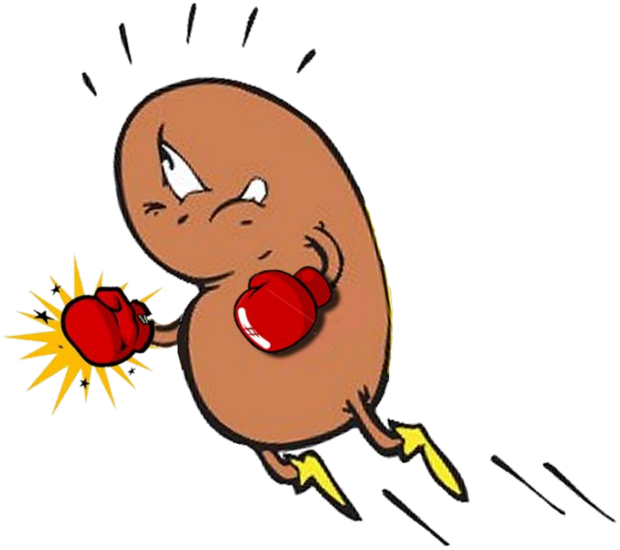
- **Extra Skeletal**
  - **Vitamin D deficiency linked to mortality and complications in CKD including:**
    - Insulin Resistance
    - Anemia
    - Inflammation
  - **In prospective studies of adults with CKD, low serum 25(OH)D concentration was an independent predictor of CKD progression and mortality**

Mehrotra et al. Kidney Int 2009, Chonchol et al. Kidney Int 2007, Stefikova et al.Physiol Res 2011,Lac et al.Clin Nephrol 2010, Patel et al. Kidney Int 2010, Isakova et al.J Ren Nutr 2010, Stubbs et al. J Am Soc Nephrol 2010

Vitamin D Renoprotective

- **Vitamin D deficiency may also contribute to podocyte injury and development of proteinuria**

- **Animal studies: treatment with activated vitamin D**
  - Inhibited the renin-angiotensin system
  - Prevented podocyte loss and glomerulosclerosis
  - Reduced hypoalbuminemia



Kuhlmann et al. Am J Physiol Renal Physiol 2004, Li et al. J Clin Invest 2002, Matsui et al. Nephrol Dial Transplant 2009, Schwarz et al. Kidney Int 1998

Vitamin D Renoprotective

- **Normal 25 (OH) D ≥ 50 ng/ml associated with:**
  - ↓ Decreased Proteinuria
  - ↑ Greater preservation of renal function
- **Analysis of 3 RCT evaluating safety and efficacy of paracalcitol in CKD stages 3-4**
  - ↓ Proteinuria
- **Subsequent RCT CKD stages 2-3**
  - ↓ Hypoalbuminemia

Shroff et al JASN 2015, Agarwal et al. Kidney Int 2005, Alborzi P et al. Hypertension 2008

Prevalence of Insufficiency

- **Insufficiency is common in children with CKD**
- **16-30 ng/mL = vitamin D insufficiency** National Kidney Foundation 2009

Author/Journal	Year	n	25(OH)D	Prevalence
Menon et al. Peds Neph	2008	57	< 30 ng/mL	77.2 %
Hari et al. Peds Neph	2010	42	< 30 ng/mL	82.1 %
Ali et al. Pediatrics	2009	88	< 32 ng/mL	72 %
Seeherunvong et al. J.Pediatrics	2009	258	< 30 ng/mL	60 %
Belostotsky et al. Arch Dis Child	2008	143	< 30 ng/mL	83.2 %

Prevalence of Deficiency

- **Deficiency is common in children with CKD**
- **5-15 ng/mL = vitamin D deficiency**

National Kidney Foundation 2009

Author/Journal	Year	n	25(OH)D	Prevalence
Menon et al. Peds Neph	2008	57	5-15 ng/mL	21.1 %
Hari et al. Peds Neph	2010	42	< 16 ng/mL	42.8 %
Ali et al. Pediatrics	2009	88	< 15 ng/mL	39 %
Seeherunvong et al. J.Pediatrics	2009	258	< 20 ng/mL	28 %
Belostotsky et al. Arch Dis Child	2008	143	< 20 ng/mL	58 %

Vitamin D and CKD

- **182 children with CKD vs. 276 healthy controls**
  - In children with ↓ 25(OH)D concentration
- **No apparent difference in 25 (OH) D concentrations between early –stage CKD and healthy children**

Table 3 | Predictors of vitamin D concentrations and vitamin D deficiency in healthy reference and CKD participants: results from multiple linear regression and logistic regression modeling

		Deficient		Severely deficient	
	25(OH)D (ng/ml)	25(OH)D <20 ng/ml		25(OH)D <10 ng/ml	
CKD stage	$P<0.0001$		$P<0.0001$		$P=0.0002$
Healthy reference (*n*=276)	24.2 ± 0.7[a]	1.00		1.00	
2–3 (*n*=74)	26.6 ± 1.1	1.12	(0.54–2.32)	1.56	(0.53–4.59)
4–5 (*n*=54)	20.9 ± 1.3	2.77	(1.32–5.81)	4.24	(1.68–10.71)
5D (*n*=54)	16.1 ± 1.3	10.28	(4.48–23.61)	6.38	(2.59–15.60)

Kalkwarf et al. Kidney Int 2012

Vitamin D and CKD

- **Statistically significant interaction between 25(OH)D concentration and CKD stage for predicting 1,25$(OH)_2$D concentrations ($p<0.0001$)**

- **For a 1 ng/ml increase in 25(OH)D concentration, 1,25$(OH)_2$D concentrations increased as follows:**
  - Healthy 0.4% (n=275, p=0.01)
  - CKD 2/3 0.7% (n=57, p=0.04)
  - CKD 4/5 4.2% (n=14, p=0.006)
  - CKD 5D 2.3% (n=8, p=0.15)

Kalkwarf et al. Kidney Int 2012

Vitamin D and CKD

- **25(OH) D**
  - Positively associated with 1,25$(OH)_2$D
  - Inversely related to Intact PTH & inflammatory markers CRP, IL-6

- **Conclusion**

↓ 25 (OH)D = ↓ 1,25$(OH)_2$D ↑ PTH & Inflammation

Kalkwarf et al. Kidney Int 2012

Vitamin D and CKD

- **Hypoalbuminemia and glomerular disease were independent risk factors for Vitamin D deficiency**
  - Adjusted for age, race, season and CKD stage
- **Adjusted mean 25(OH) D by diagnosis ($p<0.0001$):**

CAKUT (congenital abnormalities of the kidney and urinary tract)	**24.8**
Systemic inflammatory disease/ glomerulonephritis	**19.2**
FSGS (focal segmental glomerulosclerosis)	**14.6**
Other	**25.5**

- **Adjusted mean 25(OH) D by albumin <3 vs. ≥3**
  - 11.1 vs. 23.5 ng/ml ($p<0.0001$)

Kalkwarf et al. Kidney Int 2012

Vitamin D Supplementation

- **If the serum level of 25-hydroxyvitamin D is less than 30 ng/mL, supplementation with vitamin D_2 (ergocalciferol) or vitamin D_3 (cholecalciferol) is suggested.**

National Kidney Foundation 2009

Author/ Journal	Year	n	Supplement	25 (OH)	PTH	Ca & Phos
Menon et al. Peds Neph	2008	22	2000 - 4000 IU D_2 Per day	n/a	↓	No elevated levels
Hari et al. Peds Neph	2010	42	600,000 IU D_3 3 days	↑	↓	No change
Shroff et al. CJASN	2012	47	50,000 IU D_2 Per KDOQI	n/a	Delayed hyperpara onset	No elevated levels

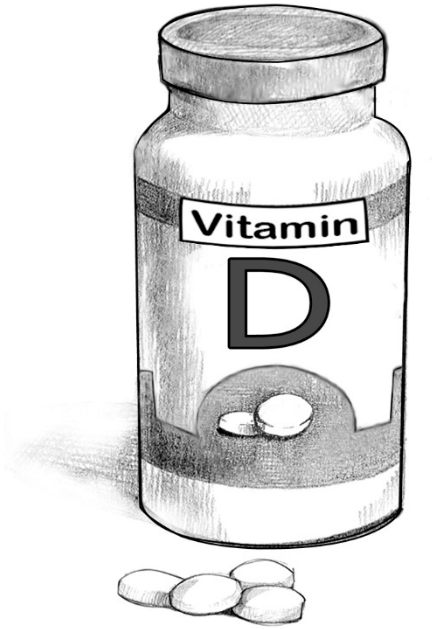
Vitamin D Supplementation

- **Cholecalciferol** (**D_3**) is Superior to **Ergocalciferol** (**D_2**)
  - Cholecalciferol appears to have higher bioefficacy than ergocalciferol
  - Greater increases in 25(OH) vitamin D levels with cholecalciferol
  - Cholecalciferol maintains higher levels of 25(OH)-vitamin D over time
  - Greater efficacy may be related to higher affinities to hepatic 25-hydroxylase, DBP, VDR, and differences in deactivation

National Kidney Foundations 2009, Trang et al. Am J Clin Nutr 1998 ,
Armas et al. J Clin Endocrinol Metab 2004, Houghton et al. Am J Clin Nutr 2006

Vitamin D Supplementation

- **Ergocalciferol (Vitamin D_2)**
  - 50,000 IU capsules -100 capsules
    - $143.40
  - Liquid 800 IU/mL - 60 mL
    - $110.82
- **Cholecalciferol (Vitamin D_3)**
  - 10,000 IU capsules - 100 capsules
    - $4.34
  - Liquid 2000 IU per drop – 30 mL
    - $11.39



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Vitamin D Supplementation

- FDA does not routinely review the manufacturing of dietary supplements, and therefore cannot guarantee their safety and effectiveness.
- **Rely on different certifying organizations:**
  - U.S. Pharmacopeial Convention (USP)
    - Products voluntarily submitted → meet stringent testing & auditing criteria
  - NSF or National Products Association
    - Third party organizations → have processes set up for facility & product inspection
- **Products not certified by USP → require certificates of analysis (COA)**
  - Confirm whether or not the dosage matches label

Vitamin D Supplementation

- **Initiate therapy with active vitamin D sterol (calcitriol)**
  - **CKD Stages 2-4**
    - 25 (OH) D >30 ng/mL and serum levels of PTH are above target range for CKD stage
  - **CKD Stage 5**
    - PTH > 300 pg/mL

Table 3. Target Range of Serum PTH by Stage of CKD

CKD Stage	GFR Range (mL/min/1.73 m²)	Target Serum PTH
2	60-89	35-70 pg/mL (OPINION)
3	30-59	35-70 pg/mL (OPINION)
4	15-29	70-110 pg/mL (OPINION)
5	<15 or dialysis	200-300 pg/mL (EVIDENCE)

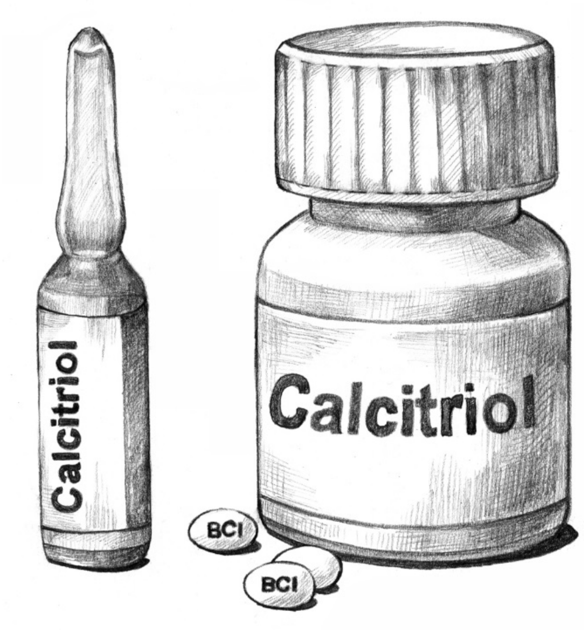
Vitamin D Supplementation

- **Use activated vitamin D to decrease PTH**
  - Activated Vitamin D
    - Limited by ↑Ca & ↑Phos
      - ✓ *Calcitriol*
      - ✓ *Alfacalcidiol*
  - Vitamin D Analogs
    - Minimize intestinal Ca & Phos absorption
      - ✓ *Paricalcitol*
      - ✓ *Doxercalciferol*
  - Calcimimetics
    - Mimics calcium at the CaSR in the parathyroid glands
      - ✓ *Cinacalcet*

Wesseling, et al. Pediatric Bone, 2012.

Vitamin D Supplementation

- **Calcitriol**
  - 0.25 mcg capsules - 30 capsules
    - $57.59
- **Paricalcitol**
  - 1 mcg capsules – 30 capsules
    - $264.67
- **Doxercalciferol**
  - 0.5 mcg - 50 capsules
    - $366.31
- **Cinacalcet**
  - 30 mg capsules – 30 capsules
    - $1084.83



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Outline

- Overview of Vitamin D
- Vitamin D and Chronic Kidney Disease
- **KDOQI Clinical Practice Guideline**
  - Bone mineral and vitamin D requirements

Calcium

- **Total oral and/or enteral calcium intake from nutritional sources and phosphate binders should be in the range of 100% to 200% of the DRI for calcium for age.**
- **Intestinal calcium absorption is impaired in CKD because 1,25$(OH)_2$D production decreased**
- **Stimulate calcium absorption with vitamin D therapy**
- **Must also worry about excessive calcium load**
  - Phosphate binders
  - High doses of calcitriol
  - Absorption from dialysis fluids

Calcium

Table 20. Recommended Calcium Intake for Children with CKD Stages 2 to 5 and 5D

Age	DRI	Upper Limit (for healthy children)	Upper Limit for CKD Stages 2-5, 5D (Dietary + Phosphate Binders*)
0-6 mo	210	ND	≤420
7-12 mo	270	ND	≤540
1-3 y	500	2,500	≤1,000
4-8 y	800	2,500	≤1,600
9-18 y	1,300	2,500	≤2,500

Abbreviation: ND, not determined.

*Determined as 200% of the DRI, to a maximum of 2,500 mg elemental calcium.

Phosphorus

- **Suggested to reduce dietary phosphorus intake to 100% of the DRI for age when serum PTH concentration is above target range for CKD stage and serum phosphorus concentration is within normal range for age.**
- **Suggested to reduce dietary phosphorus intake to 80% of the DRI for age when the serum PTH concentration is above target range for CKD stage and serum phosphorus exceeds normal range for age.**
- **Monitor serum phosphorus every 3 months in CKD stages 3 to 4 and monthly in CKD stages 5 and 5D.**
- **In all CKD stages, avoid serum phosphorus levels both above and below the normal reference range for age.**

Phosphorus

Table 23. Recommended Maximum Oral and/or Enteral Phosphorus Intake for Children With CKD

Age	DRI (mg/d)	Recommended Phosphorus Intake (mg/d): High PTH and Normal Phosphorus*	Recommended Phosphorus Intake (mg/d): High PTH and High Phosphorus†
0-6 mo	100	≤100	≤80
7-12 mo	275	≤275	≤220
1-3 y	460	≤460	≤370
4-8 y	500	≤500	≤400
9-18 y	1,250	≤1,250	≤1,000

Vitamin D

- **When should 25 (OH) D be measured?**

  - **KDOQI Ped Bone Guidelines (2005)**
    - Only if PTH elevated for CKD Stage

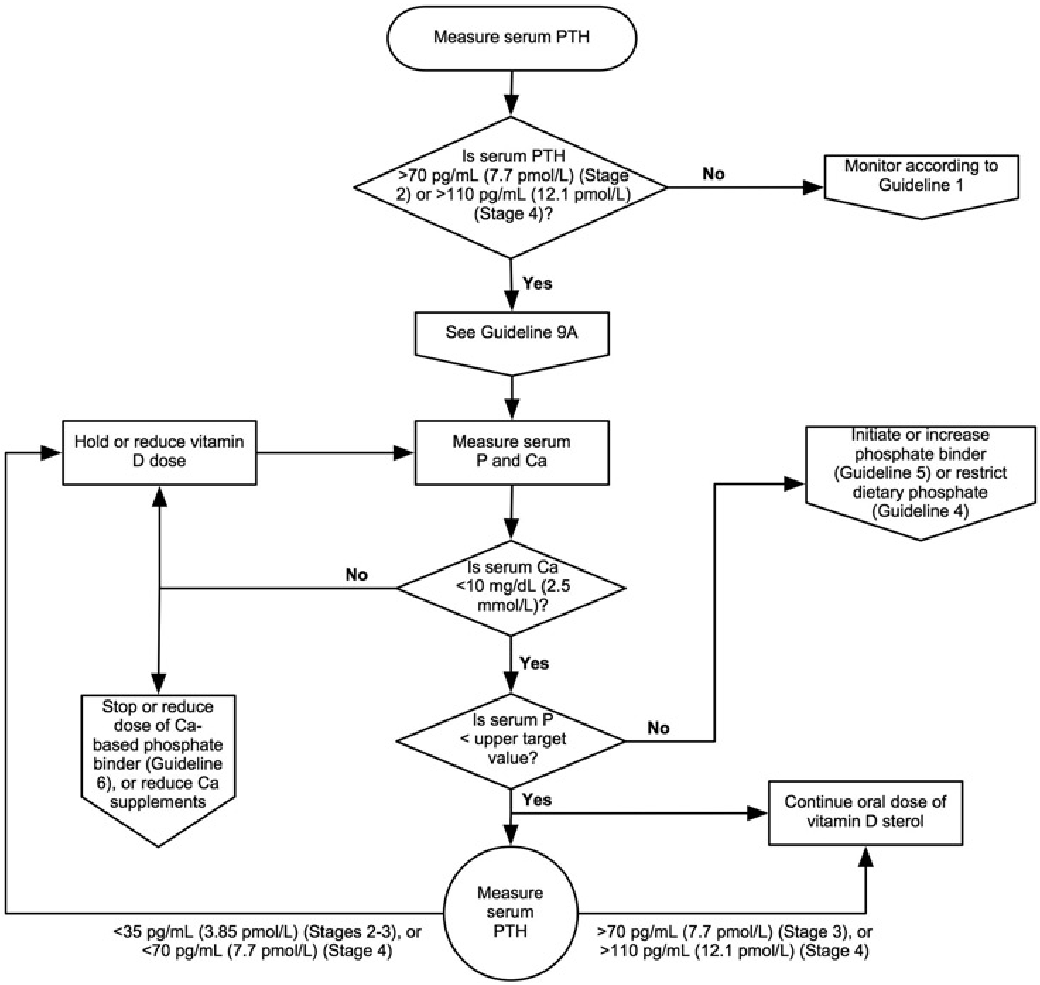
  - **KDOQI Ped Nutrition Update (2009)**
    - CKD 2-5 Measure annually

Vitamin D

- **KDOQI Ped Bone Guidelines (2005)**
  - **CKD Stages 2- 4**
    - If PTH > target range, serum 25 (OH) D levels should be measured
    - If 25 (OH) < 30 ng/mL → supplement with vitamin D
    - If serum levels of PTH are above the target range for the CKD stage & when serum levels of 25(OH)D are >30 ng/mL → initiate therapy with active vitamin D
  - **CKD Stage 5**
    - If PTH > 300 pg/mL → initiate therapy with active vitamin D sterol

Vitamin D

In CKD patients, Stages 2-4, with stable renal function, compliant with visits and medications with serum phosphorus levels < upper target value, calcium <10 mg/dL (2.5 mmol/L), and 25(OH)D ≥30 ng/mL (75 nmol/L)



National Kidney Foundation 2005

Vitamin D

Table 16. Serum Levels of PTH, Calcium, and Phosphate Required for Initiation of Oral Vitamin D Sterol Therapy, and Recommended Initial Doses in Patients with CKD Stages 2-4

Serum PTH (pg/mL or ng/L)	Serum Ca (mg/dL) [mmol/L]	Serum P (mg/dL)	Dose Oral Calcitriol
>70 (CKD Stage 2,3) >110 (CKD Stage 4)	<10 [2.37]	≤ age-appropriate levels	<10 kg: 0.05 µg every other day 10-20 kg: 0.1-0.15 µg/day >20 kg: 0.25 µg/day

Table 17. Initial Calcitriol Dosing Recommendations for Children on Maintenance Dialysis

Serum PTH (pg/mL)	Serum Ca (mg/dL) [mmol/L]	Serum P (mg/dL) [mmol/L]	CaXP*	Calcitriol Dose per HD Session	Calcitriol Dose for Patients Receiving PD (TIW) [311, 312]
300-500	<10 [2.37]	<5.5 [1.78] for adolescents <6.5 [2.10] for infants and children	<55 for adolescents <65 for infants and children	0.0075 µg/kg (maximum = .25 ?g) qd	0.0075 µg/kg (maximum = 0.25 ?g) qd
>500-1000	<10 [2.37]	<5.5 [1.78] for adolescents <6.5 [2.10] for infants and children	<55 for adolescents <65 for infants and children	0.015 µg/kg (maximum = 0.5 ?g) qd	0.015 µg/kg (maximum = 0.5 ?g) qd
>1000	<10.5 [2.50]	<5.5 [1.78] for adolescents <6.5 [2.10] for infants and children	<55 for adolescents <65 for infants and children	0.025 µg/kg (maximum = 1 ?g) qd	0.025 µg/kg (maximum = 1 ?g) qd

HD Hemodialysis, thrice weekly (TIW)
PD Peritoneal dialysis, thrice weekly (TIW)
* <65 in children below 12 years of age

Vitamin D

- **KDOQI Ped Nutrition Update (2008)**
  - **Serum 25-hydroxyvitamin D levels must be measured once per year.**
  - **If the serum level of 25-hydroxyvitamin D is < 30 ng/mL, supplementation with vitamin D_2 (ergocalciferol) or vitamin D_3 (cholecalciferol) is suggested.**
  - **In the repletion phase, it is suggested that serum levels of corrected calcium and phosphorus be measured at 1 month following initiation or change in dose of vitamin D and at least every 3 months thereafter.**
  - **When patients are replete, supplement vitamin D continuously and monitor levels yearly.**

Vitamin D

- **Levels < 5 ng/mL = severe vitamin D deficiency**
    - Osteomalacia
    - Hypocalcemia

- **Levels 5-15 ng/mL = mild vitamin D deficiency**
    - Increased risk of bone demineralization and fractures

- **Levels 16-30 ng/mL = vitamin D insufficiency**
    - Hyperparathyroidism

Vitamin D

Table 22. Recommended Supplementation for Vitamin D Deficiency/Insufficiency in Children with CKD

Serum 25(OH)D (ng/mL)	Definition	Ergocalciferol (Vitamin D_2) or Cholecalciferol (Vitamin D_3) Dosing	Duration (mo)
<5	Severe vitamin D deficiency	8,000 IU/d orally or enterally × 4 wk or (50,000 IU/wk × 4 wk); then 4,000 IU/d or (50,000 IU twice per mo for 2 mo) × 2 mo	3
5-15	Mild vitamin D deficiency	4,000 IU/d orally or enterally × 12 wk or (50,000 IU every other wk, for 12 wk)	3
16-30	Vitamin D insufficiency	2,000 IU daily or (50,000 IU every 4 wk)	3

National Kidney Foundation 2009

Summary

- Vitamin D is a key player in normal calcium and phosphorus homeostasis that involves a complex interplay between the kidney, parathyroid, intestine, and bone.
- CKD presents unique disturbances in vitamin D metabolism.
- Sufficient Vitamin D prevents skeletal deformities and has extra-skeletal benefits.
- National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines for vitamin D in children with CKD are available.

Questions?