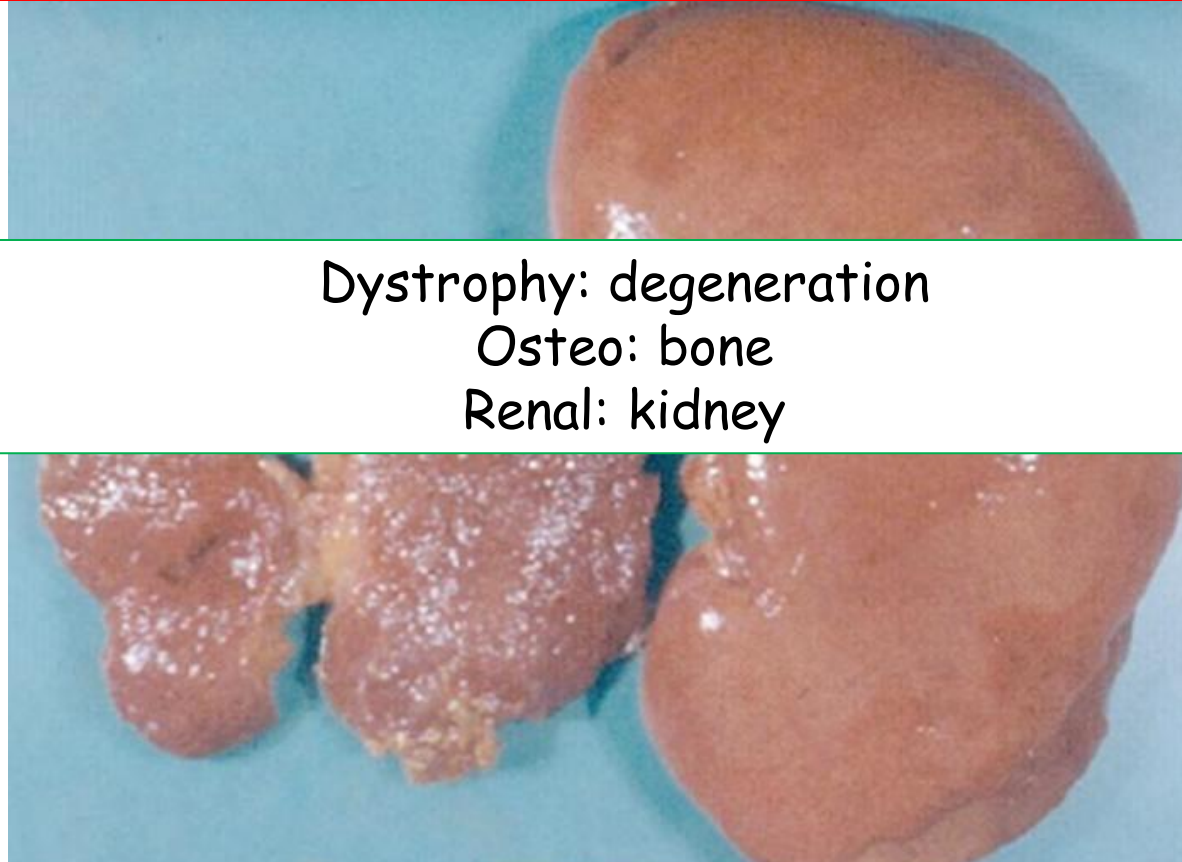


Renal Osteodystrophy



Howard J. Sachs, MD
www.12DaysinMarch.com

Renal Osteodystrophy



Dystrophy: degeneration
Osteo: bone
Renal: kidney

Howard J. Sachs, MD
www.12DaysinMarch.com

Is Sachs slipping in his old age?



Is Sachs slipping in his old age?



Why such a boring topic?

Renal

MSK

ENDO

GI

Renal

MSK

ENDO

GI

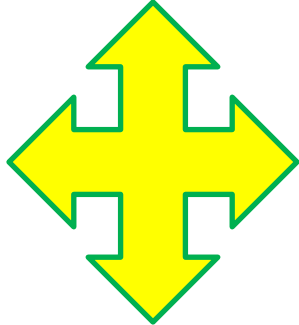


Deranged
Bone Metabolism

Hormonal
Interactions

Renal

MSK



ENDO

GI

Renal Osteodystrophy

- Definition
 - Does **NOT** represent a single pathologic entity.



Renal Osteodystrophy

- Definition
 - Does **NOT** represent a single pathologic entity.



Reflects the bone changes that take place in response to advanced CKD

Renal Osteodystrophy

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 - Does NOT represent a single pathologic entity.
 - Implication: don't expect to see a pathology specimen labeled as renal osteodystrophy.

Renal Osteodystrophy

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- Does **NOT** correspond to a single pathologic entity.

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- Reflects the disordered **pathophysiologic** state associated with advanced renal disease (GFR <15 ml/min)



Renal Osteodystrophy

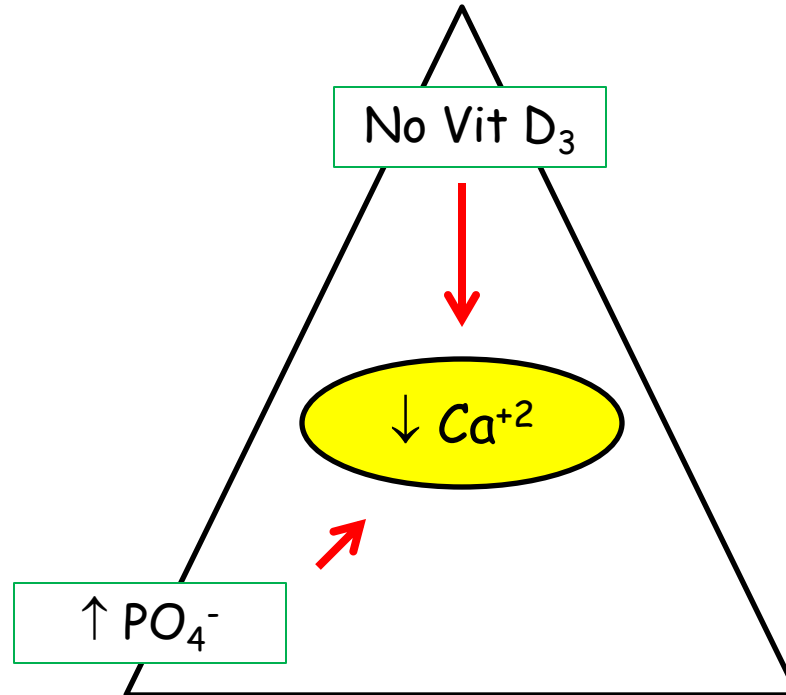
- Definition
 - Does **NOT** correspond to a single pathologic entity.
 - Implication: don't expect to see a pathology specimen labeled renal osteodystrophy.
 - Reflects the disordered **pathophysiologic** state associated with advanced renal disease (GFR <15 ml/min)
 - Implication: you need to understand the renal perturbations that permit bone to get so messed up!

Blood Urea Nitrogen	40 mg/dL	H	7-23
Creatinine	4.00 mg/dL	H	0.60-1.30

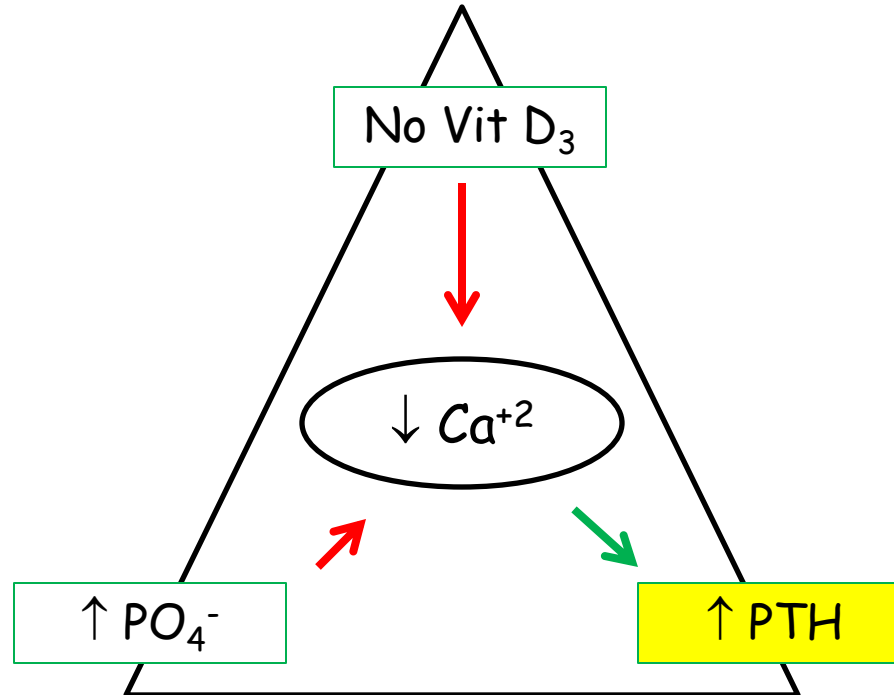
Calcium	7.5 mg/dL	L	8.7-10.7
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If you understand the basis of hypocalcemia,
And the physiologic response,
You understand renal osteodystrophy

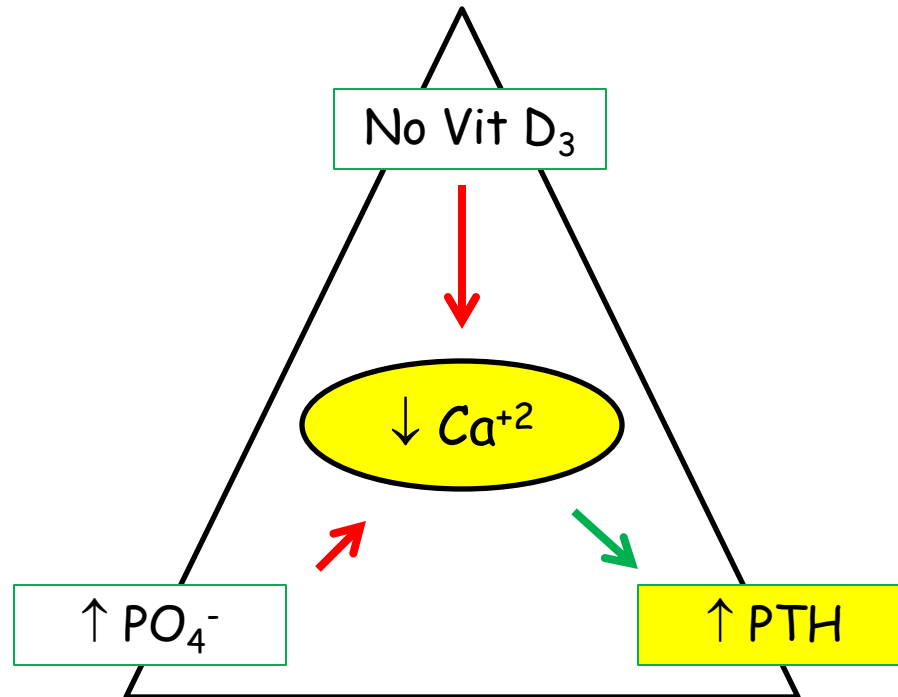
Renal Osteodystrophy



Renal Osteodystrophy: the Pyramid

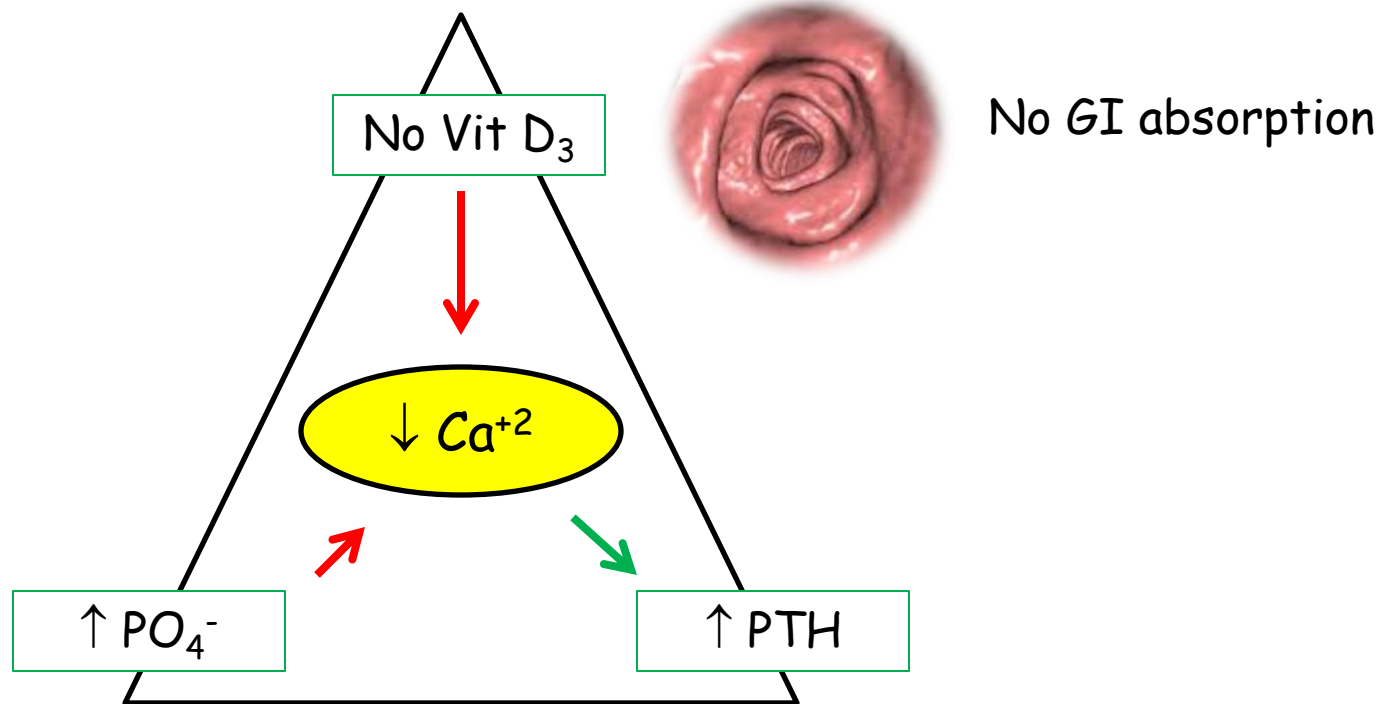


Renal Osteodystrophy: the Pyramid

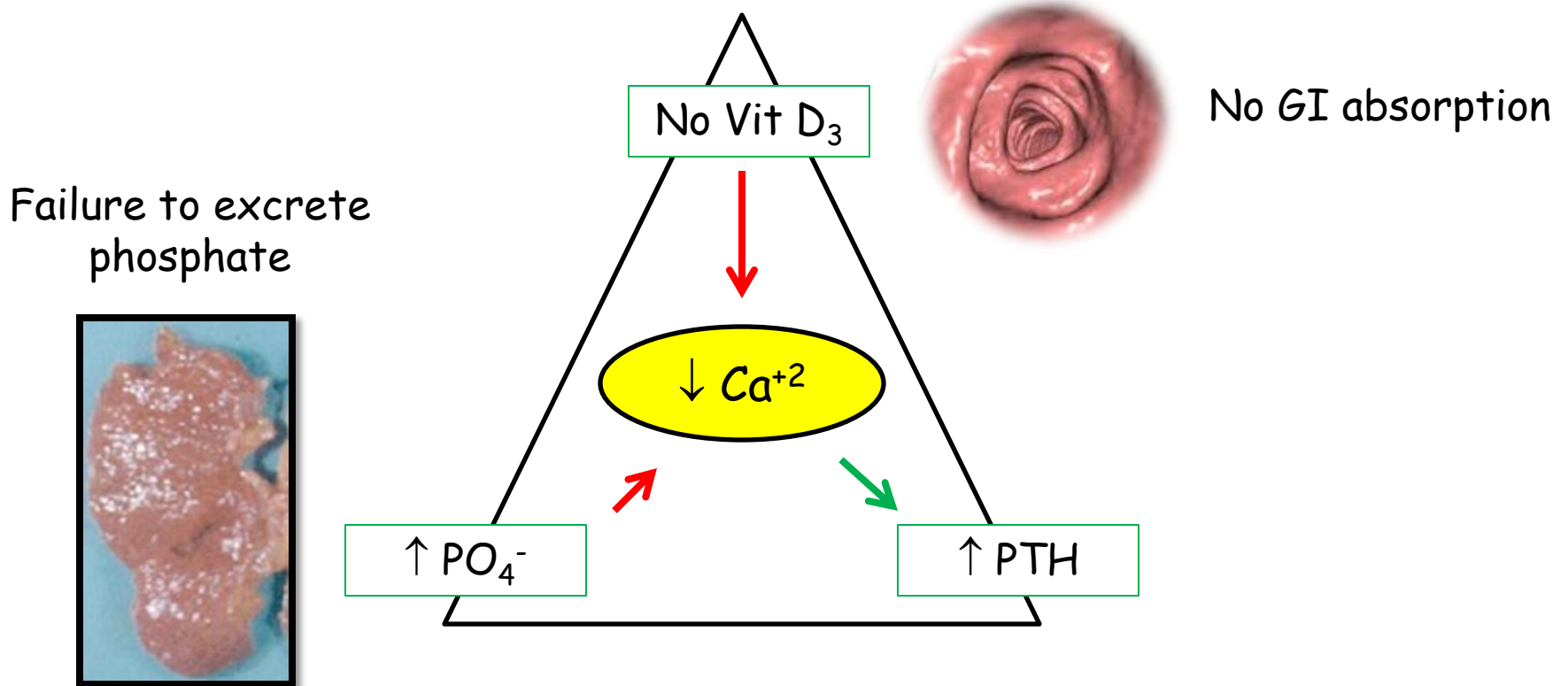


Secondary Hyperparathyroidism

Renal Osteodystrophy

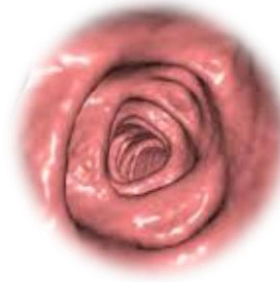
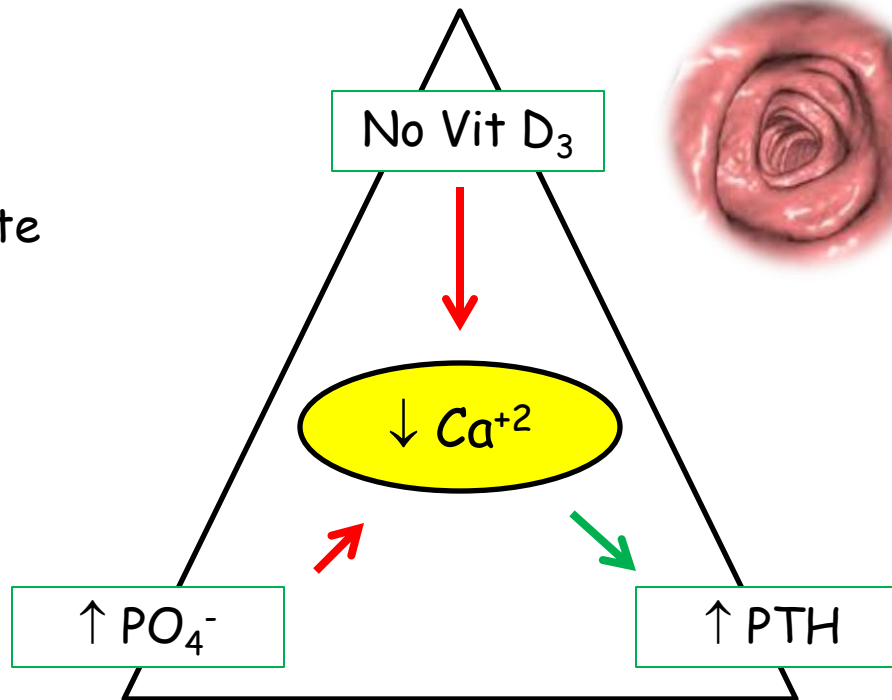


Renal Osteodystrophy



Renal Osteodystrophy

Failure to excrete phosphate



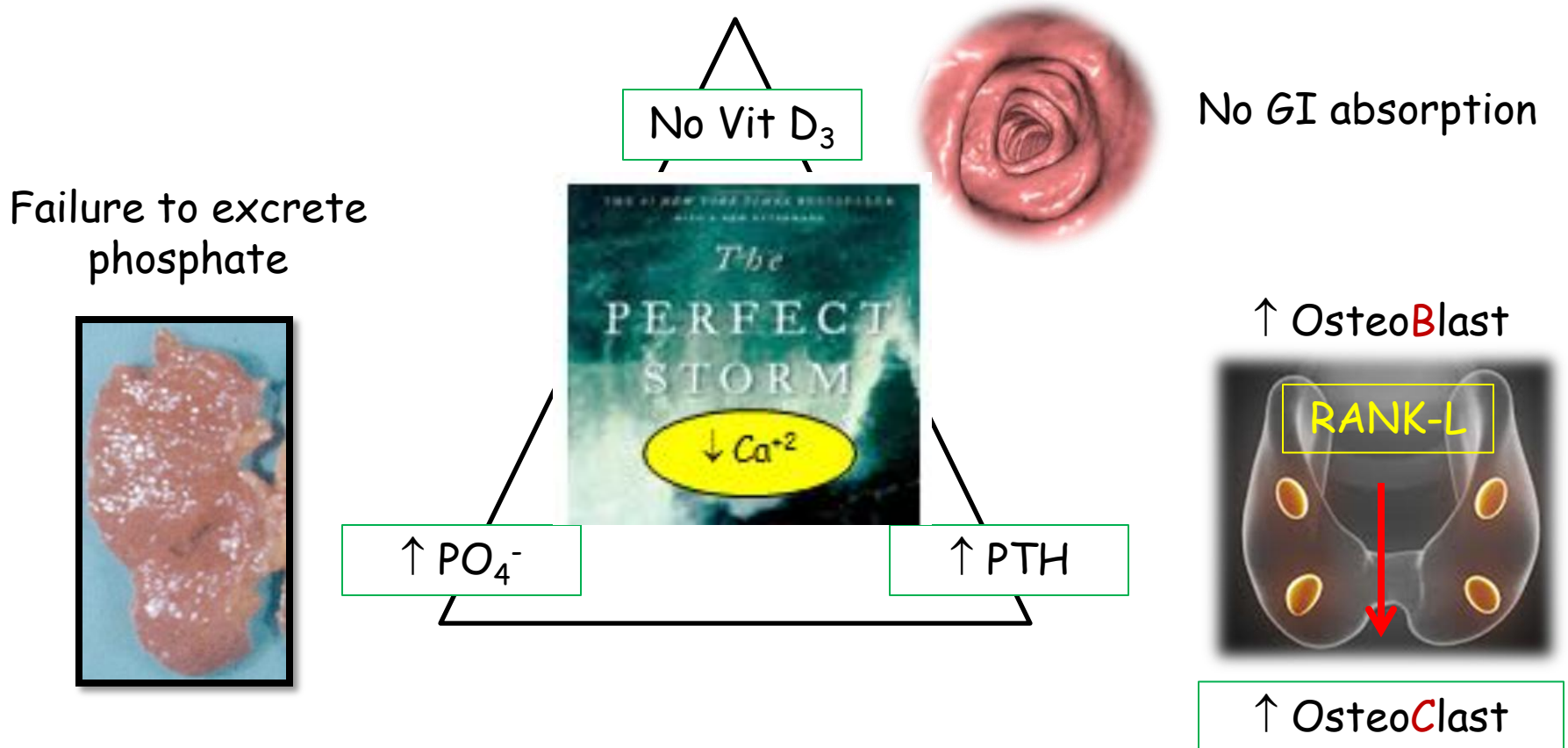
No GI absorption

↑ OsteoBlast



↑ OsteoClast

Renal Osteodystrophy

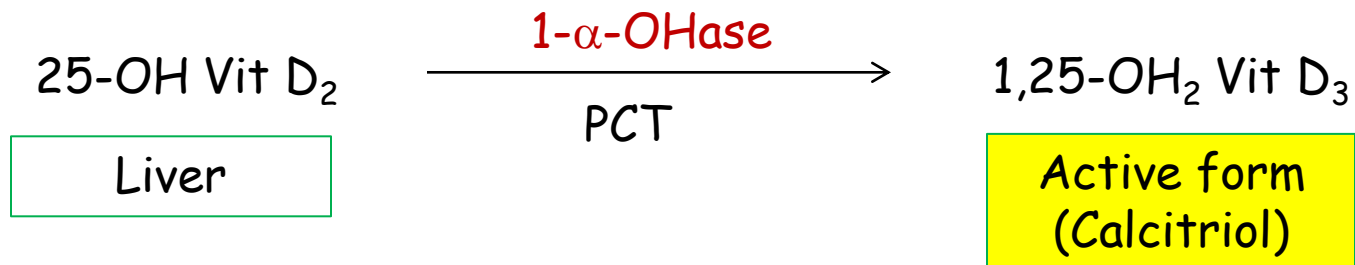


Renal Osteodystrophy

- Background

- Does not describe a single entity, rather the components of bone pathology related to **loss of renal function**

1. **Failure** to synthesize 1,25 dihydroxy Vit D₃

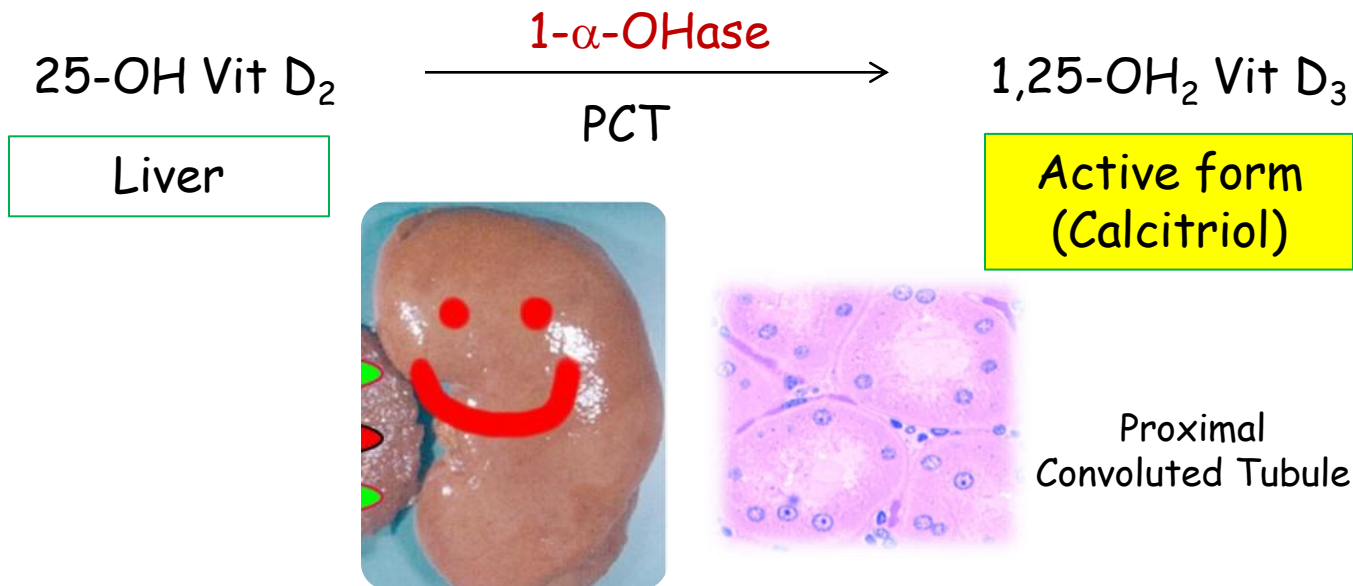


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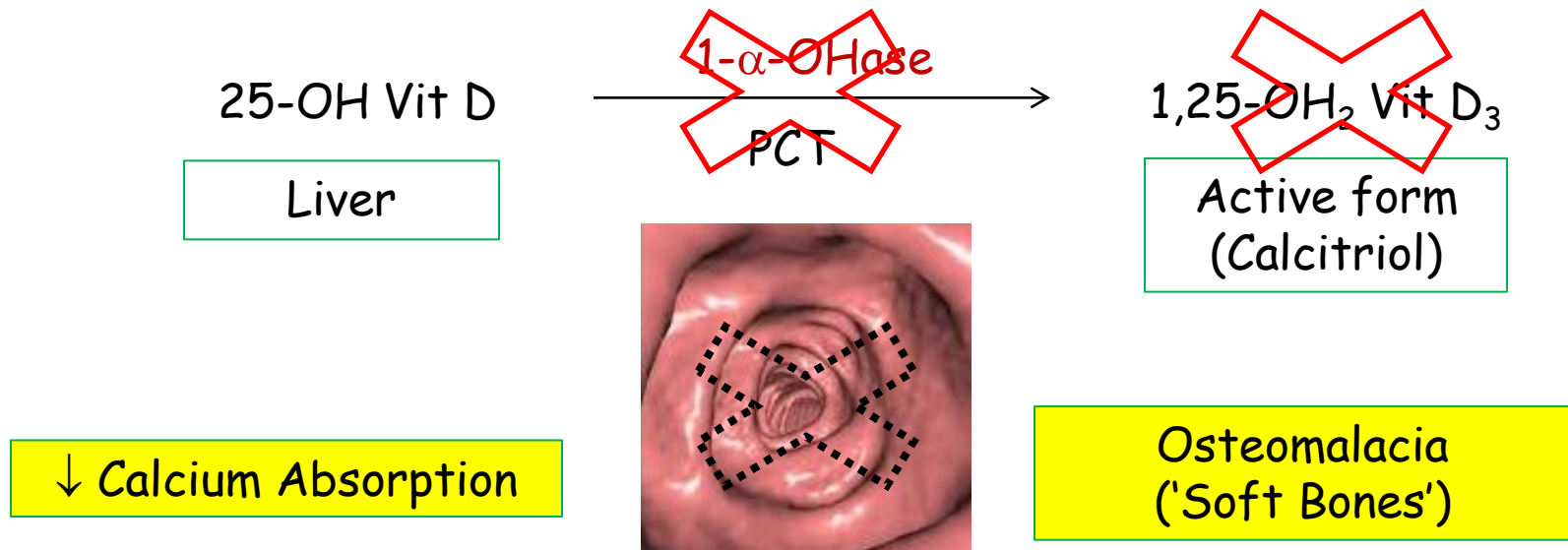


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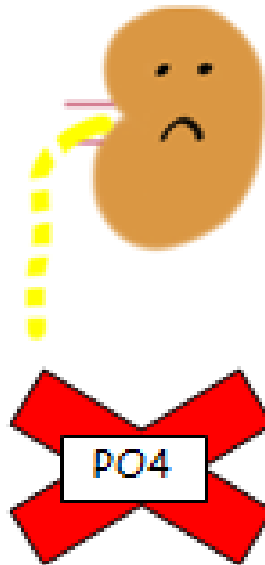
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1. Failure to synthesize 1,25 dihydroxy Vit D \Rightarrow osteomalacia

2. Failure to excrete PO₄



Renal Osteodystrophy

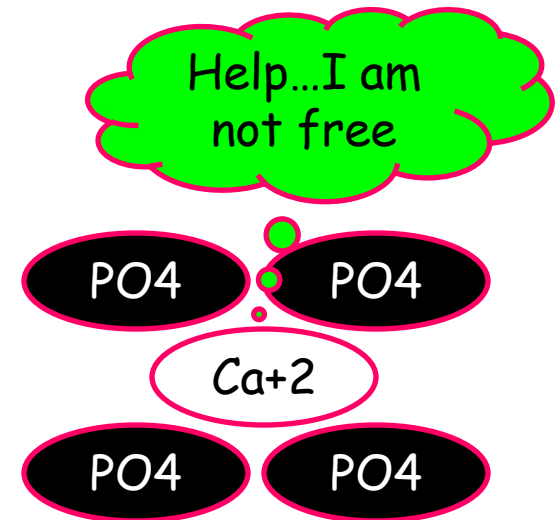
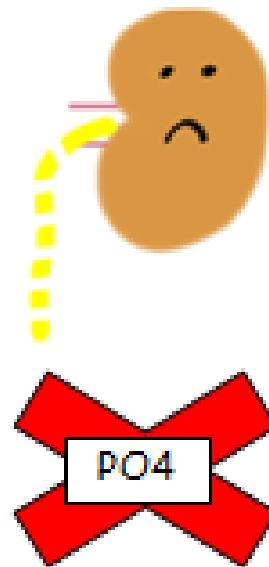
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1. Failure to synthesize 1,25 dihydroxy Vit D \Rightarrow osteomalacia

2. Failure to excrete PO₄

Hyperphosphatemia binds to serum calcium resulting in ↓ed availability of ionized free Ca⁺²



Calcium

7.5 mg/dL

L

8.7-10.7

Phosphorus

6.9 mg/dL

H

2.5-4.5

Test

Result

Flag

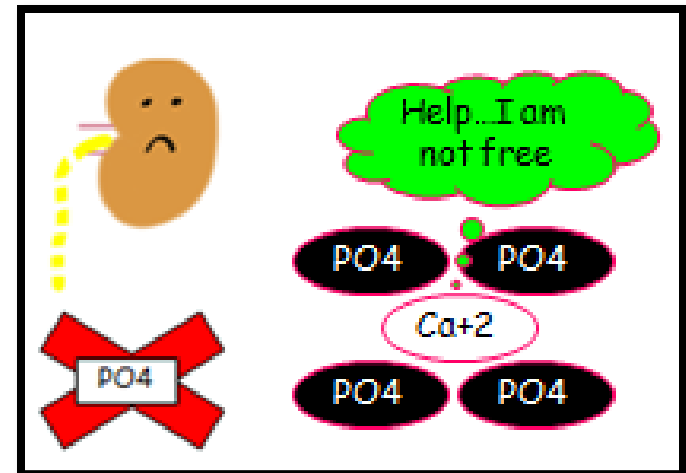
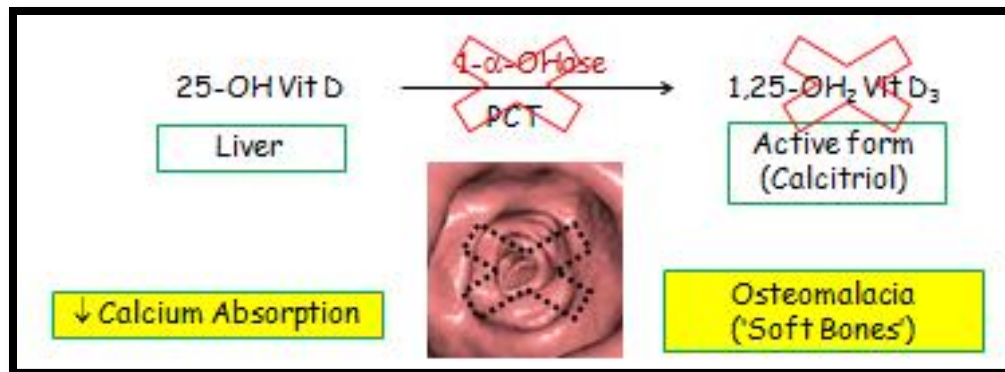
Reference

Vitamin D 25 OH

5 ng/mL

L

30-100

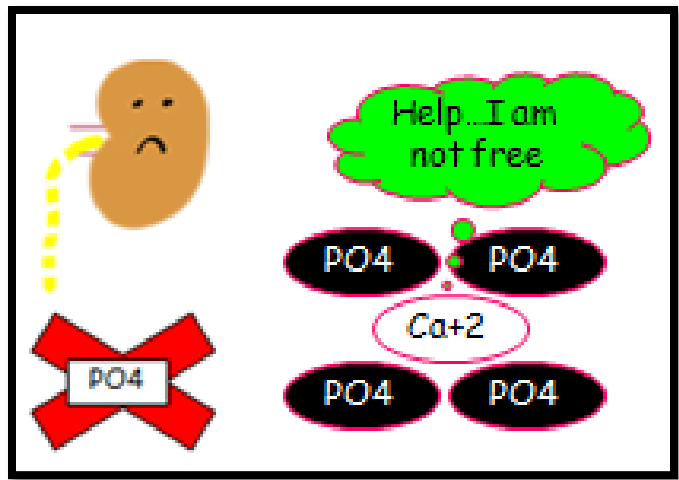
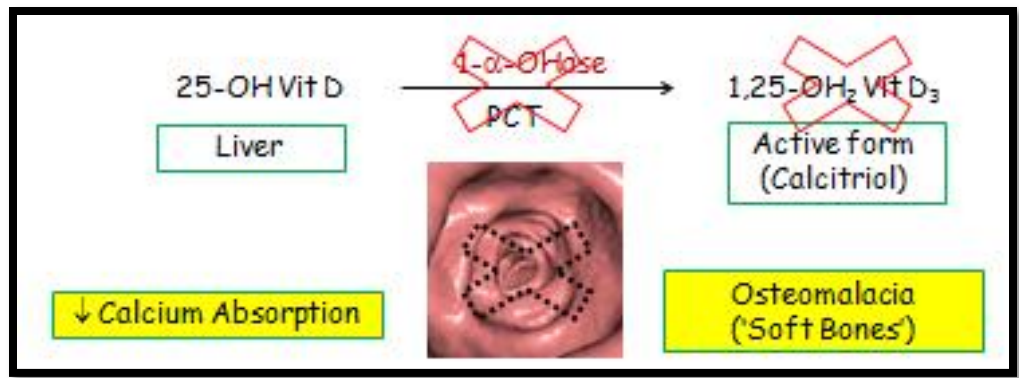


Hypocalcemia \Rightarrow Osteomalacia

Calcium	7.5 mg/dL	L	8.7-10.7
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Phosphorus	6.9 mg/dL	H	2.5-4.5
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Test	Result	Flag	Reference
Vitamin D 25 OH	5 ng/mL	L	30-100



Hypocalcemia ⇒ Osteomalacia

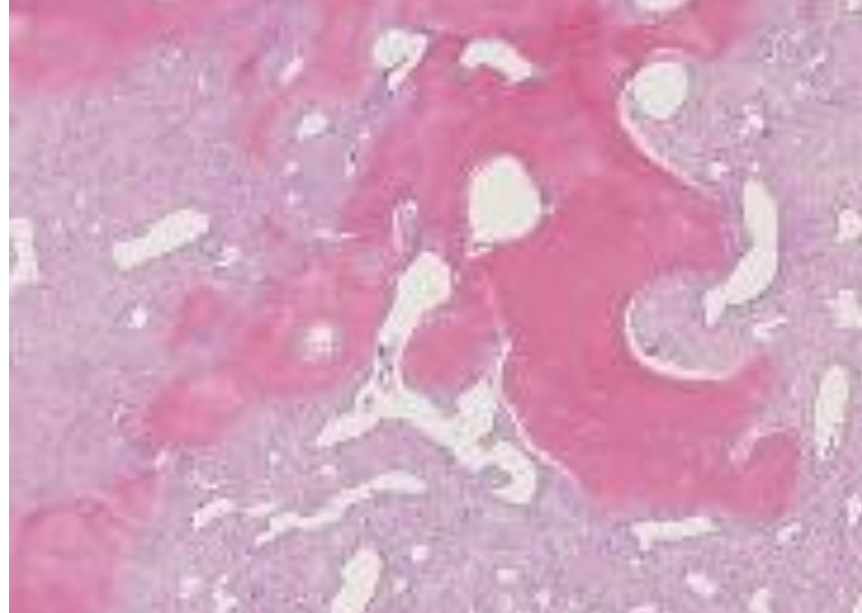
The NBME doesn't come right out and say 'Osteomalacia.'

So what vocabulary will they use?

the Histology of Osteomalacia: a Glossary



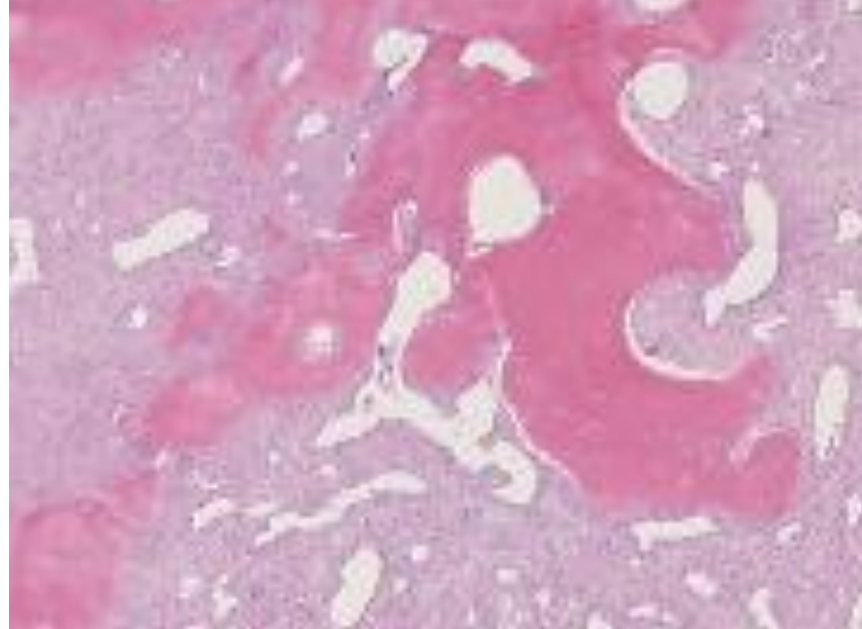
Pathologic Description:
Thickened layer of **unmineralized osteoid**



Osteoid: organic component of bone (i.e. Type I collagen)

the Histology of Osteomalacia: a Glossary

Pathologic Description:
Thickened layer of **unmineralized osteoid**



Bone Formation and/or Remodeling

1. Osteoblasts lay down collagen (osteoid).
2. After a two week delay, mineralization takes place.

the Histology of **Osteomalacia**: a Glossary

Pathologic Description:
Thickened layer of **unmineralized osteoid**
(organic matrix = collagen)



Calcium	7.5 mg/dL	L	8.7-10.7
---------	-----------	---	----------

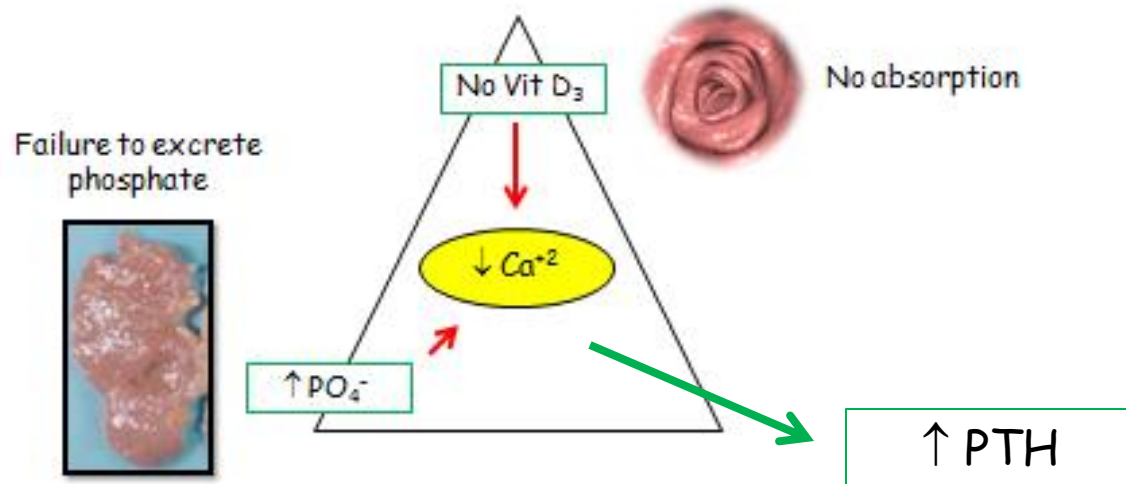
Bone Formation and/or Remodeling

1. Osteoblasts lay down collagen (osteoid).
2. After a two week delay, mineralization takes place.
 - **OMG: we have no calcium!**
 - Result: a thickened layer of **unmineralized osteoid**.

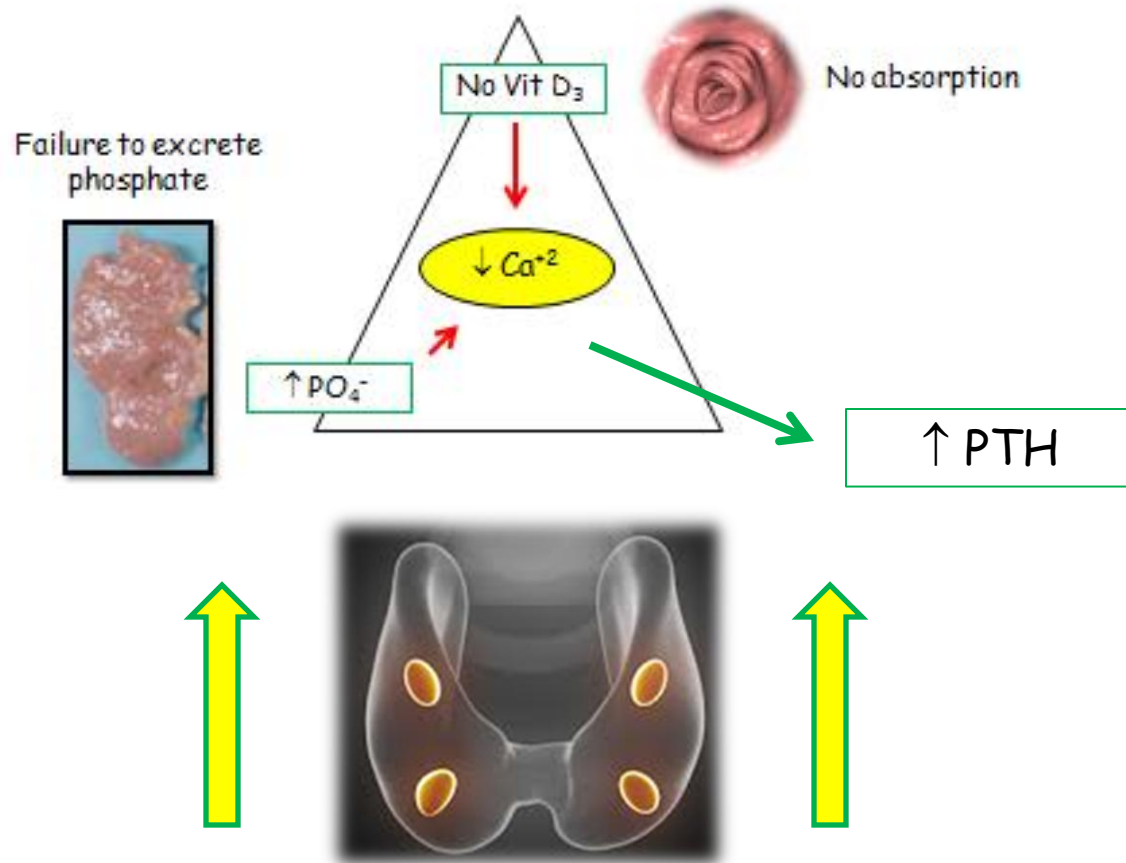
Osteomalacia: Bone that is Soft

Fractures and Pseudofractures



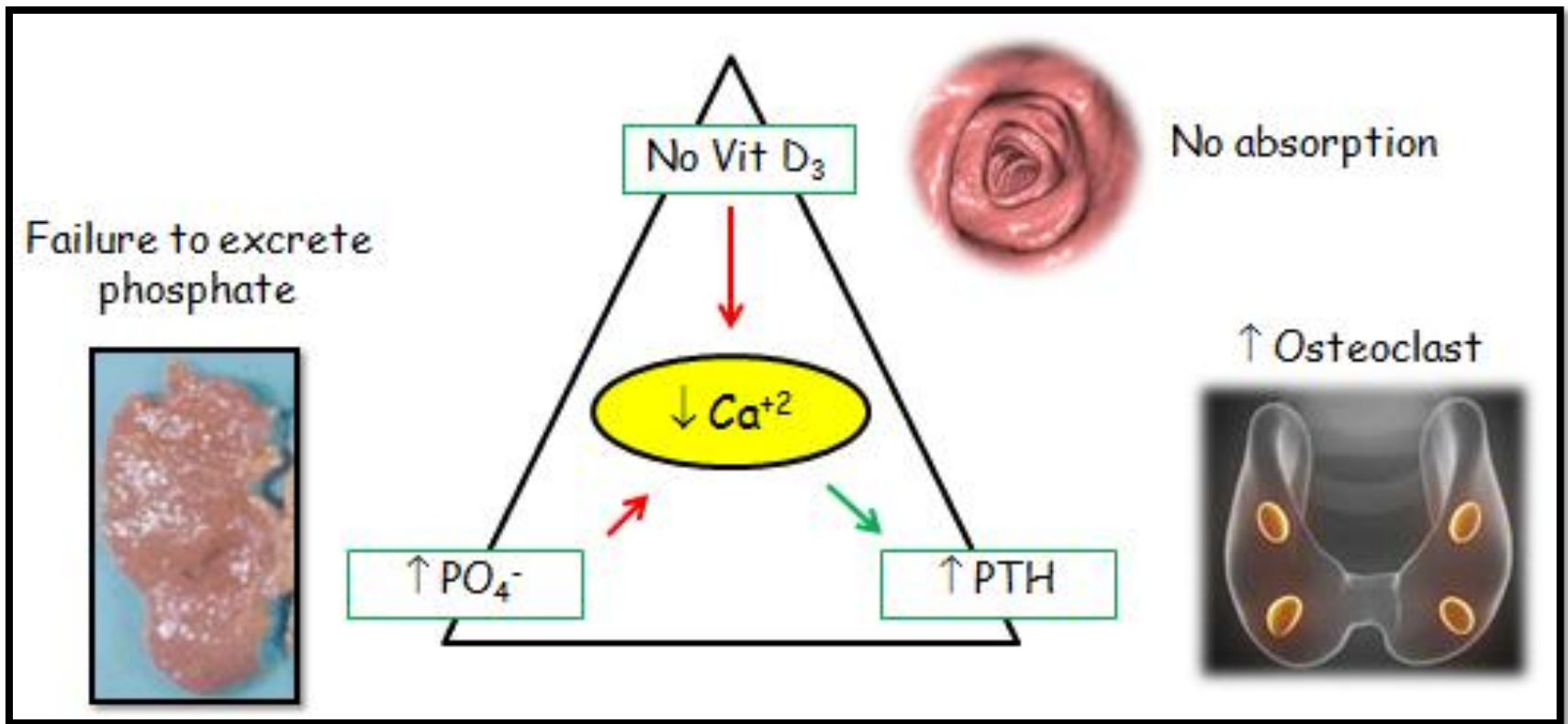


Parathyroid Gland
Only hormone-secreting gland in the body that responds to Δ 's in mineral levels



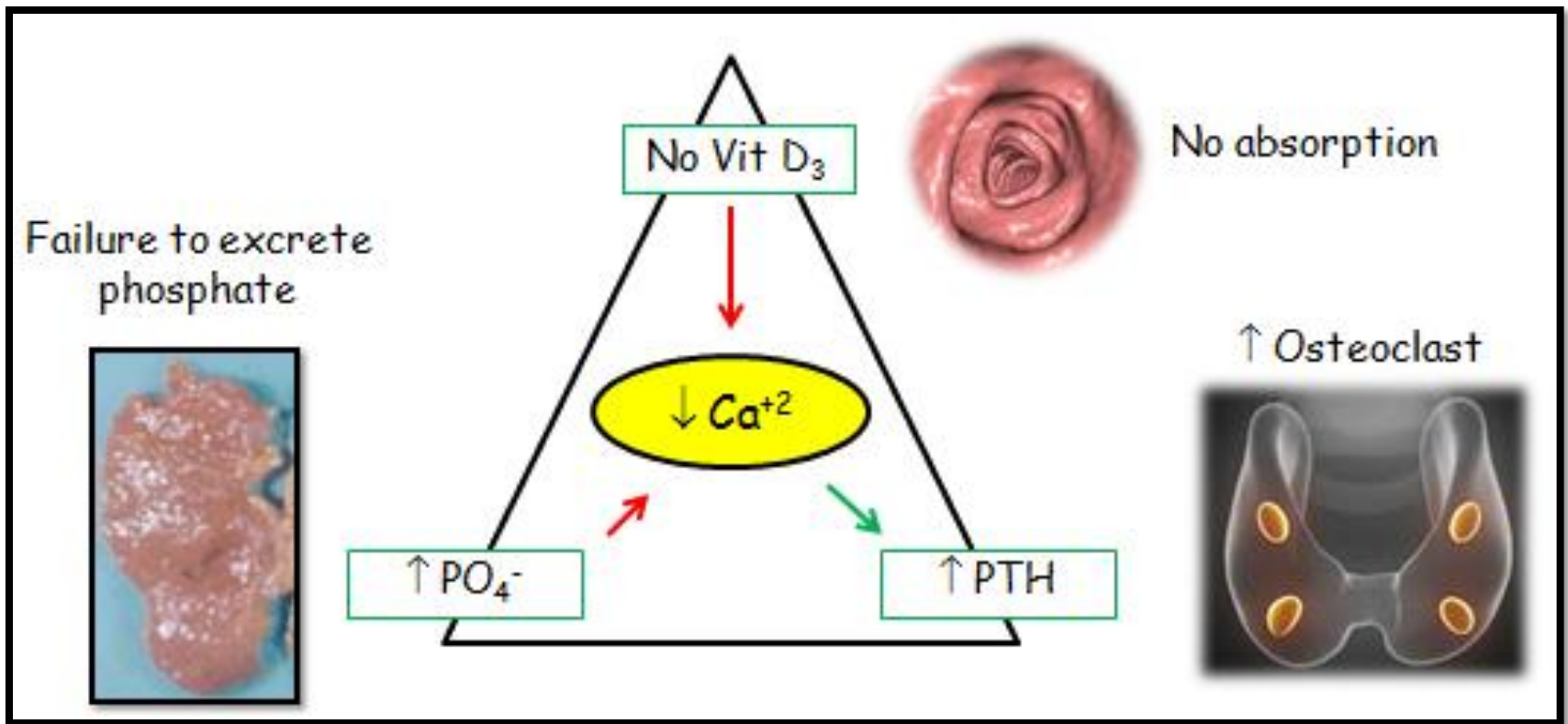
Calcium Sensing Receptor

Parathyroid Gland
 Only hormone-secreting gland in the body
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Problem: 'Secondary Hyperparathyroidism' is not okay.

It leaches calcium from bone. That's not okay.
The bones are already soft.



Problem: 'Secondary Hyperparathyroidism' is not okay.

It leaches calcium from bone. That's not okay.
The bones are already soft.

You know by now the NBME has some special nicknames to describe this process...

Problem: 'Secondary Hyperparathyroidism' is not okay.

It leaches calcium from bone. That's not OK.



When PTH leaches bone from the diaphysis, it's called **subperiosteal bone resorption**.

Subperiosteal Bone Resorption

Takafumi Taguchi, M.D., Ph.D., and Yoshio Terada, M.D., Ph.D.

N Engl J Med 2014; 370:e32 | May 22, 2014 | DOI: 10.1056/NEJMicm1308814

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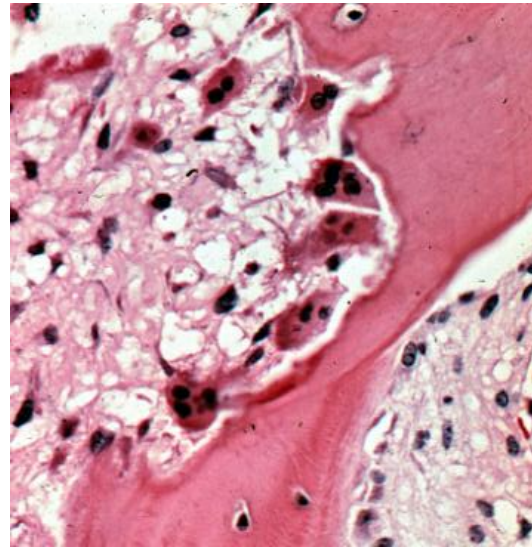
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Sometimes they call it **bowing** of the digits

Problem: 'Secondary Hyperparathyroidism' is not okay.

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Sometimes, instead of bowing, it makes **holes** in **bones**.

Osteitis Fibrosa Cystica

Problem: 'Secondary Hyperparathyroidism' is not okay.

It leaches calcium from bone. That's not OK.



Cysts



Osteoclasts

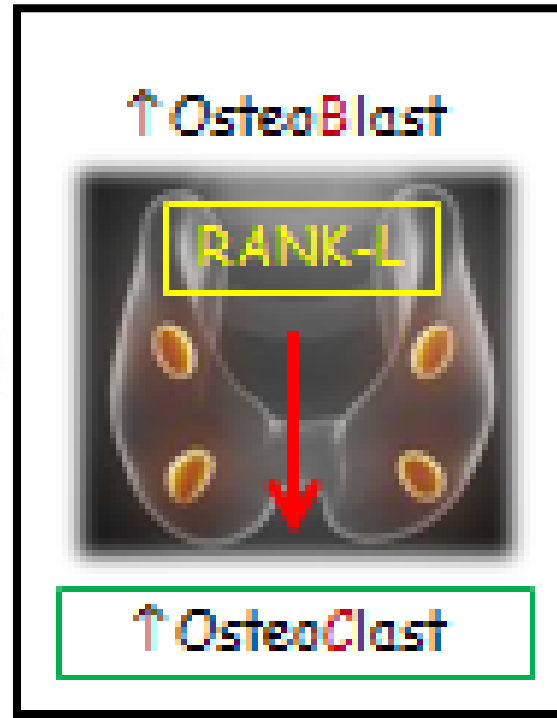


Granulation

Sometimes it makes holes in bones.

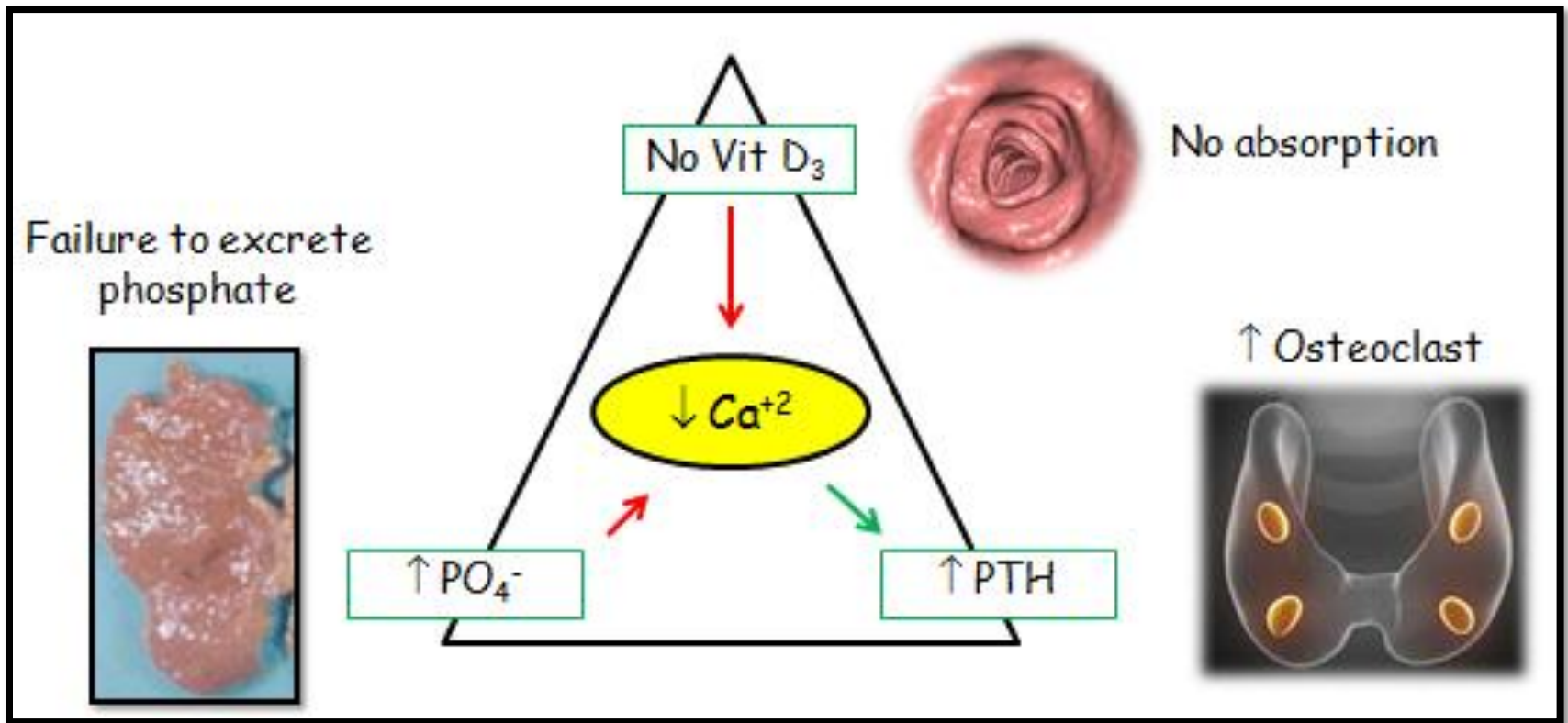
Osteitis Fibrosa Cystica

The holes come from activated osteoclasts.
They cause microfractures, bleeding and granulation tissue.
The whole mess looks brown so they are called 'Brown Tumors'



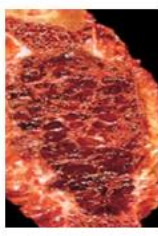
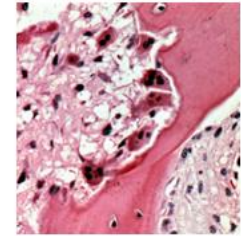
The NBME and I would like to remind you that PTH stimulates osteo**B**lasts. Osteo**b**lasts secondarily stimulate osteo**c**lasts through expression of RANK-L





So what do we have left?:

1. Applied Pharmacology
2. Favorite Question

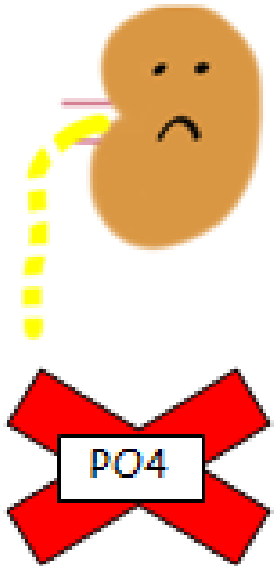




Osteomalacia

Renal Osteodystrophy

HyperPTH

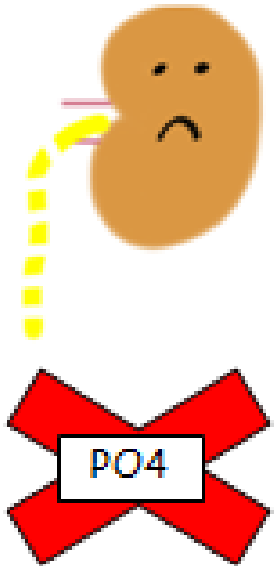


Osteomalacia

Renal Osteodystrophy

HyperPTH

- Low Phosphate Diet
- Phosphate Binders:
Sevelamer



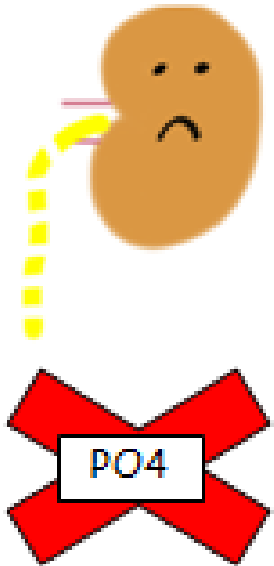
Osteomalacia

Renal Osteodystrophy

HyperPTH

Low Phosphate Diet
Phosphate Binders:
Sevelamer

1,25 Vitamin D₃
(Calcitriol)
Administer with PO₄ binder



Osteomalacia

Renal Osteodystrophy

HyperPTH

Low Phosphate Diet
Phosphate Binders:
Sevelamer

Vitamin D
(**Calcitriol**)
Administer with PO4 binder
(calcitriol stimulates calcium
AND phosphate absorption)

Cinacalcet
(calcimimetic)
Increases sensitivity of PTH
Calcium Sensing Receptor

Sen-a-Cal-Set

Sensor of calcium has been reset.



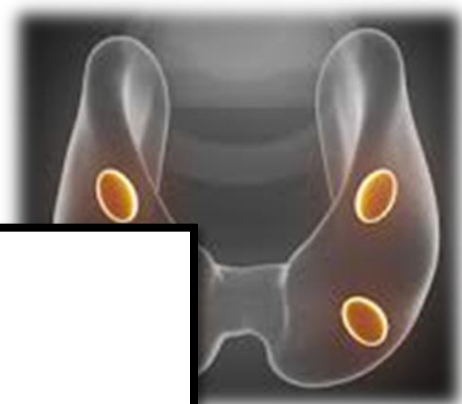
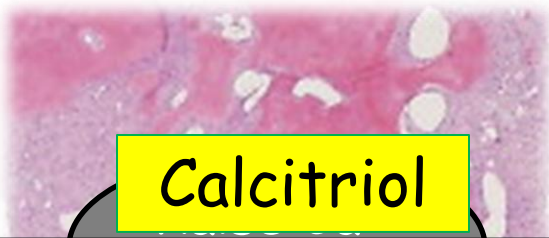
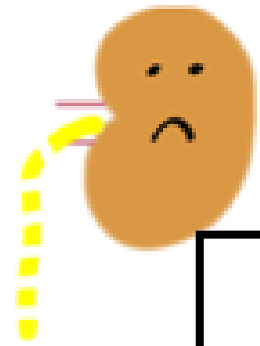
Sensipar

Sensor of Parathyroid

HyperPTH

Cinacalcet
(calcimimetic)
Increases sensitivity of PTH
Calcium Sensing Receptor





Calcitriol

PO4

No Vit D₃



rPTH

Osteon

↑PO₄⁻

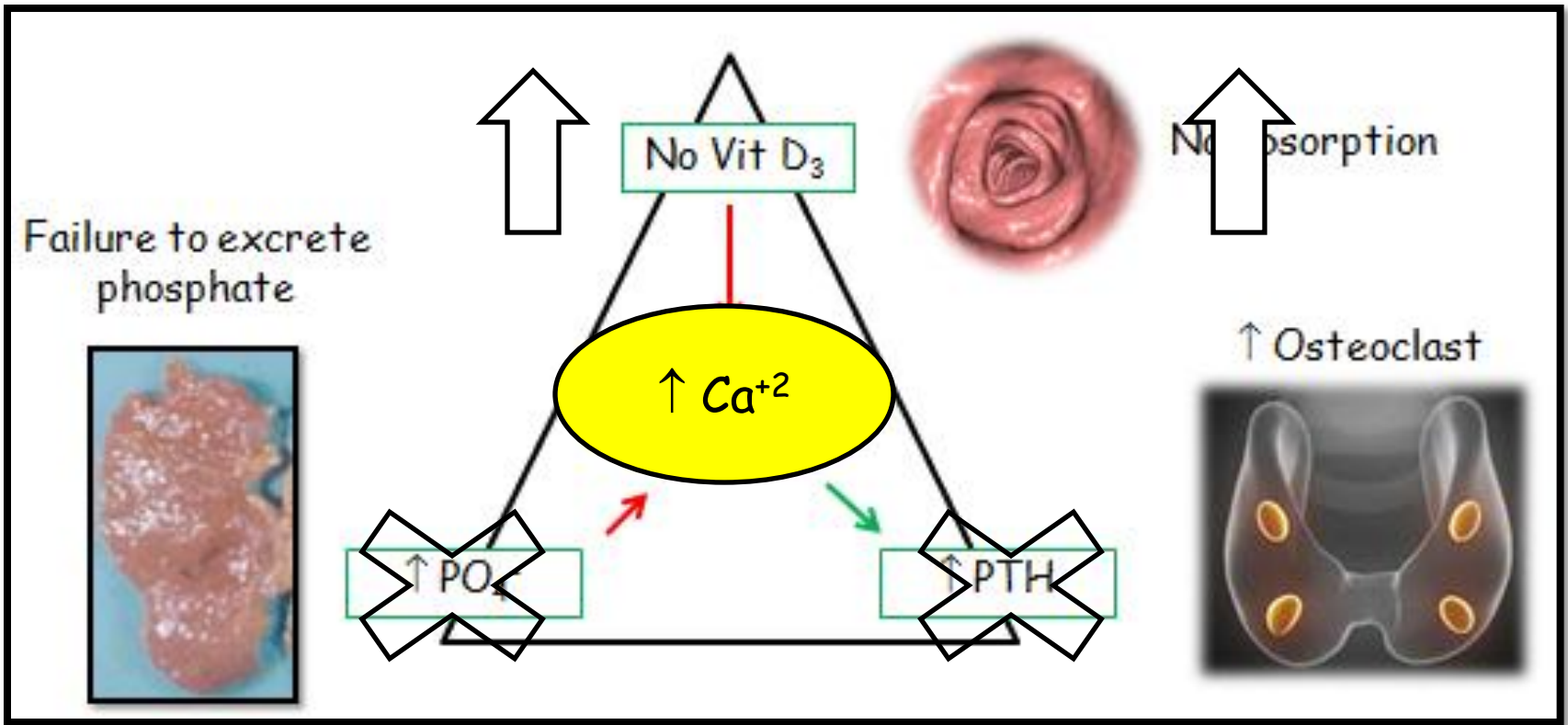
↑PTH

cinacalcet
(calcimimetic)
increases sensitivity of PTH
Sensing Receptor

Low Phosph
Phosphate
Sevela

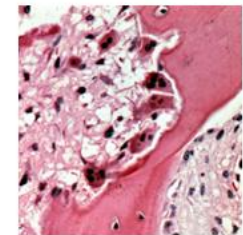
Sevelamer

Cinacalcet

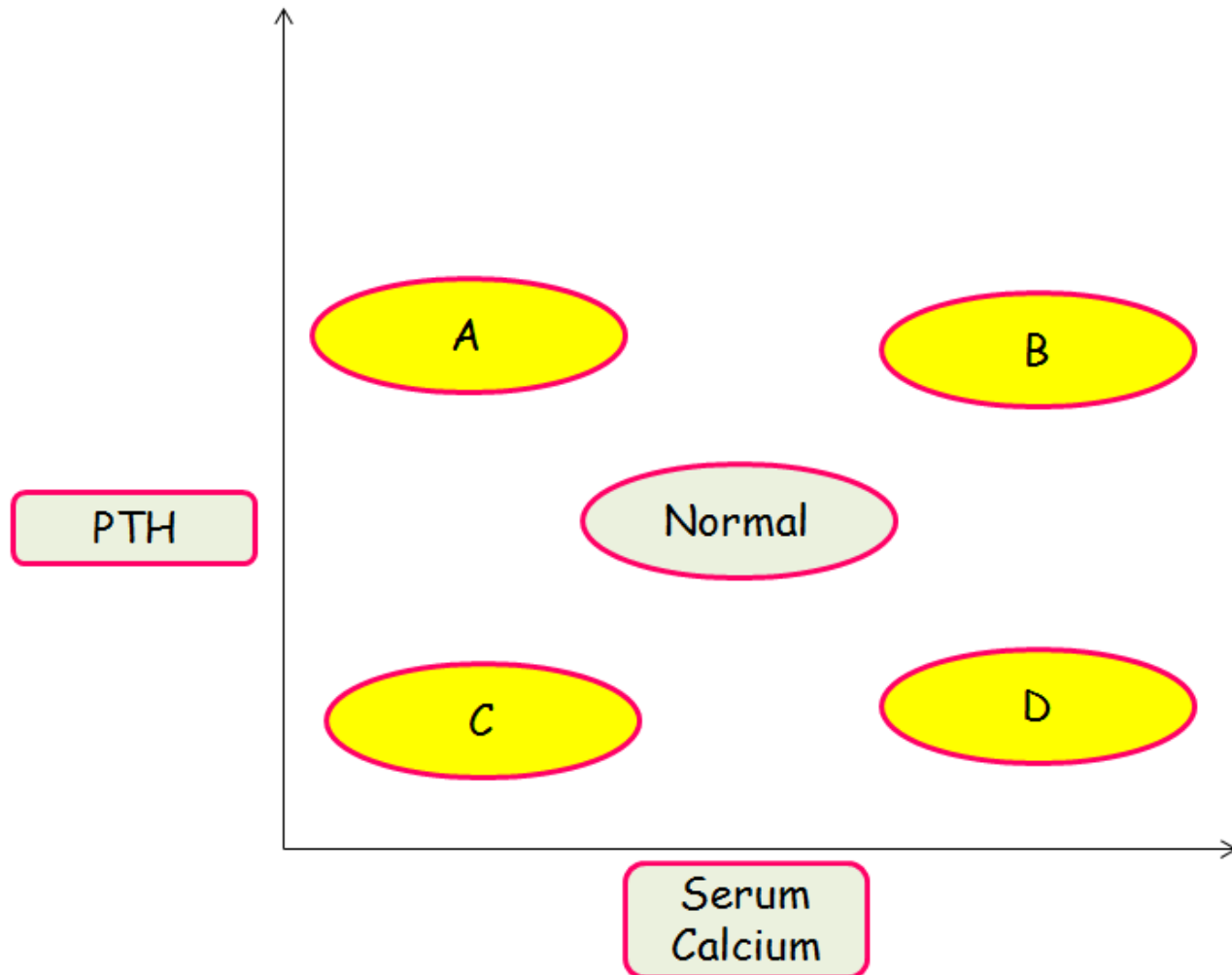


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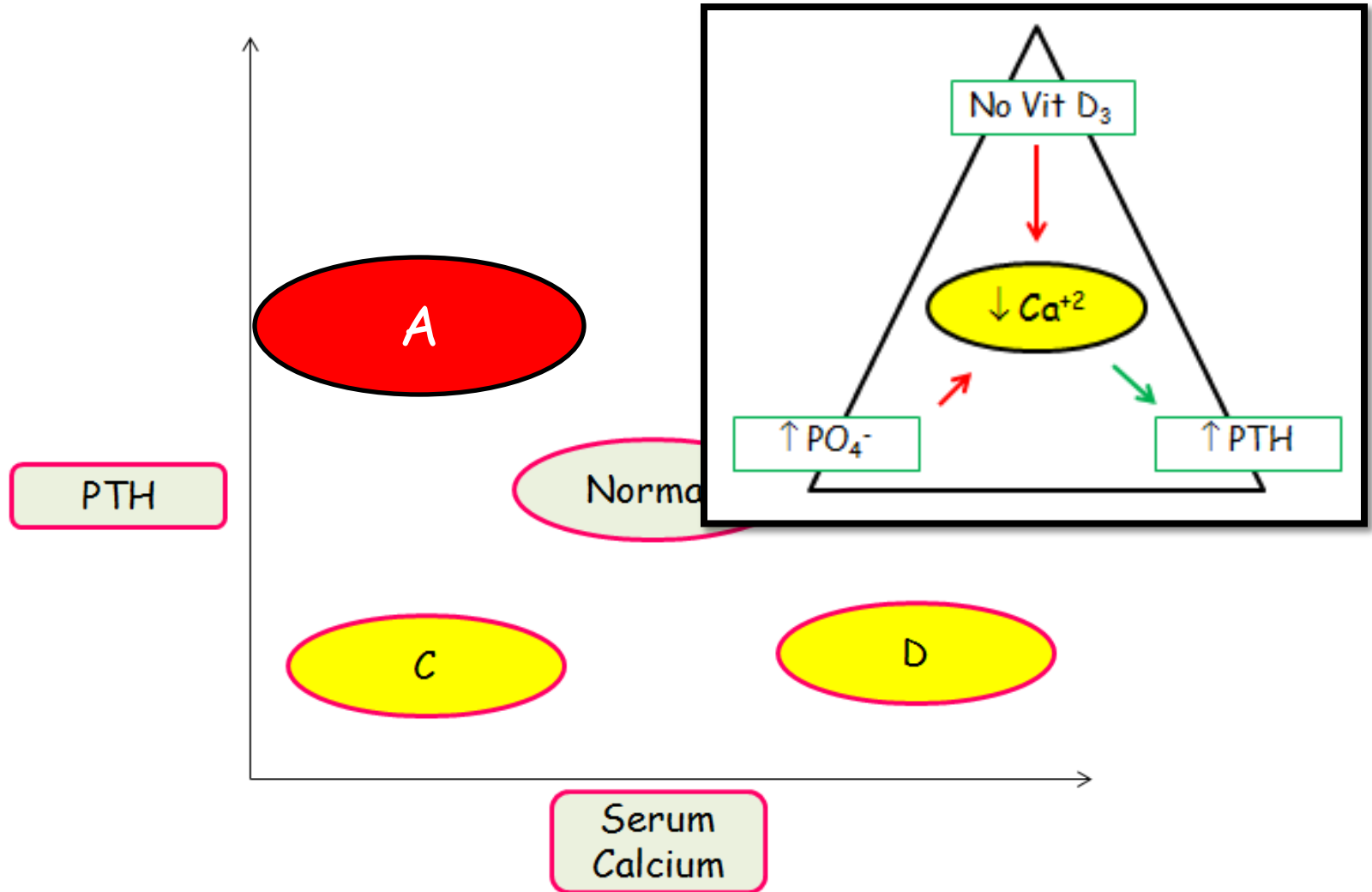
1. Applied Pharmacology
2. Favorite Question



Patient with ESRD. Which of the areas below represent the patient's current metabolic state?

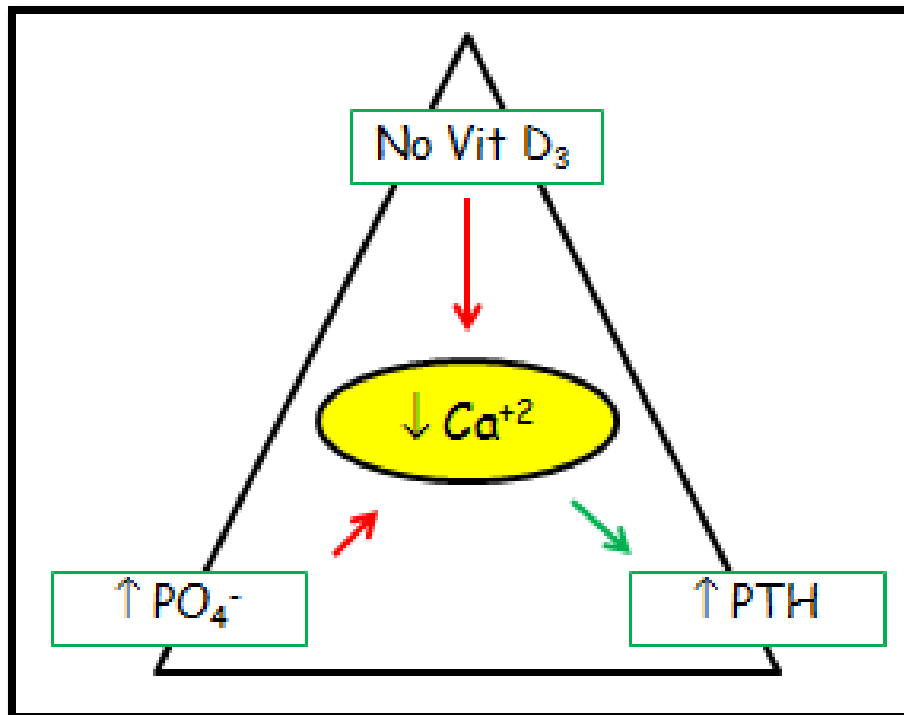


Patient with ESRD. Which of the areas below represent the patient's current metabolic state?



Patient with ESRD. Which of the areas below represent the patient's current metabolic state?

PTH	Calcium	Phosphate	Calcitriol
Inc	Dec	Inc	Dec



↓ Ca²⁺: ↑ PO₄, ↓ D₃

Renal

MSK

ENDO

hyperPTH

GI

↓ Ca²⁺ 2° ↓ D₃

↓ Ca²⁺: ↑ PO₄, ↓ D3

Renal

Osteomalacia
Unmineralized

MSK

Osteitis Fibrosa Cystica
Subperiosteal resorption

Osteoblasts



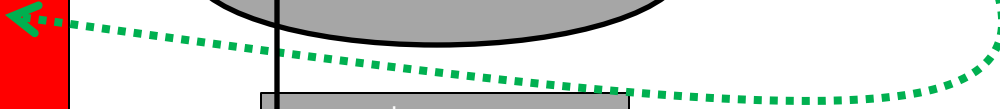
Osteoclasts

ENDO

hyperPTH

GI

↓ Ca²⁺



Calcitriol

↓ Ca²⁺: ↑ PO₄, ↓ D3

Renal

Osteomalacia
Unmineralized

MSK

Osteitis Fibrosa Cystica
Subperiosteal resorption

Osteoblasts



Osteoclasts

Cinacalcet

ENDO

hyperPTH

GI

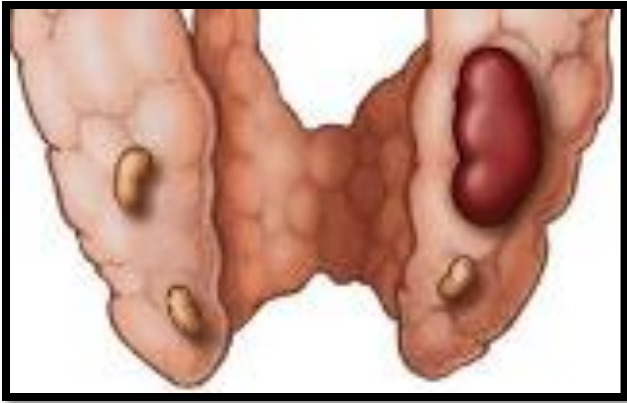
↓ Ca²⁺ 2° ↓ D3

Sevelamer



Material NOT covered (but vaguely related and key in diff dx)

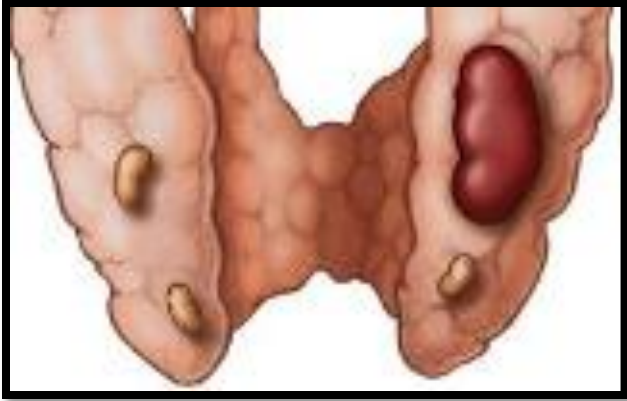
Primary HyperPTH



Characterized by
Hypercalcemia ($\uparrow \text{Ca}^{+2}$)
Hypophosphatemia ($\downarrow \text{PO}_4$)

Material NOT covered (but vaguely related and key in diff dx)

Primary HyperPTH



Characterized by
Hypercalcemia
Hypophosphatemia

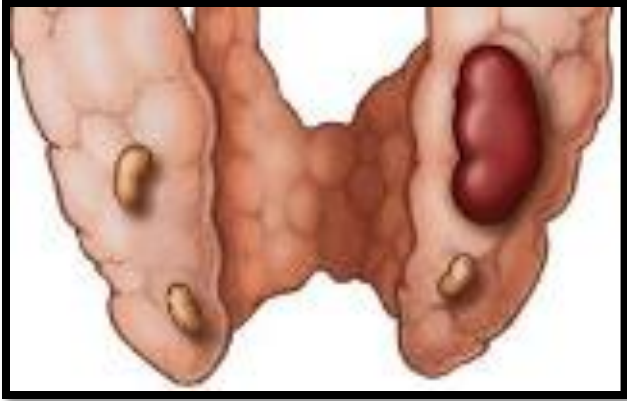
'Periosteal disorders' for the NBME



Codman's triangle
Osteosarcoma

Material NOT covered (but vaguely related and key in diff dx)

Primary HyperPTH



Characterized by
Hypercalcemia
Hypophosphatemia

'Periosteal disorders' for the NBME



Codman's triangle
Osteosarcoma



Hypertrophic
Osteoarthropathy
AdenoCa, Lung

'Periosteal disorders' for the NBME



Subperiosteal Bone Resorption

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HyperPTH
Subperiosteal resorption

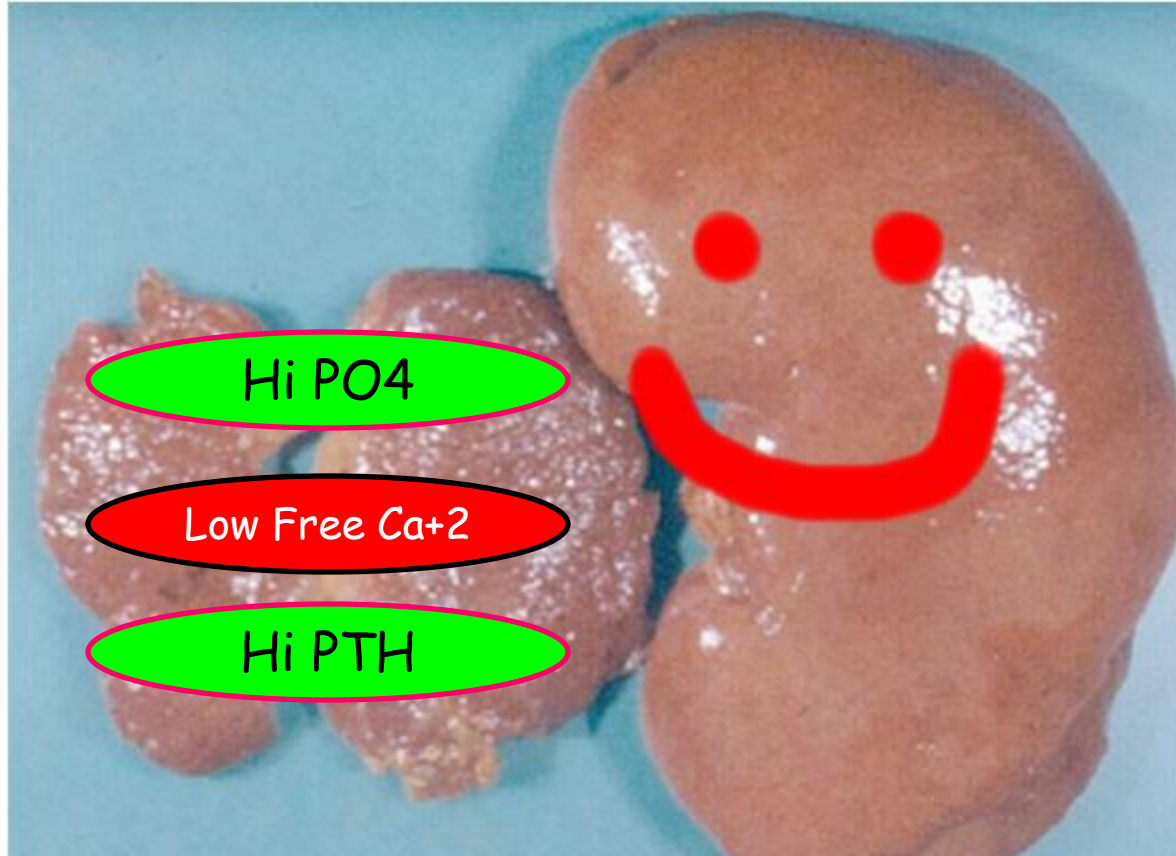


Codman's triangle
Osteosarcoma



Hypertrophic
Osteoarthropathy
AdenoCa, Lung

Renal Osteodystrophy:



Howard J. Sachs, MD
E-mail: Howard@12daysinmarch.com