

Ca, Phos and Vitamin D Metabolism in Pre-Dialysis Patients

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Case: 22 y/o referred to Renal Clinic

Phosphate: 3.9 mmol/L

Calcium: 1.9 mmol/L

PTH: 99 pmol/L

What do you fix first ?

Case: A.M. 29 y/o Man with ESRD on Peritoneal Dialysis

- Renal Diagnosis: ESRD due to FSGS
- Jan/1999 started Peritoneal Dialysis
- With no OHIP coverage
- Jan/1999 Advanced 2-HPT (PTH 99)
- Multiple Ectopic Calcifications by 2003:
 - Left shoulder, right elbow, right hip vascular calcifications.

SECONDARY HYPERPARATHYROIDISM (HPT) IN PATIENTS WITH
CHRONIC RENAL DISEASE (CRD).



Secondary Hyperparathyroidism

- 1993: CRD, Biopsy: FSGS
- 1999: 23 y/M: started CAPD

complaining of joint and muscle aches;

X-rays showed multiple soft tissue calcifications

	<u>1999</u>	<u>2001</u>	<u>2003</u>	<u>2006</u>	
Ca	1.90	2.10	2.55	2.23	mmol/L
P	3.9	2.5	1.96	1.73	mmol/L
PTH	99	100	30	11	pmol/L

Case: 56 man on hemodialysis

- Renal Dx: ESRD 2o SLE; Failed kidney Tx.
- On PD from 1991 to 1997
- Kidney Transplant 1997
- 2000 failed Transplant, back on Hemodialysis
- 2000: PTH 50; Phos 2.07 Ca 2.10
- 2001: PTH 81; Phos 2.03 Ca 2.10
- 2002: PTH 10; Phos 1.46 Ca 2.70

11-Oct-05
SE:100
IM:0

261602
St: 15450 Se: 4371
2005/10/06
14:44:40
CB
CT
MIP Mag: 1.26

CREDIT VALLEY FERGUSON, ROBERT
Brilliance16
Brilliance16
Slab: 4.00



kV:
mm
W 255 : L 127

140.00 kV
218.00 mA
Tilt: 0.00
FOV: 220.00
Thickness: 1.00 mm

10.00mm/div

W : 825 L : 260
LeftButton : Rotate

CYRIACJASON

What is the life expectancy of patients on dialysis?

- The mean life span at age 49 in the USA is 30 years in the general population.
- In a patient starting dialysis at age 49 in the USA the life span is 6 to 10 years (AJKD: 2006).
- Compare this to the waiting list for transplants.
- What is the cause of death for most patients?
- Cardiovascular disease.

Morbidity and Mortality in ESRD

- What is the life expectancy of patients with ESRD?
- What factors increase the Morbidity and Mortality in ESRD?
- General Factors: Age, Sex, Renal Diagnosis
- Disease Factors: Cardiovascular Disease, DM
- Cardiovascular Disease Factors: smoking, DM, HTN, **disruption of Ca/P Metabolism.**

K/DOQI Target range of P04, PTH & Ca

■ <u>CRD-3</u>	<u>PO4</u>	<u>Ca</u>	<u>PTH</u>
30-59 *	<1.49*	2.1-2.54	<8.0 pmol/L
■ <u>CRD-4</u>			
15-29*	<1.49	2.1-2.54	<12.1
■ <u>CRD-5</u>			
Dialysis	<1.78	2.1-2.54	<33.0

*PO4 0.87-1.49 mmol/L

Ca 2.1-2.54 mmol/L

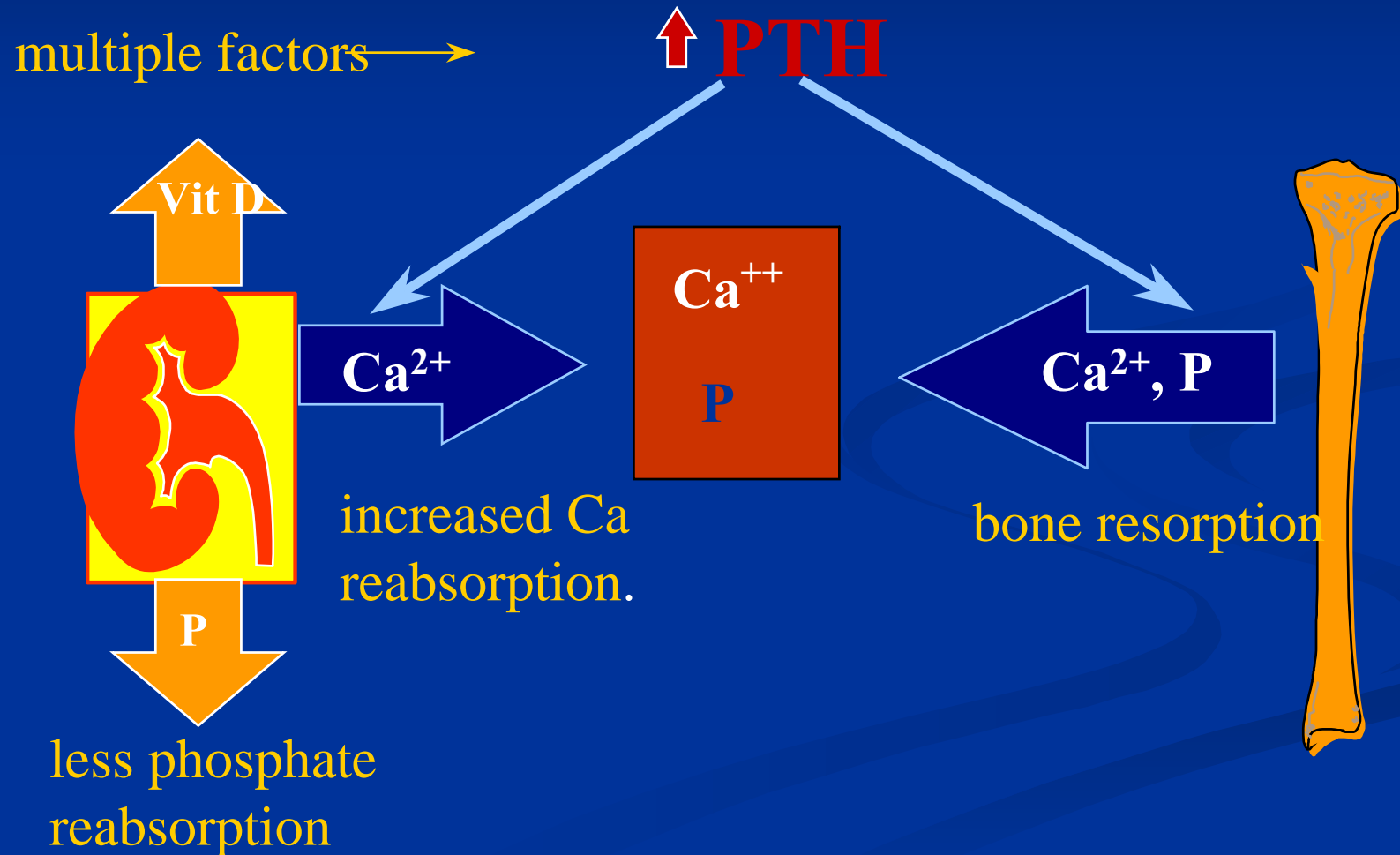
PTH: 3.8-7.7 pmol/L

When do you measure Vitamin-D?

Questions

- Why does Phosphate (**PO₄**) goes up during chronic renal disease (**CRD**)?
- What happens to Calcium (**Ca**) during the progression of **CRD**?
- Why does **PTH** goes up during **CRD**?
- What are the consequences of this abnormalities? How do we treat them?

PTH biological actions



What happens in CRD ?

Initial fall in GFR:

Reduced filtered PO₄



↑ PO₄



Renal Damage:

Reduced 1,25-Vit-D



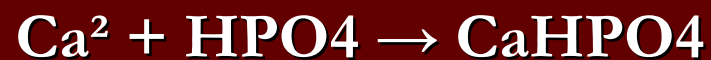
↓ Ca



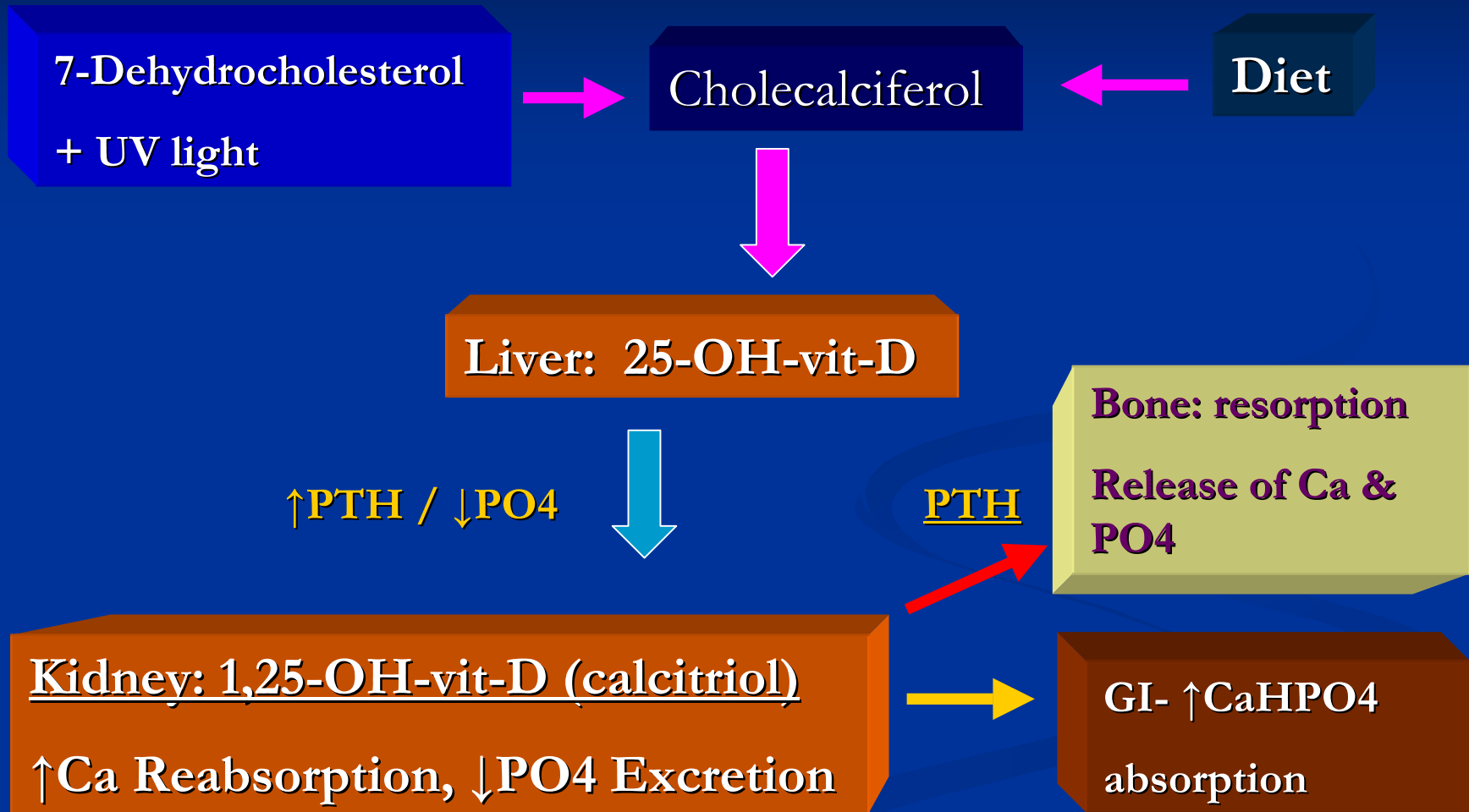
↑ PTH



Secondary Hyperparathyroidism:



Vitamin D Metabolism



Controversies in the Management of Secondary Hyperparathyroidism

- What is the result of bringing PTH levels down? Is that good or bad?
- Does it improve morbidity and mortality?
- Does correcting PTH levels increase the incidence of dynamic bone disease?
- Does it reverse calcifications in tissues?
- Does it reduce cardiovascular mortality?
- Block, GA: KI 2005; 68:1815

Table 1. Characteristics of a stage 3 & 4-CRD
Clinic Population (n=508 patients)

■ Age (mean)	67 (range 22-89)
■ Females	35 %
■ Males	65 %
■ Cause of ESRD	
Diabetes	43 %
Hypertension	17 %
Primary Renal Disease	40 %
■ PTH > 20 pmol/L (3x normal)	34 %
■ Ca < 2.2 mmol/L	40 %
■ PTH > 20 & Ca < 2.2	22 %
■ Serum Creatinines Range	150-500 umol/L

Age-Mean PTH in CRD

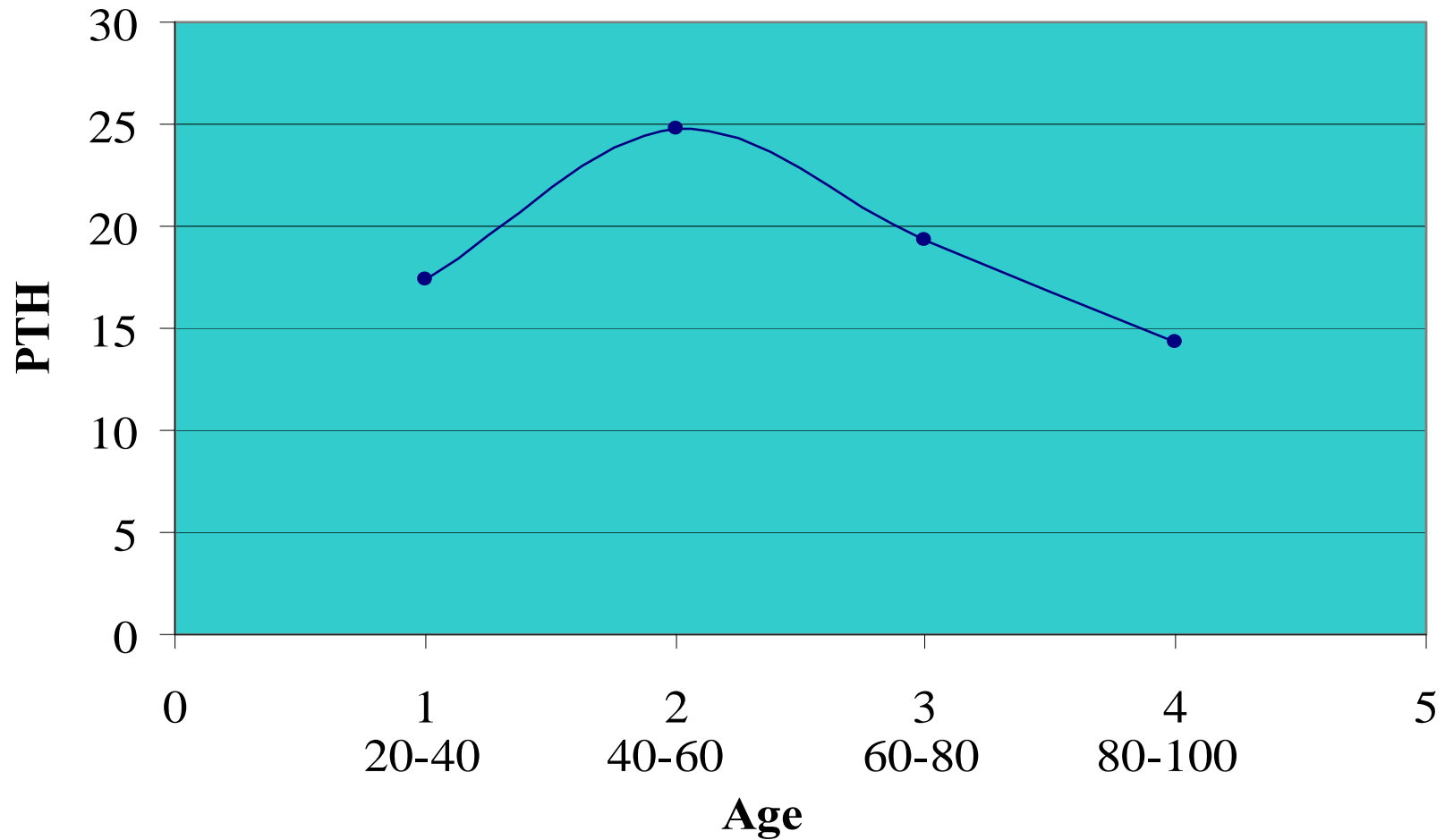


Table 3. Baseline characteristics of the treatment groups

	<u>Alfacalcidol</u>	<u>Calcitriol</u>
■ Patients (number)	43	33
■ Gender (female/male)	13/30	18/15
■ Age (mean \pm SD)	60 \pm 15	63 \pm 11
■ Diabetics (number)	13	14
■ Hypertension/Vascular	7	6
■ Primary Renal Disease	23	13
■ Creatinine (mmol/L; mean +SD)	372 \pm 112	351 \pm 85
■ Creatinine Clearance (ml/s)	0.31 \pm 0.13	0.29 \pm 0.1
■ Ca (mmol/L)	2.13 \pm 0.24	2.17 \pm 0.17
■ P (mmol/L)	1.53 \pm 0.38	1.45 \pm 0.24
■ PTH (pmol/L)	38 \pm 23	44 \pm 22

Management of 2° HPT

- Diet restriction of PO₄
- Phosphate binders: CaCO₃ & Renagel
- Vitamin D sterols: Calcitriol & Alfacalcidol & Doxercalciferol
- Calcimimetics: Cinacalcet

Cost of Treatment

CaCO ₃	500 mg	\$0.05/tab	6.00/mo
Calcitriol	0.25 mcg	\$0.97/cap	\$30.00/mo
Alfacalcidol	0.25 mcg	\$0.45/cap	\$15.00/mo
Hectorol	2.5 mcg	\$1.70/cap	\$82.00/mo
Renagel	800 mg	\$1.72/tab	\$200-400/m
Sensipar	30 mg	\$10.70/tab	\$320-960/m

Conclusions

- HPT and Hyperphosphatemia should be identified and treated early in CRD
- Approximately 30% of patients with CRD stage 3-4 already have HPT
- In the future treatment for HPT should be tailored to each patient and may include combinations of diet, phosphate binders, vitamin-D and Cinacalcet

Conclusions

- In order to reduce the risk of adynamic bone disease and
- To reduce the incidence of tissue calcification and
- To reduce morbidity and mortality
- Therapy has to achieve perfect balance of Ca, P and PTH

Vitamin D metabolism

Vitamin D₃
cholecalciferol

← foods

← UV light on skin

1,25(OH)₂D₃
calcitriol (active)

25-hydroxylase

simple, fast
hydroxylation

25(OH)D₃
calcifediol

controlled

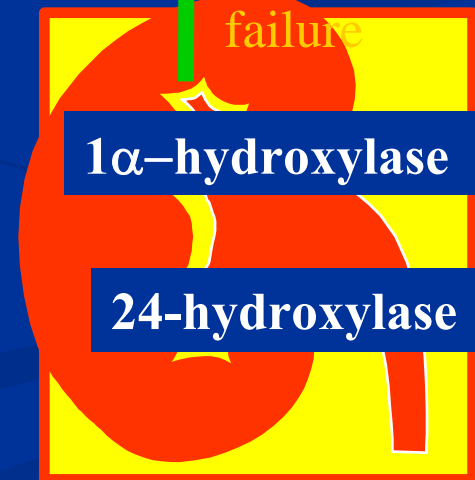
less active

24,25(OH)₂D₃

1α-hydroxylase

24-hydroxylase

less
conversion
with renal
failure



Case: 20 yr old man w CRD-5

- Just started dialysis; his monthly routine results:
- Lab:
- PO₄: 2.12 mmol/L
- Ca: 2.32 mmol/L
- PTH: 93 pmol/L

- What should be fixed first?

