Incorporating K/DOQI Using a Novel Algorithm Approach: Regina Qu'Appelle's Experience

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BC Nephrology Days

There is a “strong association among higher concentrations of serum phosphorus and calcium and an increased risk of death”.[1]

[1] Block et al. Mineral Metabolism, Mortality, and Morbidity in Maintenance Hemodialysis. J Am Soc Nephrol 15: 2208-2218, 2004

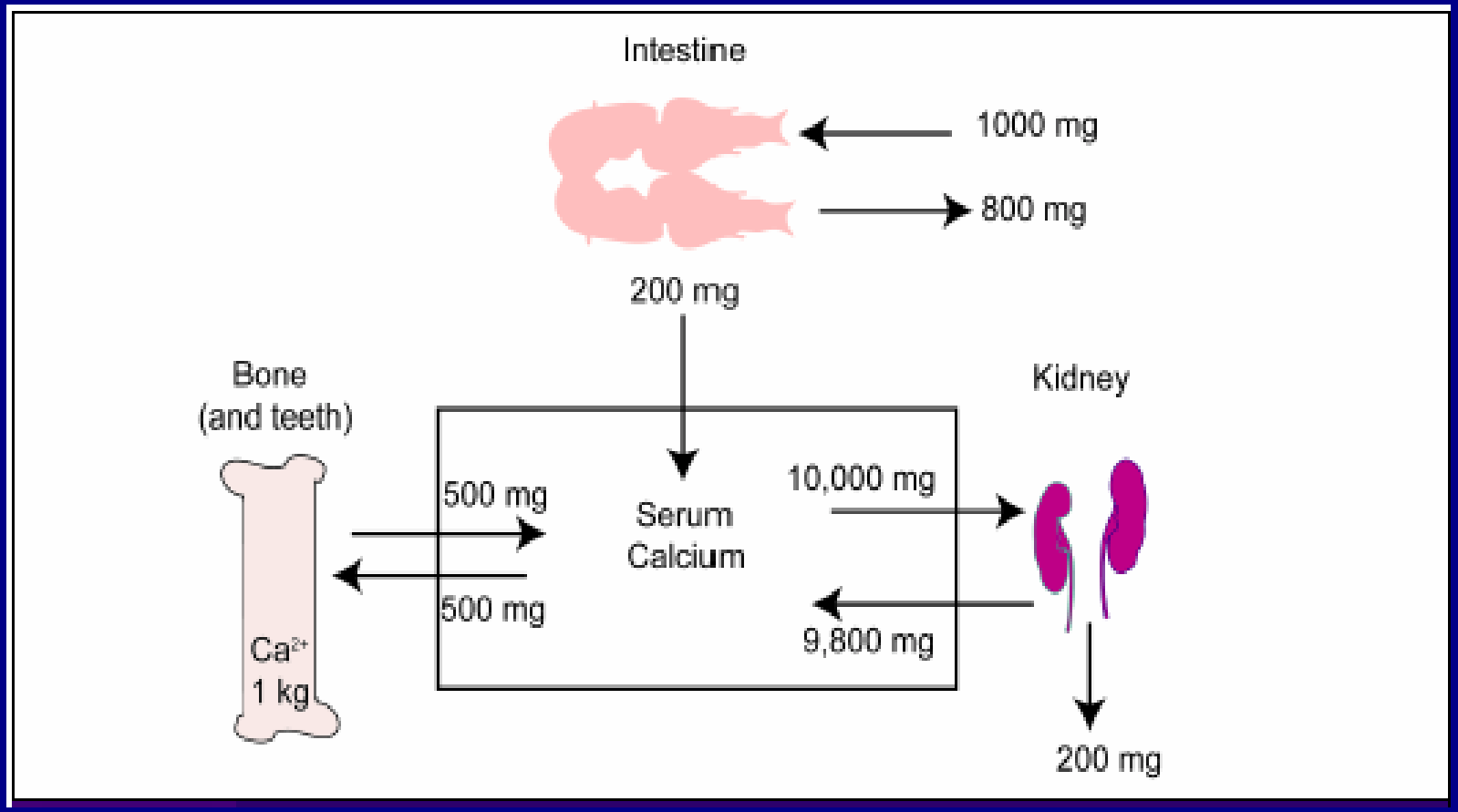
“Treatment of the complex bone and mineral metabolism abnormalities in CKD requires a coordinated team effort…..”[2]

[2] McCann, Journal of Renal Nutrition , Volume 15, No 2 (April) 2005, pp.265-274

A Complex Process

- Minerals: calcium, phosphorus, and magnesium
- Regulators: parathyroid hormone, vitamin D
- Target Organs: kidney, intestine, bone

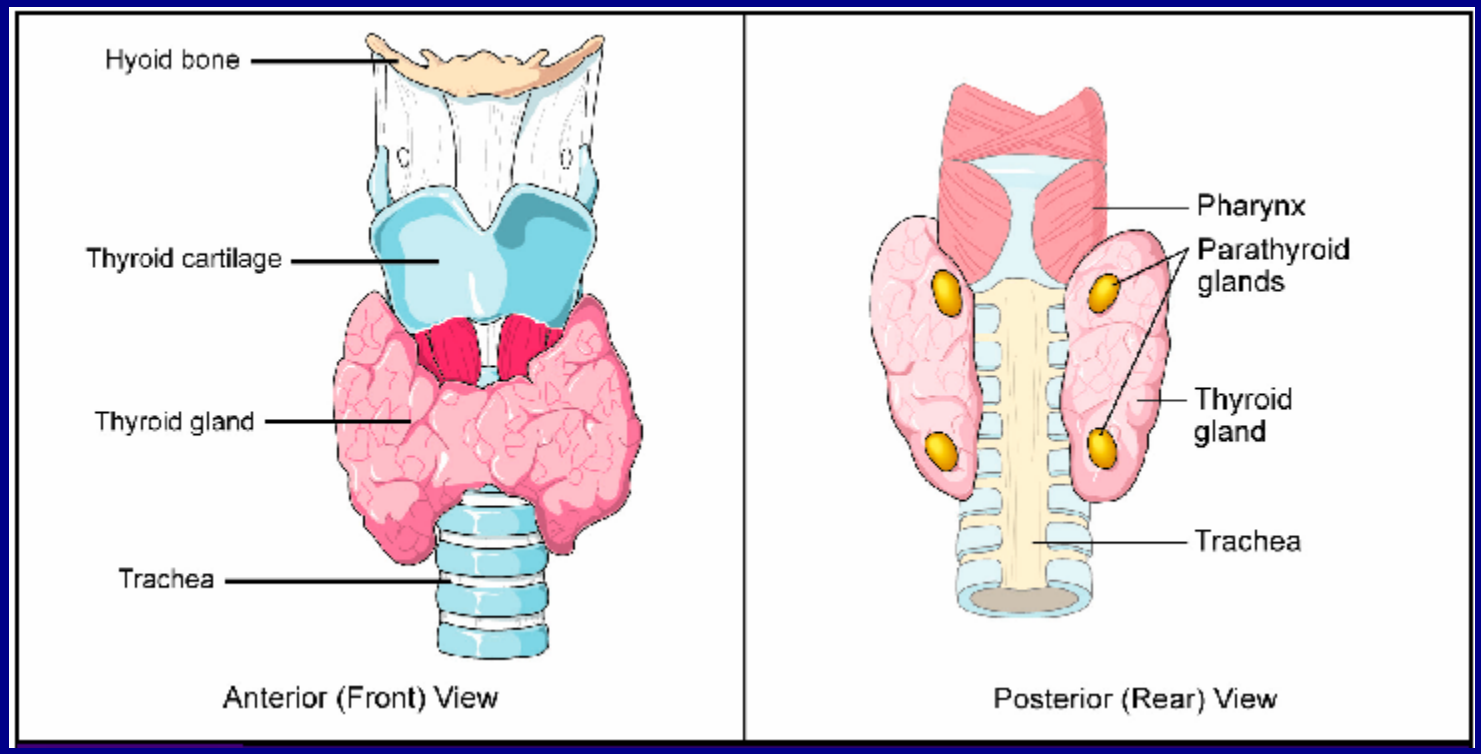
Target Organs



A Complex Process

- The thyroid gland, parathyroid glands and kidneys play an important role in the maintenance of the serum levels of calcium and phosphorus.

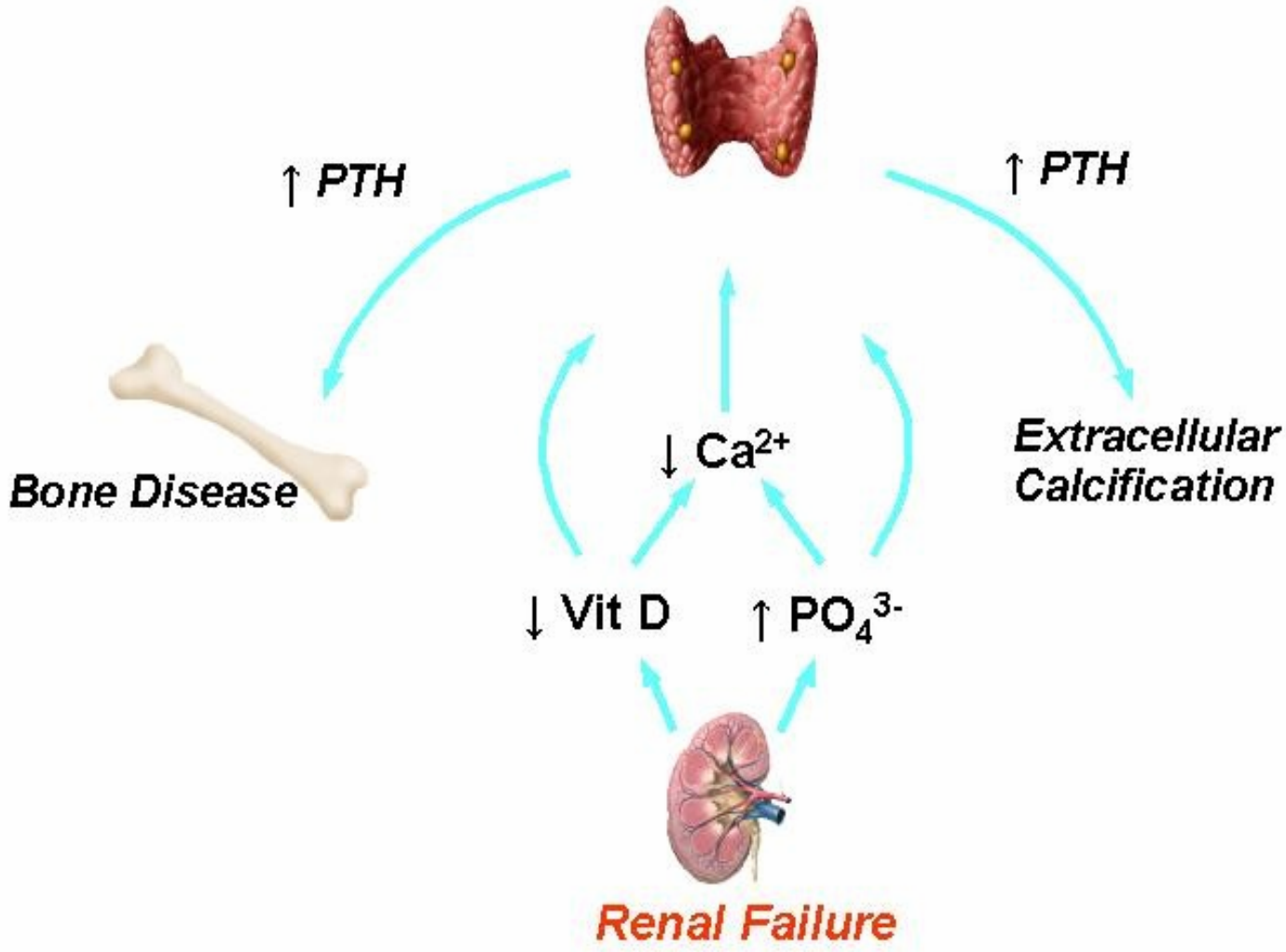
Thyroid/Parathyroid Gland



Disorders of Mineral Metabolism

- Hyperphosphatemia
- Hypocalcemia
- Secondary hyperparathyroidism
- Altered vitamin D metabolism
- Bone disease
- Calcification

Secondary Hyperparathyroidism

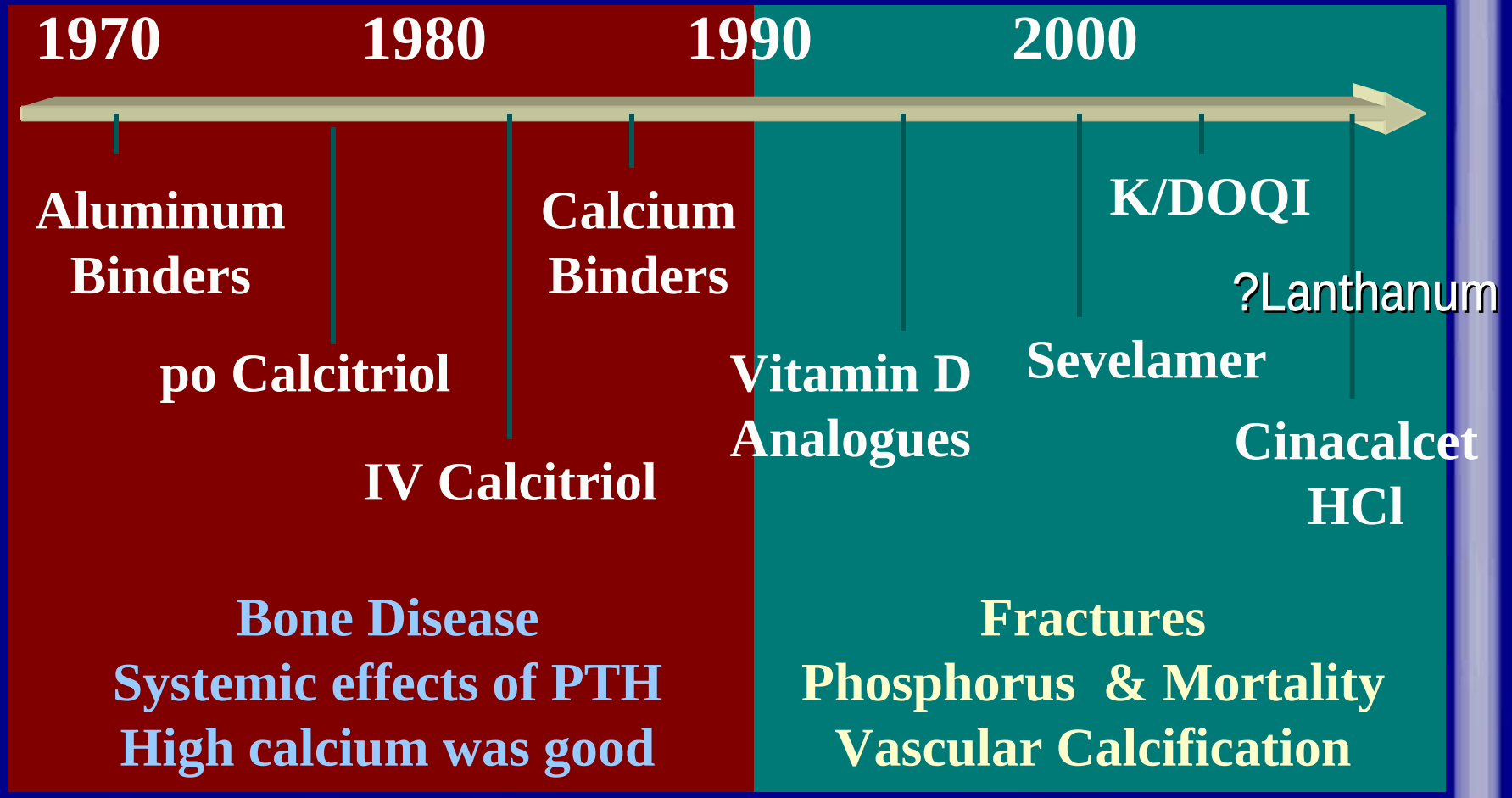


"Virtually every treatment directed at one of these abnormalities can adversely impact another area of bone and mineral balance and result in a new and undesirable complication."[3]

Best example of this is the history of managing hyperphosphatemia…

[3] McCann, Journal of Renal Nutrition , Volume 15, No 2 (April) 2005, pp.265-274

History of Treatment Strategies for Secondary Hyperparathyroidism



Normal Bone Remodeling

- The majority of the body's calcium and phosphorus is stored in bone (99%). When osteoclasts resorb bone, these minerals are released for use in other physiologic processes.

Normal Bone Remodeling

- The actions of osteoclasts and osteoblasts allow bone to continually remodel, replacing old weaker bone with new stronger bone. Under normal circumstances, osteoblast activity matches osteoclast activity with no net loss or gain of bone mass.

Normal Bone Remodeling

- Bone remodeling starts with resorption of bone by osteoclasts, then deposition of collagen by oseoblasts, and finally mineralization with calcium and phosphorus.

Normal Bone Remodeling

- PTH stimulates production of active Vitamin D in the kidneys, which increases the supply of calcium and phosphorus from the gastrointestinal tract for mineralization of the new bone.

Hypocalcemia and Hyperphosphatemia

- In Renal Failure, Two processes no longer performed adequately.
- 1. Phosphorus is no longer excreted by the kidney
- 2. Kidney no longer adequately converts Vitamin D to active form, thus causing a decrease in serum calcium

Secondary Hyperparathyroidism

- PTH is stimulated by the low calcium, high phosphorus, and low Vitamin D.
- As kidney function declines, disorders of calcium and phosphorus metabolism lead to overstimulation of the parathyroid glands resulting in excessive secretion of PTH.

Secondary Hyperparathyroidism

- Vitamin D deficiency develops, causing decreased intestinal absorption of calcium

Secondary Hyperparathyroidism

- The resulting hypocalcemia causes secondary hyperparathyroidism.
- High PTH levels stimulate osteoclasts which increase bone resorption.

Bone Disease in Renal Patients

Renal Osteodystrophy

High Turnover
(rapid or abnormal bone remodelling)

- Osteitis fibrosis (hyperparathyroid bone disease)
- Mixed uremic osteodystrophy

Low Turnover
(delayed or inadequate bone mineralization)

- Osteomalacia and aluminum related bone disease
- Adynamic uremic osteodystrophy

Other age and disease related conditions

Osteoporosis
-post menopausal
-age related
-medications
corticosteroids

Amyloid bone disease
(resulting from constant stimulation of immune system by exposure of blood to dialyzer)

Calcification

- Chronically high levels of PTH lead to bone disease and extraskeletal calcification.

Metastatic Calcification

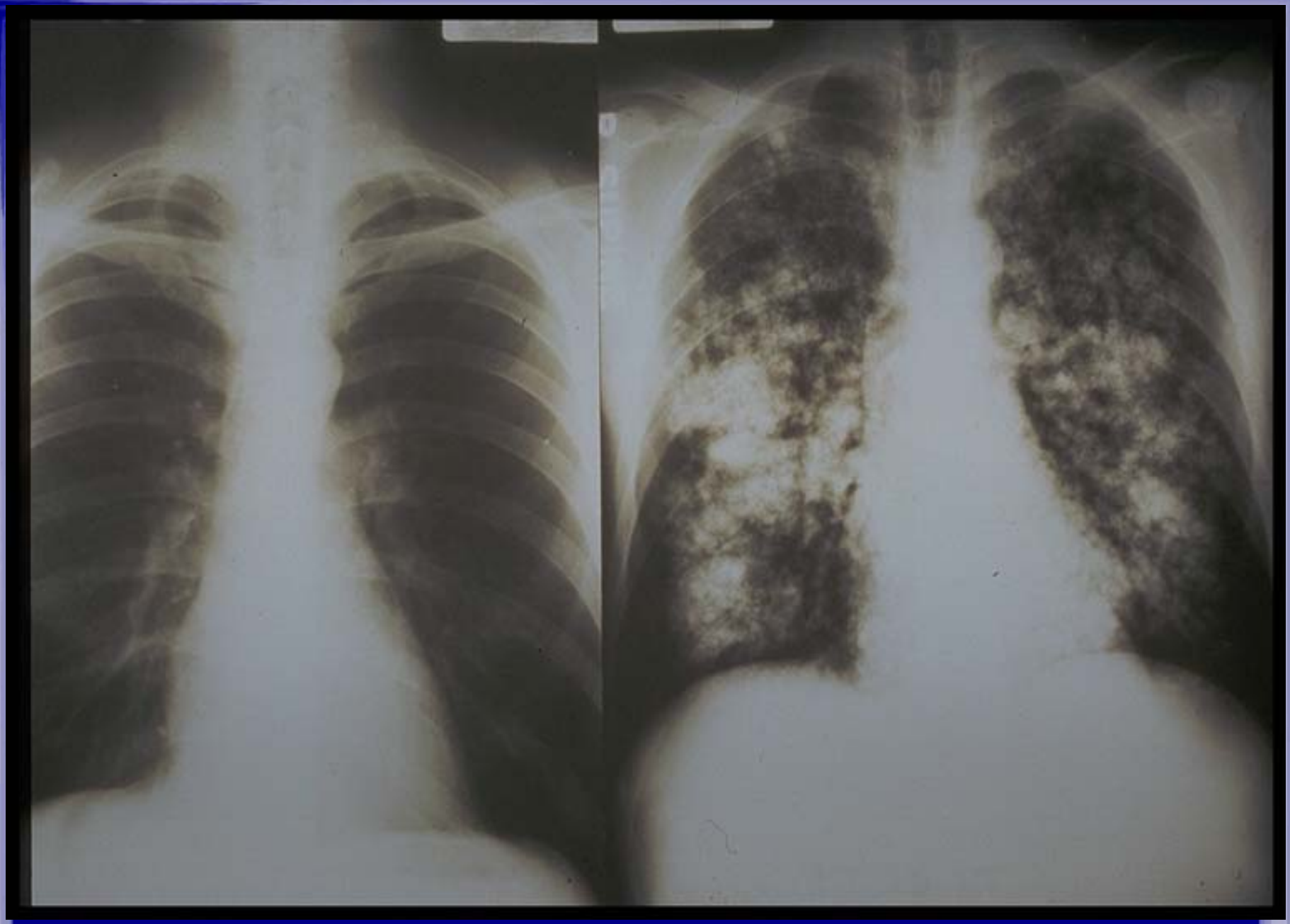
Calcium and Phosphorus are Deposited in One of Two Forms

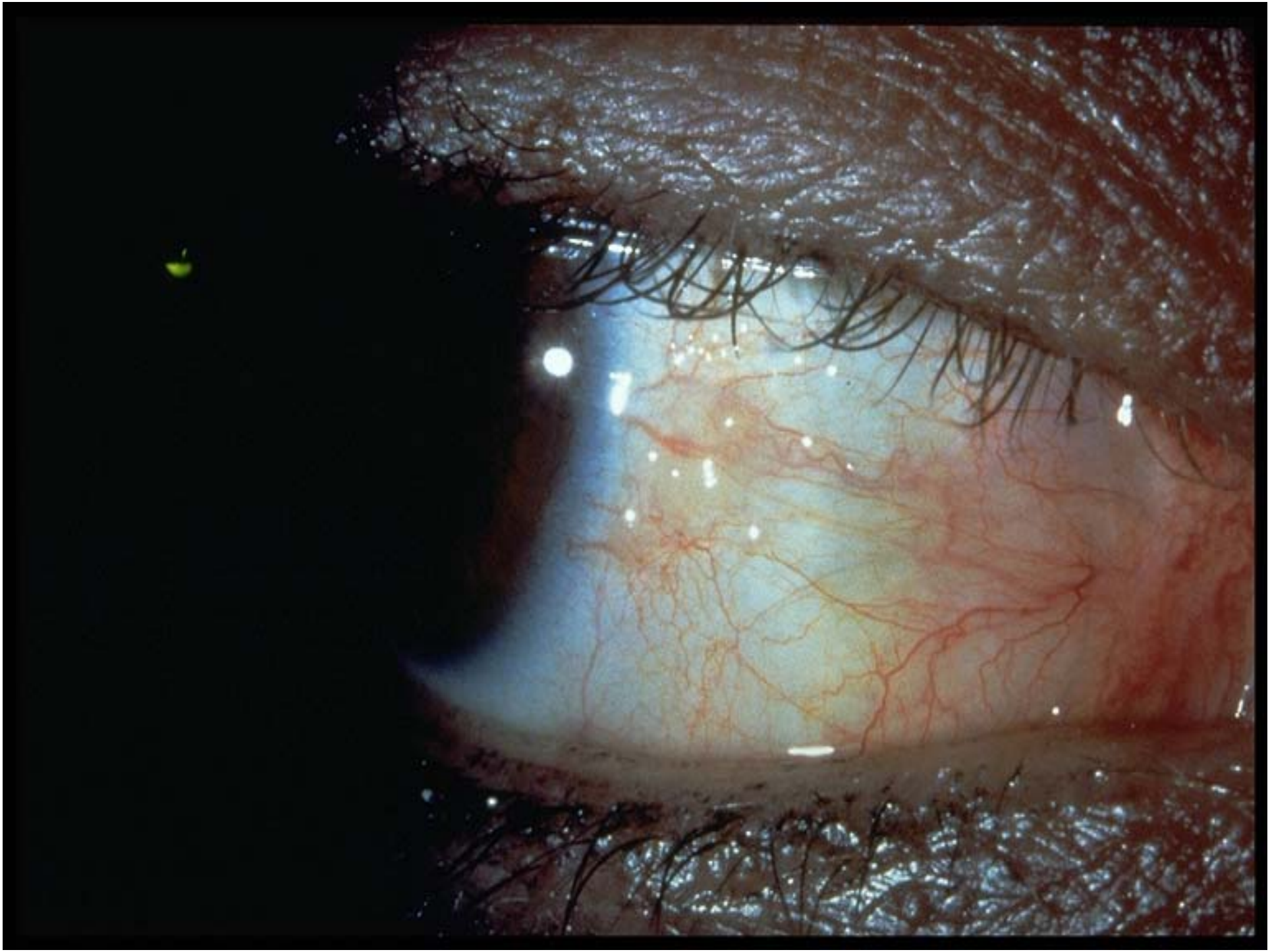
- **Amorphous**
- $(CaMg)_3(PO_4)_2$

- **Soft tissue**
  - **Heart**
  - **Lungs**
  - **Kidneys**

- **Hydroxyapatite**
- $Ca_{10}(PO_4)_6(OH)_2$

- **Vascular**
- **Valvular**
- **Joints**
- **Ocular**





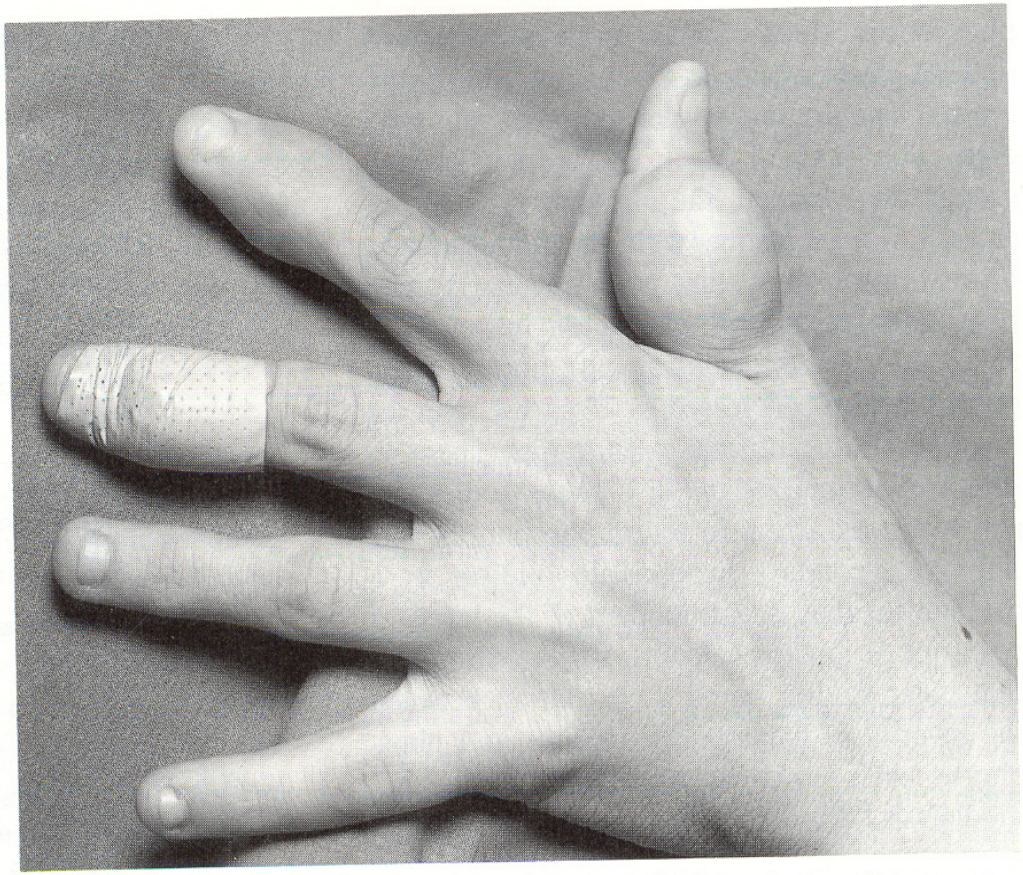
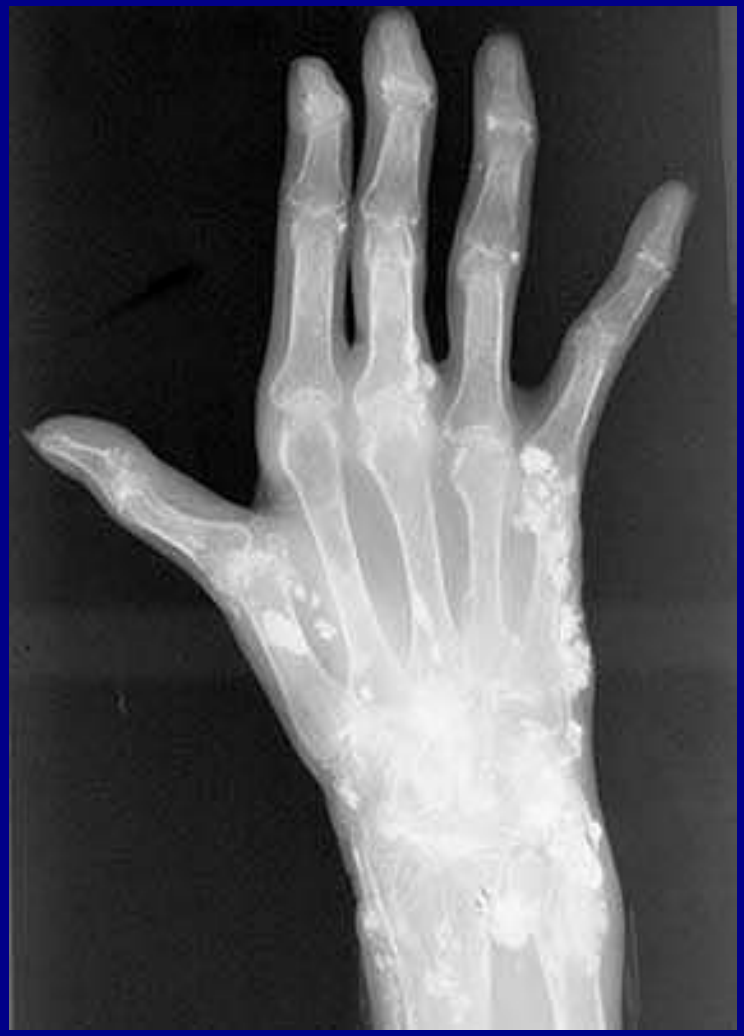
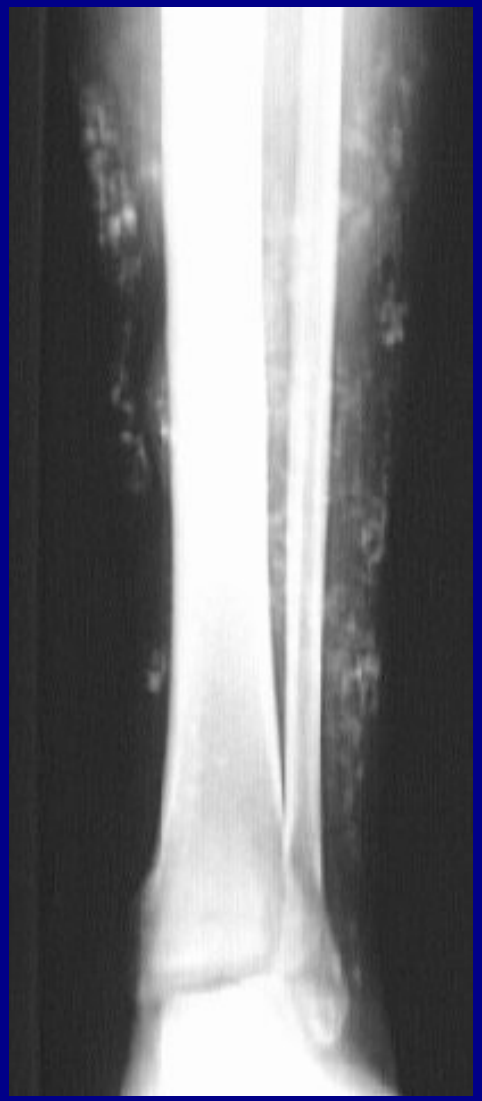


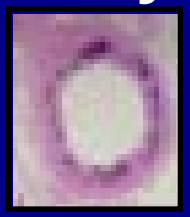
Fig 2. Periarticular calcification in a dialysis patient with a persistently elevated calcium-phosphorus product.





Arterial media calcification in ESRD: impact on all-cause and cardiovascular mortality

Arterial Intimal Calcification

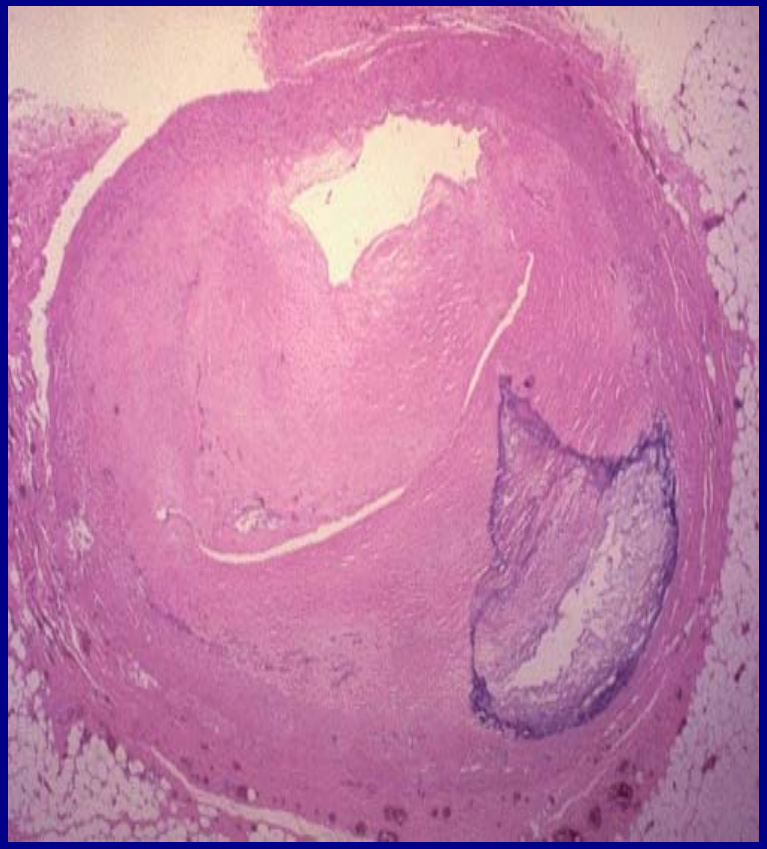


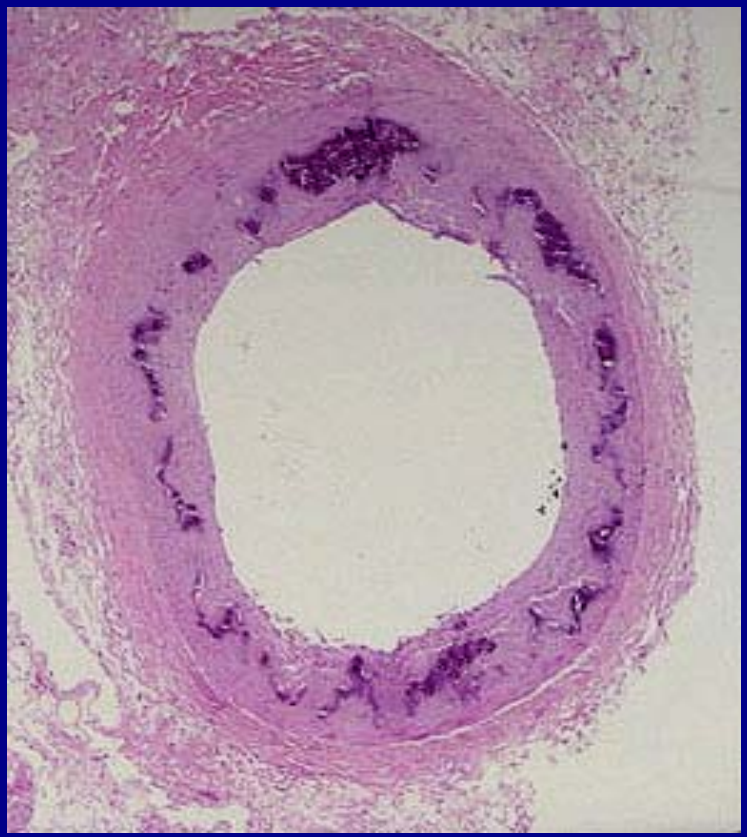
Arterial Medial Calcification

- "usually observed in …"
  - older patients with a clinical history of atherosclerosis before starting HD
  - typical risk factors associated with atherosclerotic disease
- "closely associated with …"
  - duration of HD
  - calcium-phosphate disorders
  - oral dose of elemental calcium prescribed as a phosphate binder ($CaCO_3$)

London GM, et al.*NephrolDial Transplant* 2003;18:1731-1740

AIC vs AMC





General Population **Chronic Kidney Failure**

Wide Pulse Pressure

- 120/80 = WPP of 40
- 160/90 = WPP of 70

- Increasing WPP indicates calcification

Nurse assessment

- Chest Xray
- Blackened area on skin (necrotic area may indicate calcifilaxis, more around the ankle or shin area)
- Soft tissue calcification
- Blood shot eyes

Symptoms

- Itchiness (high phosphorus, high calcium, high product)
- Bone pain, Joint pain

Morbid Effects of Calcification

Type of Calcification	Morbid Effects
Coronary arteries, valvular and large vessel disease arrhythmia, left and right ventricular hypertrophy	Atrioventricular block, cardiac failure, pulmonary hypertension,
Peripheral arteries amputation	Bone and soft tissue necrosis,
Skin arterioles	Calciphylaxis
Pulmonary defects, decreased diffusion, hypoxia	Cough, dyspnea, restrictive

K/DOQI Guidelines
Stage 5

K/DOQI Disclaimer

- These Guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision-making. They are not intended to define a standard of care, and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.
- Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every health care professional making use of these Guidelines is responsible for evaluating the appropriateness of applying then in the setting of any particular clinical situation.
- The recommendations for research contained within this document are general and do not imply a specific protocol.

K/DOQI Guidelines Stage 5

- Serum Phosphorus 1.13-1.78 mmol/L
- Serum Calcium 2.10-2.38 mmol/L
- PTH 16.5-33.0 pmol/L
- Ca x Phos < 4.44 $mmol^2/l^2$

- Max 2000 mg elemental calcium/d (includes 1500 mg binders and 500 mg diet)
- Use of non calcium based binders:
  - hypercalcemia (>2.54 mmol/L),
  - evidence of calcification (ie. x-ray, wide pulse pressure),
  - PTH ≤16.5 pmol/L

K/DOQI Guidelines for Binders

Key is to choose binder based on:

- patient profile (#, size, appetite)
- comorbid illness
- associated side effects
- cost
- ability of binder to control serum P04 without causing increase in Ca, a Ca x P04 product above range
- limit elemental calcium to <1500mg/day

[4]McCann, Journal of Renal Nutrition , Volume 15, No 2 (April) 2005, pp.265-274

Interpretation of Labs

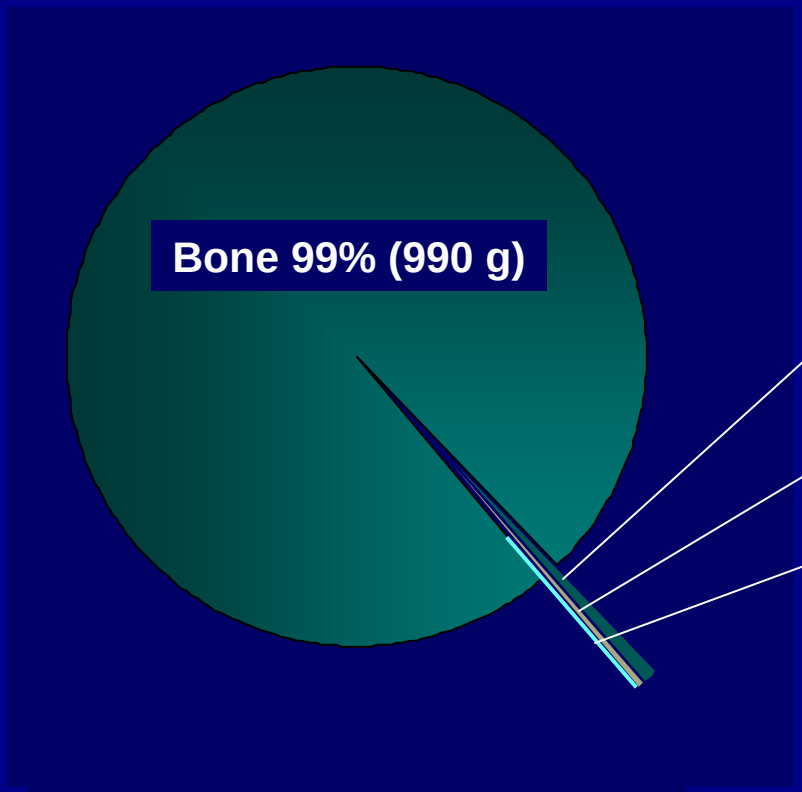
- Lab results may give a false impression of what is really going on
- Need to critically evaluate
- Result may have many interpretations
- Takes time
- It is everyone's responsibility

Case 1

	January	February	March
urea	33.6	24.8	18.5
creatinine	789	534	427
albumin	42	38	35
potassium	5.6	5.5	4.1
calcium	2.45	2.36	2.39
phosphorus	2.01	1.80	1.43
PTH			43

What questions do we need to ask?

Distribution of Calcium in the Body



- **Intracellular Ca**
  0.9% (9 g)
- **Interstitial Ca**
  0.075% (0.75 g)
- **Plasma Ca**
  0.025% (0.25 g)

Total Body Calcium = 1000 g

Incorporating the Guidelines

- Challenge is to use the guidelines to best manage the patient
- We need help
- The algorithm

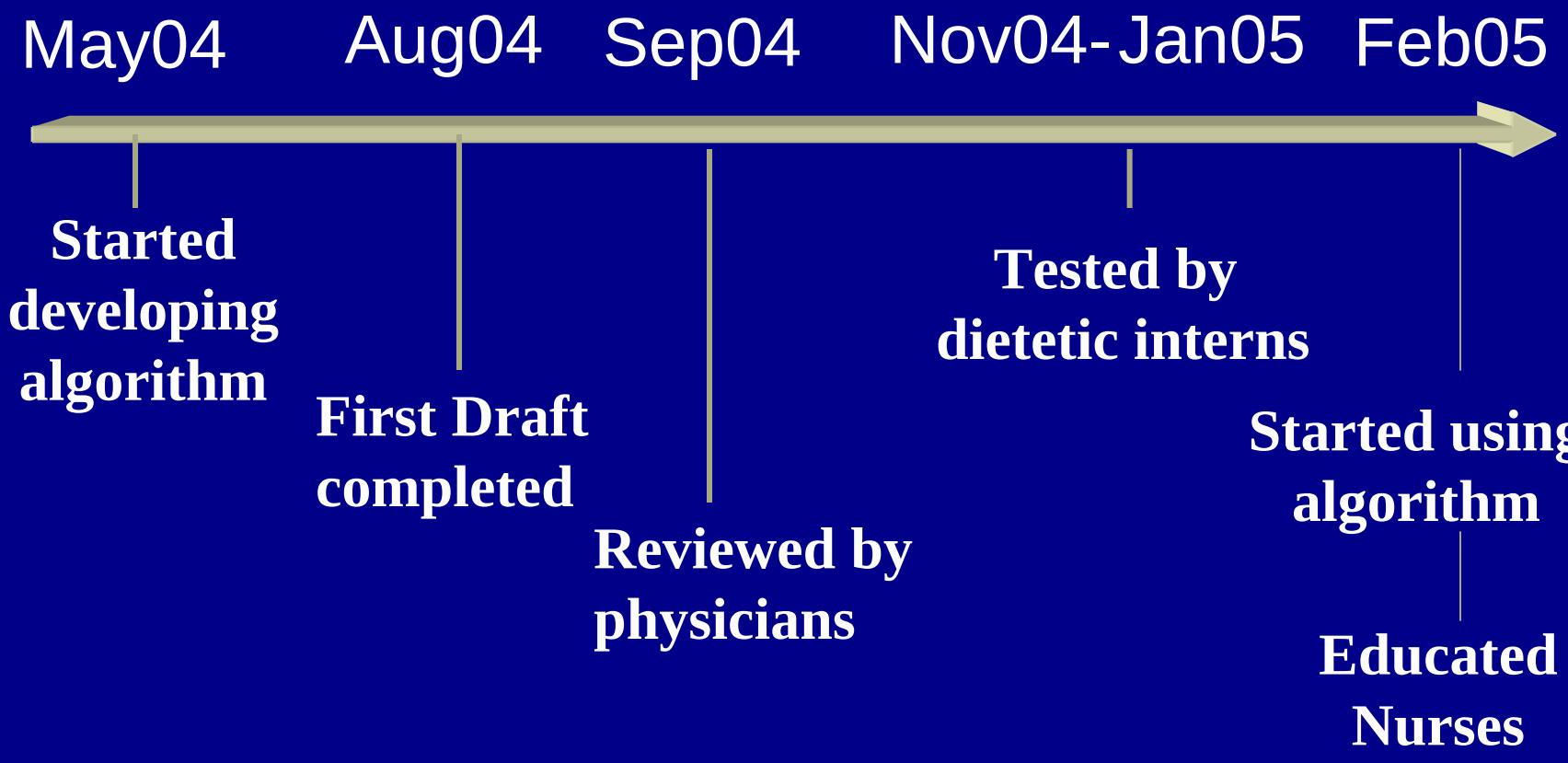
Why the Algorithm Was Developed?

- To assist health care professionals understand and manage the complexity of calcium and phosphorus metabolism
- To incorporate K/DOQI guidelines
- Will provide for the improvement of patient management using this CQI tool

Development and Implementation of Algorithm

- Driven by dietitian and pharmacist in May 2004
- Reviewed updated literature and incorporated reimbursement criteria
- Reviewed by nephrologist and team
- Draft trialed with students
- Comments were incorporated

Timeline for Development of Algorithm



PHOSPHORUS/CALCIUM MANAGEMENT (Stage 5 CKD)

Target Values K/DOQI Guidelines[1]

Phosphorus	1.13 - 1.78 mmol/L
Calcium	2.10 - 2.38 mmol/L
Ca x P	<4.4 mmol^2/L^2
PTH	16.5 - 33 pmol/L

INDICATIONS FOR NON CALCIUM BASED PHOSPHOROUS BINDER

- Hypercalcemia (corrected serum calcium > 2.54 mmol/L)
- Severe Calcification
- PTH levels less than 16.5 pmol/L

Initial Binder Therapy

calcium carbonate 500 mg/meal
max 1500 mg elemental calcium/day
(or non calcium based binder)

Phosphorus <1.13 mmol/L

- dietary review
- decrease or stop phosphorus binders
- phosphorus supplement

Calcium <2.10 mmol/L
- change timing of calcium carbonate to between meals
- review PTH
- adjust vit D as required

Calcium 2.10-2.38 mmol/L
- dietary review
- decrease or stop phosphorus binders
- phosphorus supplement
- review PTH
- adjust vit D as required

Calcium > 2.38 mmol/L
- consider calcium dialysate
- review PTH
- adjust vit D as required

Phosphorus > 1.78 mmol/L

- assess adherence to diet and meds
- adequacy of dialysis

If adherent with diet and meds

Calcium < 2.10 mmol/L
- increase calcium carbonate (max. 1500mg/day)
- start non calcium based binder eg. Renagel
- review PTH
- adjust vit D as required

Calcium 2.10-2.38 mmol/L
- increase calcium carbonate (max. 1500mg/day)
- start non calcium based binder eg. Renagel
- review PTH
- adjust vit D as required

Calcium >2.38 mmol/L
- discontinue calcium carbonate if Ca >2.54 mmol/L
- start non calcium based binder eg. Renagel
- review PTH
- adjust vit D as required
- consider calcium dialysate

Phosphorus 1.13 - 1.78 mmol/L

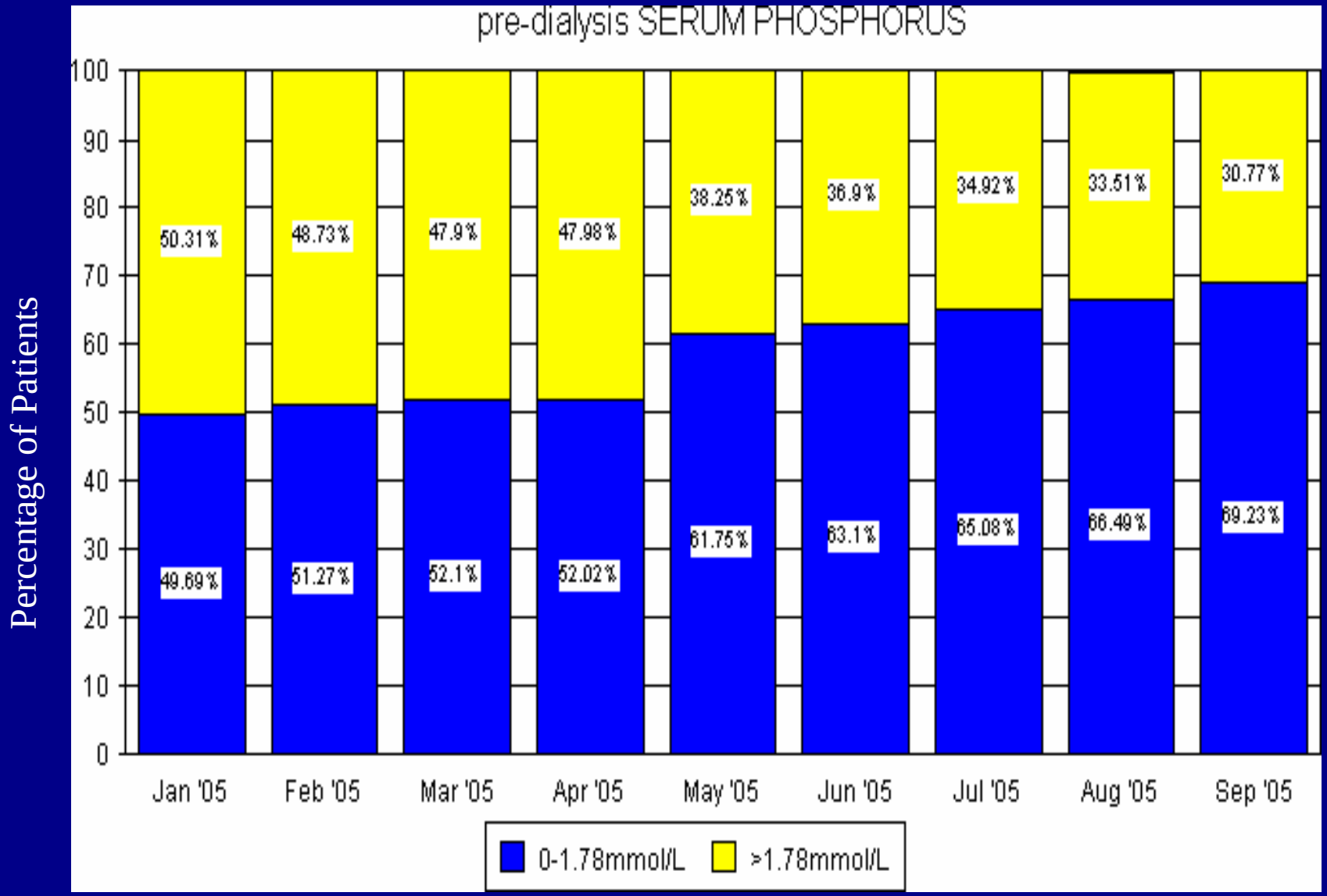
Calcium <2.10 mmol/L
- increase calcium carbonate (max. 1500mg/day)
- consider adding calcium carbonate between meals
- review PTH
- adjust vit D as required
- consider calcium dialysate

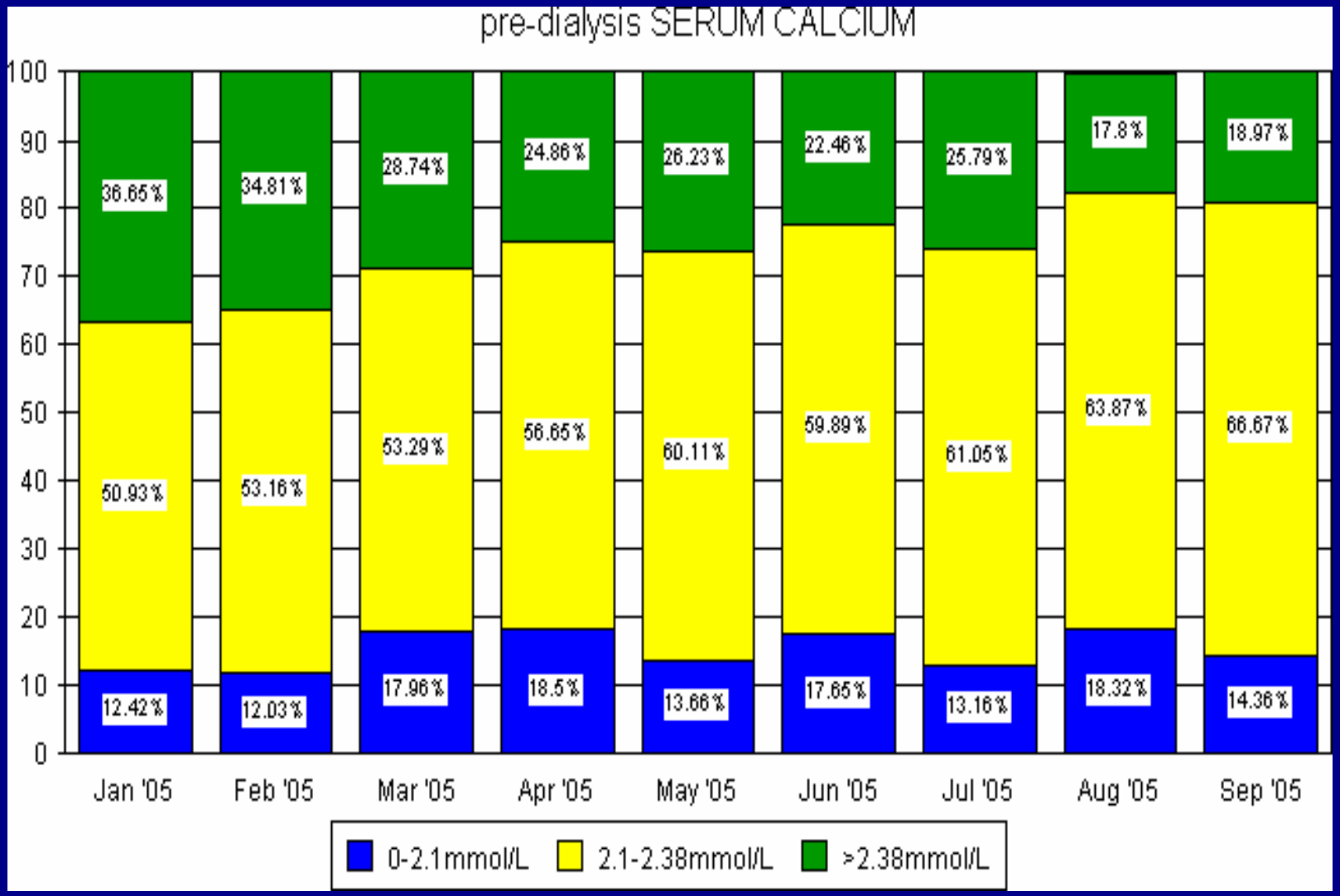
Calcium 2.10-2.38 mmol/L
- continue with current therapy
- review PTH
- adjust vit D as required

Calcium >2.38 mmol/L
- assess diet
- consider non calcium based binder (Renagel) if on calcium carbonate
- discontinue calcium carbonate if Ca >2.54 mmol/L
- review PTH
- adjust vit D as required
- consider calcium dialysate

1. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease. *Am J Kidney Dis.* 2003; 42 (suppl 3)

Developed by Michael Chan and Bruce Lang, Regina Qu'Appelle Health Region with special thanks to Sharon Skiba, Genzyme Canada Inc.


pre-dialysis SERUM PHOSPHORUS
Percentage of Patients
100
90
80
70
60
50
40
30
20
10
0
50.31%
48.73%
47.9%
47.98%
38.25%
36.9%
34.92%
33.51%
30.77%
49.69%
51.27%
52.1%
52.02%
61.75%
63.1%
65.08%
66.49%
69.23%
Jan '05
Feb '05
Mar '05
Apr '05
May '05
Jun '05
Jul '05
Aug '05
Sep '05
0-1.78mmol/L
>1.78mmol/L


pre-dialysis SERUM CALCIUM
Percentage of Patients
100
90
80
70
60
50
40
30
20
10
0
36.65%
34.81%
28.74%
24.86%
26.23%
22.46%
25.79%
17.8%
18.97%
50.93%
53.16%
53.29%
56.65%
60.11%
59.89%
61.05%
63.87%
66.67%
12.42%
12.03%
17.96%
18.5%
13.66%
17.65%
13.16%
18.32%
14.36%
Jan '05
Feb '05
Mar '05
Apr '05
May '05
Jun '05
Jul '05
Aug '05
Sep '05
0-2.1mmol/L
2.1-2.38mmol/L
>2.38mmol/L

Hemodialysis Report Card

Name _____

Date _____

Weight _____

Lab Test	Your Result	Target Level	Side Effects	Ways to Improve
Potassium		3.5 - 5.5	• irregular heart beat • muscle weakness • heart stops	• limit high potassium foods.
Albumin (blood protein)		35 - 50	• weight loss • muscle loss • weakness	• eat more protein like beef, pork, poultry, fish, and eggs.
Calcium   Phosphorus		2.10 - 2.38 1.13 - 1.78	• muscle cramping • itching • bone pain • bone disease • weak bones • joint pain	• limit foods such as milk and dairy products, dried beans and peas, nuts, colas, whole grain products. • take phosphorus binders with meals and snacks.
Fluid gain		Less than 3 kg	• shortness of breath • swelling • high blood pressure	• drink less liquid. • reduce salt and salty foods.

Are you taking these?

multi vitamin rocaltrol calcium carbonate (take with meals)

folic Acid one-alpha renagel (take with meals)

Comments: _____

Case 2

- Pt on hemo 3x/wk
- labs: Alb 37, Ca 2.66, Phos 2.01, iPTH 44.6
- meds: $CaCO^3$ with meals, one-alpha 0.25 od

Important Points to Remember

- Abnormal calcium and phosphorus balance will happen in CKD
- Renal osteodystrophy is a complex group of disorders
- Both high- and low-turnover bone disease can increase vascular and extraskeletal calcification

Important Points to Remember

- Bone and mineral abnormalities persist throughout CKD
- Morbidity and mortality are increased with high PTH, hyperphosphatemia, hypercalcemia, high Ca x P04 product
- Need to measure to improve patient care
- Need to incorporate newer and updated therapies such as Renagel appropriately

Dialysis Clinical Outcomes Revisited (DCOR) Trial

DCOR Trial


1053 Sevelamer
2103 Patients
36 Months
1050 Calcium Binder
Age
Race
Gender
Diabetes
HD > 3 months

Dialysis Clinical Outcomes Revisted DCOR Results

- Renagel reduced all-cause mortality risk by 9% relative to calcium-based phosphate binders (p=0.30)

- Patients treated for more than 2 years, Renagel reduced all-cause mortality risk by 34% relative to calcium-based phosphate binders (p=0.02)

- Patients 65 years of age or older, Renagel significantly reduced the risk of all-cause mortality by 22% (p=0.03)

- In older patients treated for more than 2 years, risk reduction 54% (p=0.0009)

DCOR

Where does DCOR fit in and how will it change the way in which we manage our patients?

References

- Getting to Goal: A Multidisciplinary Approach to Phosphorus Management.. NKF 2004
- NKF.K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis. 2003;42(suppl 3).
- Block et al. Mineral Metabolism, Mortality, and Morbidity in Maintenance Hemodialysis. J. Am Soc Nephrol 15:2208-2218, 2004

Thank you to Sharon Skiba, Genzyme, Canada