BONE AND MINERAL METABOLISM in the PD PATIENT

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Spectrum of Bone Diseases in CKD

Miller, p6, Table 1

- **Osteitis fibrosa cystica**
  - Increase in bone turnover secondary to increased PTH
- **Adynamic bone disease:**
  - Decrease in bone turnover
  - Prevalent in the advanced stages of CKD
- **Mixed uremic osteodystrophy**
- **Osteoporosis**

Miller PD. *Curr Osteoporos Rep.* 2005;3:5-12.

Spectrum of Bone Diseases in CKD

LESS COMMONLY SEEN

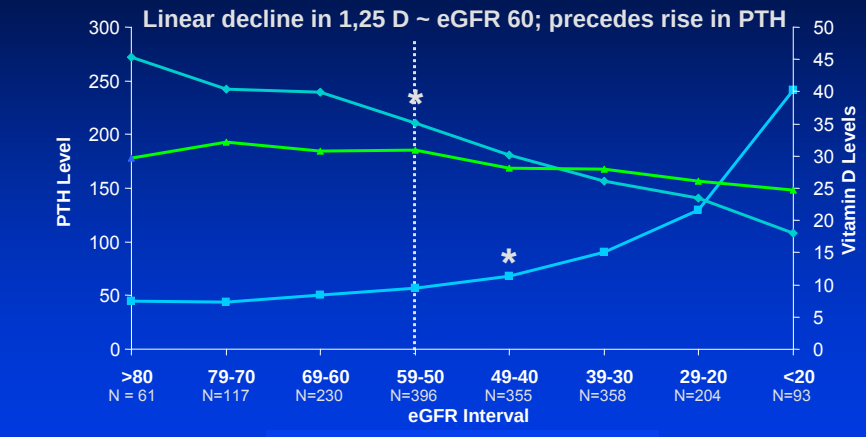
- Osteomalacia
- Aluminum accumulation
- Amyloid bone disease
- Phosphate depletion
  - Affects a minority of patients with CKD or ESRD

Miller PD. *Curr Osteoporos Rep.* 2005;3:5-12.

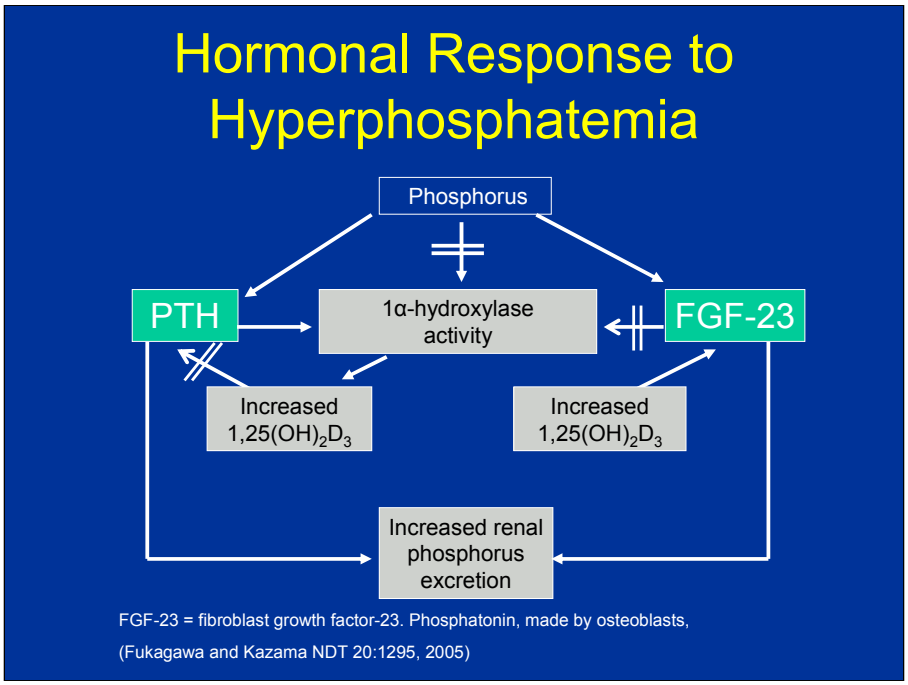
CKD-BMD MORE THAN A BONE PROBLEM

- You also see:
- Elevated PO4 levels
- Elevations of PTH
- Abnormalities in Ca levels
- Decrease in 1,25 Vitamin D and any of its non PTH related effects

Hormonal Changes in CKD

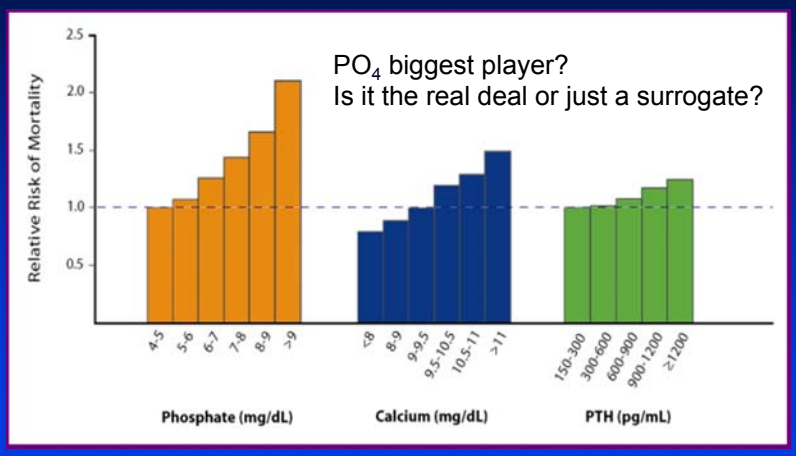


A. Levin et al., **Kidney International (2007) 71, 31-38**



Fibroblast growth factor- 23 has recently been found to be a regulator of phosphorus balance independent of calcium regulation. When stimulated it increases renal phosphate excretion (is phosphaturic) In this diagram,once phosphorus levels start to rise in CKD patients, PTH and FGF-23 are stimulated promoting phosphate excretion; 1^{α} hydroxlase activity is suppressed by phosphorus and FGF-23 but promoted by PTH; 1,25 Vitamin D stimulates both PTH and FGF-23. These factors are all inter-related in an attempt maintain acceptable plasma concentrations of phosphorus and calcium.

CKD-BMM Biochemical Markers Associated with Greatest Mortality Risk



Multivariable-adjusted relative risk

Adapted from Block GA, et al. JASN 2004

META-ANALYSIS OF BMM LAB TESTS AS PREDICTOR OF DEATH RISK

REVIEW

Serum Levels of Phosphorus, Parathyroid Hormone, and Calcium and Risks of Death and Cardiovascular Disease in Individuals With Chronic Kidney Disease

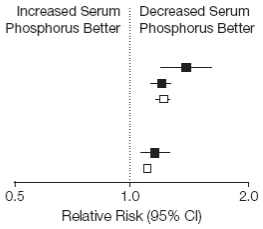
A Systematic Review and Meta-analysis

Palmer et al. JAMA V305:11:1119-1127, 2011

META-ANALYSIS OF BMM LAB TESTS AS PREDICTOR OF DEATH RISK

Figure 3. Summary Estimates for Risks of All-Cause Mortality and Cardiovascular Mortality Associated With Levels of Serum Phosphorus, Parathyroid Hormone, and Calcium

Phosphorus	No. of Cohorts	No. of Participants	Relative Risk (95% CI) Per Unit Increase
All-cause mortality			
Adequate adjustment	3	4651	1.35 (1.16-1.57)
Partial adjustment	10	87 694	1.16 (1.09-1.23)
All studies combined	13	92 345	1.18 (1.12-1.25)
Cardiovascular mortality			
Adequate adjustment	1	17 326	Not estimable
Partial adjustment	2	5881	1.14 (1.05-1.24)
All studies combined	3	23 207	1.10 (1.06-1.13)



Palmer et al. JAMA V305:11:1119-1127, 2011

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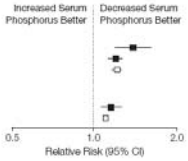
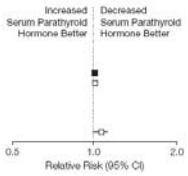
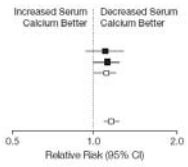
Adequate adjustment	3	4651	1.35 (1.16-1.57)
Partial adjustment	10	87694	1.16 (1.09-1.23)
All studies combined	13	92345	1.18 (1.12-1.25)
Cardiovascular mortality			
Adequate adjustment	1	17326	Not estimable
Partial adjustment	2	5881	1.14 (1.05-1.24)
All studies combined	3	23207	1.10 (1.06-1.13)



Parathyroid hormone	No. of Cohorts	No. of Participants	Relative Risk (95% CI)
All-cause mortality			
Adequate adjustment	1	17326	Not estimable
Partial adjustment	3	83732	1.01 (0.99-1.03)
All studies combined	4	101058	1.01 (1.00-1.02)
Cardiovascular mortality			
Adequate adjustment	1	17326	Not estimable
Partial adjustment	1	5041	Not estimable
All studies combined	2	22367	1.05 (0.99-1.11)



Calcium	No. of Cohorts	No. of Participants	Relative Risk (95% CI)
All-cause mortality			
Adequate adjustment	2	22367	1.07 (0.91-1.24)
Partial adjustment	6	83789	1.09 (0.99-1.20)
All studies combined	8	106156	1.08 (1.00-1.16)
Cardiovascular mortality			
Adequate adjustment	1	17326	Not estimable
Partial adjustment	1	5041	Not estimable
All studies combined	2	22367	1.15 (1.08-1.23)



META-ANALYSIS OF BMM LAB TESTS AS PREDICTOR OF DEATH RISK

Palmer et al. JAMA V305:11:1119-1127, 2011

BOTTOM LINE CKD-MBD

- Not just a Bone Disease
  - Fractures
  - Pain
- A systemic mineral metabolism disease
  - Extra-osseous calcification
  - Vascular “ossification” / calcification
  - Is any of our increased CV risk profile related to poorly managed CKD-BMD?

Phosphate Facts - I

- Total Body Phosphate = about 700 g
  - 85% in bone and teeth as hydroxyapatite
  - 14% intracellular fluids mainly as organic phosphate
  - < 1% in extracellular fluid as inorganic phosphate
    - This is component easiest to get at with dialysis
- Main source of Phosphorous:
  - Dietary
  - Bone efflux (Increased PTH)
- Phosphate removal
  - Renal
  - Dialysis
  - ?Saliva and GI (prevent absorption with binders)

Badve PDI 28:S2, 2008
Hsu, AJKD Dis 1997
Weisinger Lancet 352:391-, 1998

Phosphate Facts - II

- Dietary intake (about 1000 mg/day)
  - Typical western diet 800-2000 mg (26-67 mmol)
  - Most Dialysis patients prescribed a dietary phosphate content of 550 to 1100 mg (18-36 mmol)
  - Phosphate content /gram protein – 14-15 mg/g
- Typical fractional absorption from gut (60-86%)
  - Reported absorption in patients ON binders 44 to 80%
  - Reported total PO_4 absorbed
    - No Binders or restriction (3,360-13,040 mg/wk)
    - Restricted diet and on binders (1,500-6,160 mg/wk)

Badve and McCormick PDI 28:S2, 2008
Hsu, Am J Kidney Dis 1997 Musci KI 53:1399-1404, 1998

PHOSPHOROUS FACTS – III

Removal by dialysis

Phosphorous Statistics:

- Molecular weight - 96 Daltons
- Radius - 2.8 Angstroms
  - (urea 1.8A; Creat 3.0A)
- Hydrophobic (surrounded by water)
  - Radius functionally larger than 2.8A
- Slow to move from ICF to ECF
  - Unlike urea which readily does move
  - Remember most PO_4 in bone, teeth or ICF
- About 50% of circulating PO_4 is a Na, Ca or Mag salt
- Negatively charged
  - Not freely diffusible across all membranes
  - Living membrane vs. synthetic membrane

Kuhlman Blood Purif 2010; 29:137-144

PO_4 REMOVAL BY DIALYSIS

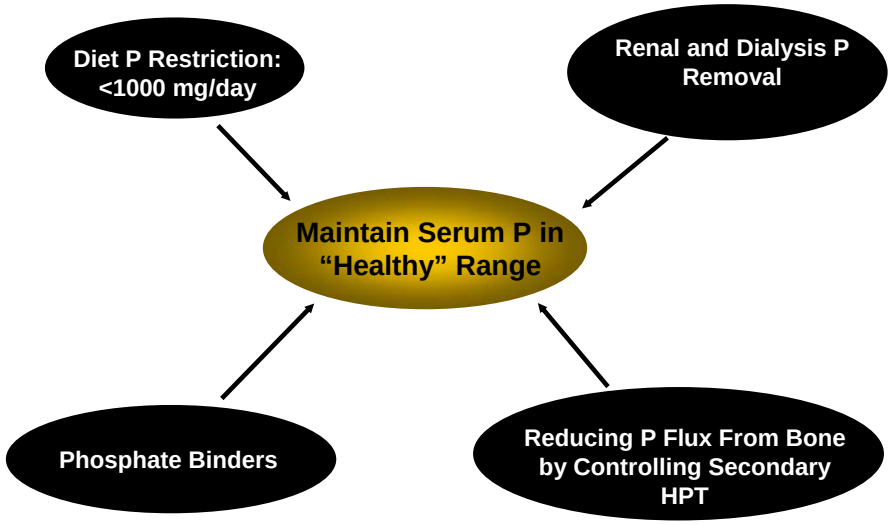
Bottom line:

- Acts more like a middle molecule than like Urea, Creatinine, Na.
- Kinetics vary markedly between PD and HD
- For PD: PO_4 removal correlates with Creatinine removal
- Residual renal function contributes in large part to phosphate excretion and subsequent phosphate balance

PO_4 REMOVAL BY DIALYSIS(cont'd)

- Peritoneal PO_4 removal/week is on the same magnitude of conventional 3/week HD.
- Peritoneal PO_4 clearance is from both diffusive and convective properties.
- Membrane transport characteristics DO play a role in phosphate clearance

Treatment of Hyperphosphatemia



National Kidney Foundation. Am J Kidney Dis. 2003;42(suppl 3):S1-S201.

CONTROLLING PHOSPHOROUS

- Must limit PO intake
  - Diet

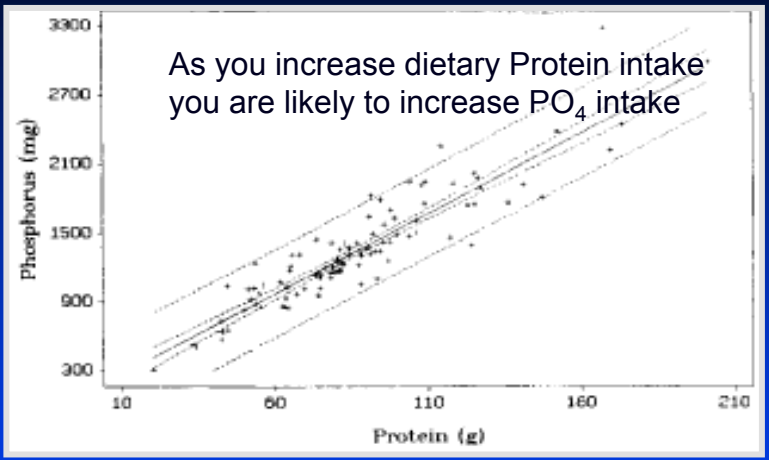
DIETS AND PHOSPHOROUS

- Unfortunately PO_4 in everything and if not there naturally we are adding it to everything. (Processed foods etc)
- However can reduce PO_4 in diet
  - Restrict Protein / PO_4 content
  - IF possible, use
    - Whey proteins
    - Boiled meats

PO_4 and PD

- If one encourages increased protein intake i.e. in patients with:
  - Malnutrition
  - Low serum albumin
  - Protein losses in dialysate
- As you recommend protein intake you also receive obligate PO_4 ingestion.

Phosphate and Protein Intake



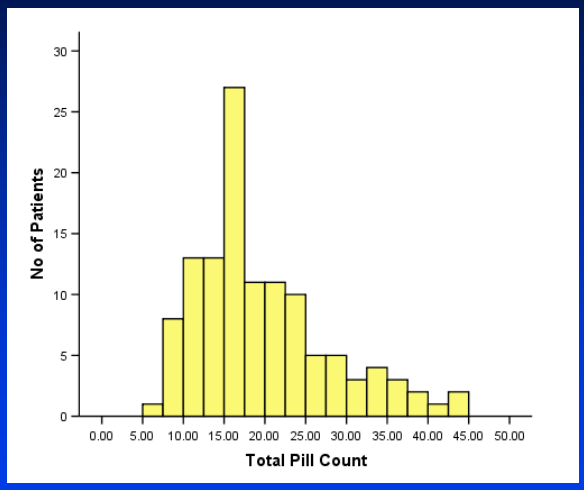
PO_4 (mg) =128 + 14 x protein (gms)
104 CRF pts, semiquantatative food frequency questionaire, Nutr III software

J Am Diet Assoc. 96: 1268, 1996

CONTROLLING PHOSPHOROUS

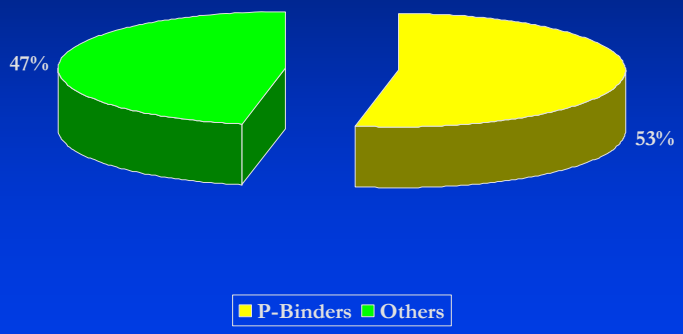
- Must limit PO intake
  - Diet
- **Must limit absorption from gut**

PILL BURDEN IN ESRD



ChiuYW et al, ClinJAmSocNephrol 2009;4:1089-96

P-Binders:
Major Source of Pill Burden



Chiu et al, 2009

Selection Of P-Binders

- Efficacy:
  - Published clinical data indicates similar efficacy of available P-binders
- Adherence considerations:
  - Be mindful of pill burden
  - Lower frequency of administration not effective in recent RCTs
- Limit Toxicity:
  - GI tolerance greatest limitation for most P-binders
  - Limit/avoid calcium-based binders in most patients
  - Watch for metabolic acidosis with sevelamer hydrochloride
  - Watch LFTs with lanthanum carbonate (no reported evidence of abnormalities in humans)

CONTROLLING PHOSPHOROUS

- Must limit PO intake
  - Diet
- **Must limit absorption from gut**
  - **Binders – Do work; will likely be needed**
  - **Minimize active Vitamin D (1,25 D) levels or analogues to minimize uptake from food**

CONTROLLING PHOSPHOROUS

- Must limit PO intake
  - Diet
- Must limit absorption from gut
  - Binders
  - Minimize active Vit D (1,25 vit D) levels or analogues
- **Minimize PO_4 efflux from bones**

MINIMIZE PO4 EFFLUX FROM BONES

Decrease PTH activity

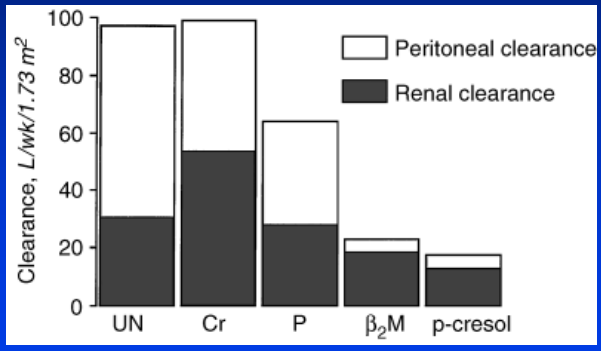
- Calcimemetics
- VDRAs
  - VDRAs have increased PO4 aborption as side effect
- Activity

CONTROLLING PHOSPHOROUS

- Must limit PO intake
- Minimize absorption from gut
- Minimize PO_4 efflux from bones
- Maximize PO_4 removal with:
  - Maintain Renal function

CLEARANCE OF VARIOUS SOLUTES NATIVE KIDNEY FUNCTION vs PD

Contribution of RRF to Clearance of Small *vs* Large Solutes



Bammens et al, 2003

CREATININE CLEARANCE in PD
Importance of RKF

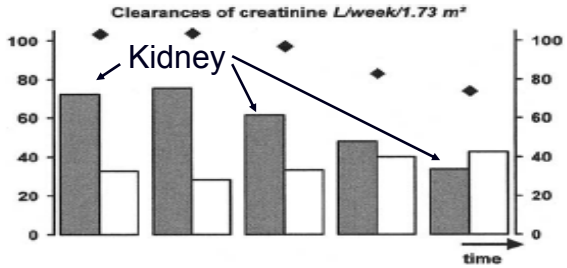


Fig 3. Time course of renal (gray bars), peritoneal (white bars), and total clearances (◆; liters per week per 1.73 m^2) of creatinine from visits 1 to 5 (N = 24). For display purposes, data were grouped per visit. Median values are shown.

Bammens et al, AJKD 46,#3;2005:512-519

PHOSPHATE CLEARANCE IN PD
Importance of RKF

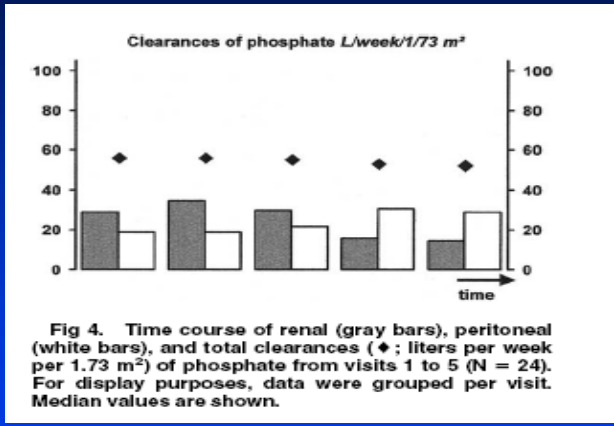


Fig 4. Time course of renal (gray bars), peritoneal (white bars), and total clearances (◆; liters per week per 1.73 m²) of phosphate from visits 1 to 5 (N = 24). For display purposes, data were grouped per visit. Median values are shown.

Bammens et al, AJKD 46,#3;2005:512-519

P Clearance and RRF

	N	Serum P	Total P clearance* (ml/min/1.73 m^2)	Daily P excretion (mg/d)
With RRF	18	5.13 ± 1.41	6.74 ± 2.95	471.6 ± 216.3
Anuric	38	5.27 ± 1.54	5.25 ± 1.14	399.9 ± 141.8

* $P < 0.05$

Study in PD patients; unaware of studies in HD patients

Sedlacek et al, Am J Kidney Dis, 2000; 36: 1020-1024

RESIDUAL KIDNEY FUNCTION AND PO4 REMOVAL

Native Kidney function plays a major role in PO4 homeostasis

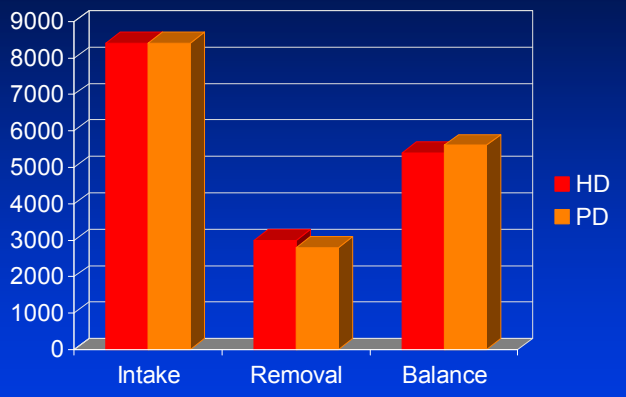
- Contribution of total PO_4 removal by native kidneys in PD:*
  - 63% of total PO_4 removal at baseline
  - 49% at 7 months.
- In a cross section study of 252 PD patients**
  - Of those with RKF: 29% PO4 > 5.5
  - In anuric patients: 44% PO4 > 5.5

**Bammens et al AJKD 46:512-519, 2005*
***Wang et al AJKD 43:712-720, 2004*

CONTROLLING PHOSPHOROUS

- Must limit PO intake
- Minimize absorption from gut
- Minimize PO_4 efflux from bones
- Maximize PO_4 removal with:
  - Renal function
  - Dialysis

Phosphate Balance in Dialysis



HD remove about 1000 mg per treatment x 3 = 3000 mg/wk
PD remove about 400 mg per day x 7 = 2800 mg/week

DIALYTIC REMOVAL OF VARIOUS SOLUTES

Table 4 | Total mass removal (mg/week) in HD (*n*=20), APD (*n*=34), and CAPD (*n*=16) patients

	HD	APD	CAPD	Overall ANOVA
UN	89 349 ± 34770	92 025 ± 27429	11 1649 ± 40506	0.2
Cr	4746 ± 2009^{x,y}	6522 ± 1952^{x}	6918 ± 2572^{y}	0.008
P	2356 ± 864	2739 ± 1042	2790 ± 1022	0.4
p-Cresol	351 ± 232^{x}	175 ± 108^{x}	214 ± 147	0.003

ANOVA, analysis of variance; APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; HD, hemodialysis.
^{x,y}Parameters with same suffix differ significantly.

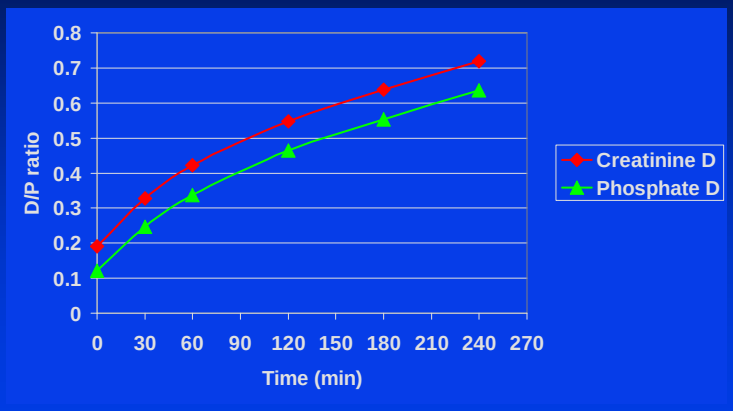
Evenepoel et al. KI 70:794-799, 2006

Phosphate Facts - IV

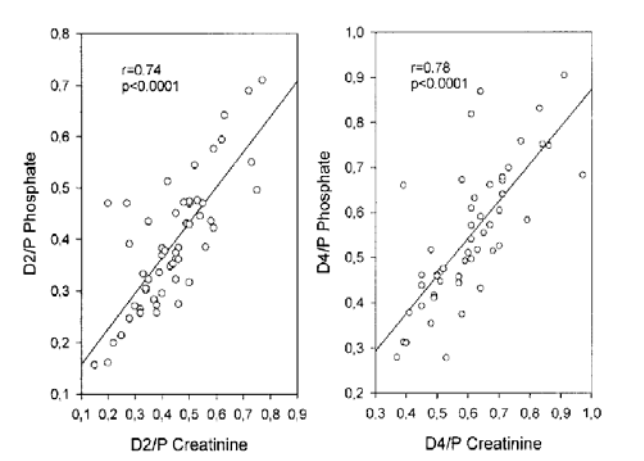
- Dietary intake (1000 mg/day)
  - Most Dialysis patients prescribed a diet phosphate content of 550 to 1100 mg / day (18-36 mmol)
  - Reported absorption in patients ON binders 44 to 80%
  - Total absorbed: (1,500-6,160 mg/wk)
- Conventional hemodialysis removal:
  - 800 to 1000 mg/Rx times 3 = 2400-3000 mg/wk
- Typical reported PD clearance:
  - 55-66 L/1.73m2/wk
  - Removal related to serum PO_4
  - If serum PO_4 is 5.5 mg/dL removal is 55mg/L x 60L=3300 mg/week

Badve and McCormick PDI 28:S2, 2008
Hsu, Am J Kidney Dis 1997

D/P for Creatinine and PO_4 are similar

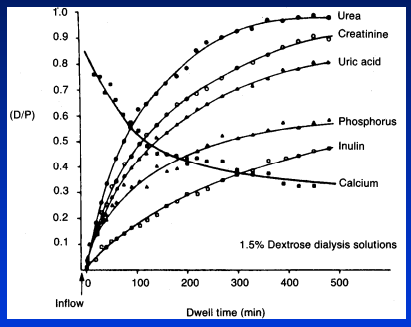


RATES OF DIFFUSION FOR CREATININE AND PO_4 ARE SIMILAR



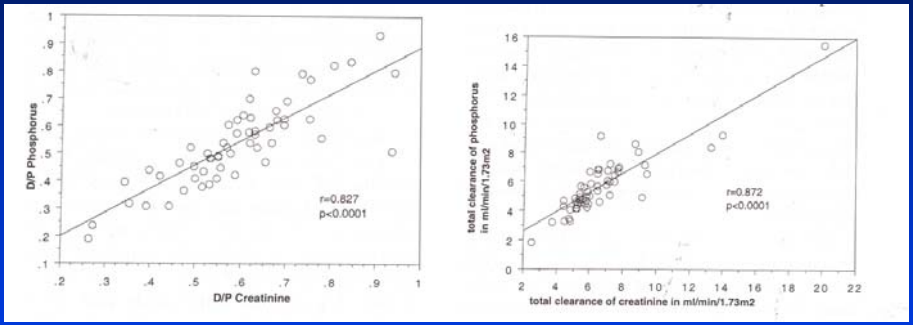
Schmitt et al, PDI 49:465-471, 2009

INFLUENCE OF MOLECULAR WEIGHT ON DIFFUSION RATE



Note D/P values for PO_4, Creatinine and Urea – Molecular weight influences rates of diffusion

PHOSPHOROUS CLEARANCE ON PD IS RELATED TO CREATININE CLEARANCE

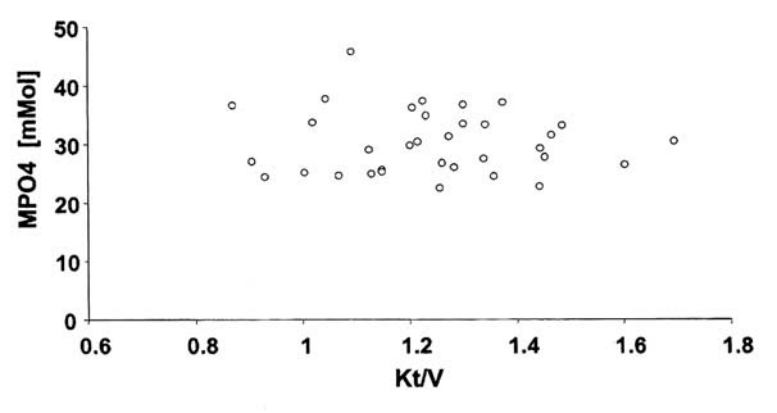


Among patients with similar Kt/V, those with wCrCl < 60 had lower P clearance (4.3 ml/min) than those with wCrCl > 60 (7.0 ml/min).

Former had higher serum P (5.9 mg/dl) than latter (4.8 mg/dl)

Sedlacek et al, Am J Kidney Dis, 2000; 36: 1020-1024

Phosphate Removal on PD MAY NOT be related to Kt/V (N=13 patients)



Guzwiller et al, Clin Nephrol 2003

PO_4 REMOVAL CORRELATES WITH CREATININE REMOVAL

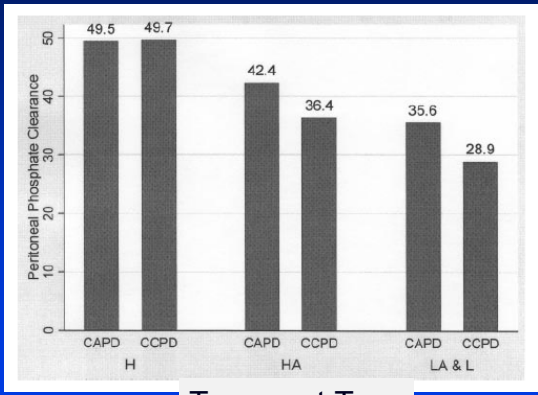
Table 2a. Fluid and solute clearances, comparison across PD modality

Variable	Total	CAPD	CCPD	*P* Value
Dialysate volume (L/day)	11.4 ± 4.2	8.2 ± 1.6	14.4 ± 3.5	< 0.001
Ultrafiltration on PD (L/day)[a]	1.04 (0.67–1.43)	1.16 (0.63–1.45)	0.99 (0.67–1.36)	0.478
Peritoneal Kt/V	1.74 ± 0.4	1.62 ± 0.3	1.86 ± 0.4	< 0.001
Peritoneal creatinine clearance (L/wk/1.73 m^2 BSA)	45.6 ± 10.8	44 ± 8.1	47 ± 12.8	0.11
Peritoneal P/phosphate clearance (L/wk/1.73 m^2 BSA)	39.5 ± 11.3	40.9 ± 10.4	38.3 ± 12	0.199

[a]Median (interquartile range). *P* value by ANOVA if parametric variable, and by Kruskal-Wallis test if nonparametric. BSA, body surface area.

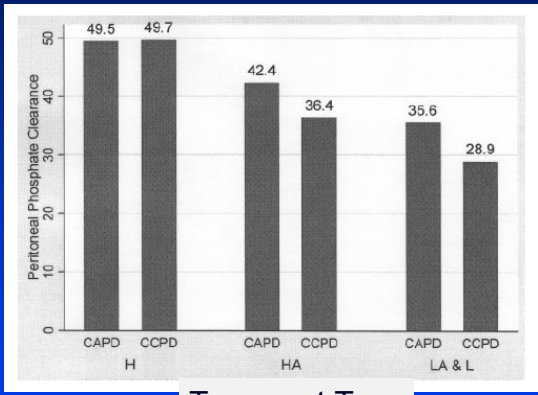
Badve et al, CJASN Vol3:1711-1717, 2008

PO_4 REMOVAL IS RELATED TO TRANSPORT TYPE (and Rx)



Badve et al, CJASN Vol3:1711-1717, 2008

PO_4 REMOVAL IS RELATED TO TRANSPORT TYPE (and Rx)



Badve et al, CJASN Vol3:1711-1717, 2008

PO_4 REMOVAL ON PD CORRELATES WITH:

Dialysis Modality, Independent of Peritoneal Transport Characteristics

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*Division of Nephrology, Department of Medicine, University of Ottawa and The Ottawa Hospital Ottawa, Canada, †Kidney Research Centre and ‡The Clinical Epidemiology Program, Ottawa Health Research Institute, Ottawa, Canada

Background and objectives: Hyperphosphatemia is an independent risk factor for mortality in ESRD, but factors regulating phosphate clearance on peritoneal dialysis (PD) are incompletely understood. The objective of this study was to test the hypothesis that peritoneal phosphate clearance is better with continuous ambulatory PD (CAPD) as compared with continuous cyclic PD (CCPD) after adjusting for membrane transport status.

Design, setting, participants, & measurements: In this cross-sectional and retrospective study, measurements of peritoneal phosphate clearance of 129 prevalent PD patients were reviewed. Patients were divided according to membrane transport status (high, high average, low average-low categories) and PD modality (CAPD or CCPD).

Results: Among high transporters, peritoneal phosphate clearances were comparable in both modalities. However, treatment with CAPD was associated with increased peritoneal phosphate clearance compared with CCPD among high-average transporters (42.4 ± 11.4 *versus* 36.4 ± 8.3 L/wk/1.73 m^2, $P = 0.01$), and low-average-low transporters (35.6 ± 5.9 *versus* 28.9 ± 11 L/wk/1.73 m^2, $P = 0.034$). On multivariate linear regression, PD modality, membrane transport category, and peritoneal creatinine clearance, but not Kt/V urea, were independently associated with peritoneal phosphate clearance.

Conclusions: Peritoneal phosphate clearance is determined by PD modality and membrane transport category, suggesting that PD regimes with longer dwell times may help control hyperphosphatemia in lower transporters.

Clin J Am Soc Nephrol 3: 1711–1717, 2008. doi: 10.2215/CJN.00190108

PERITONEAL PO_4 REMOVAL IS MORE RELATED TO CREATININE REMOVAL THAN Kt/V

Table 2b. Fluid and solute clearances, comparison across peritoneal membrane transport status

Variable	High	High-Average	Low-Average and Low	*P* Value
Dialysate volume (L/day)	12.7 ± 4	11.4 ± 4.5	10.6 ± 3.5	0.213
Ultrafiltration on PD (L/day)[a]	1.07 (0.69–1.5)	1.03 (0.62–1.40)	1.23 (0.86–1.45)	0.468
Peritoneal Kt/V	1.94 ± 0.5	1.71 ± 0.4	1.68 ± 0.3	0.035
Peritoneal creatinine clearance (L/wk/1.73 m^2 BSA)	53.9 ± 14.2	45.8 ± 8.8	39.2 ± 8.5	< 0.001
Peritoneal phosphate clearance (L/wk/1.73 m^2 BSA)	49.6 ± 11.4	39.2 ± 10.3	33.2 ± 8.5	< 0.001

[a]Median (interquartile range). *P* value by ANOVA if parametric variable, and by Kruskal-Wallis test if nonparametric.

Badve et al, CJASN Vol3:1711-1717, 2008

PO_4 REMOVAL BY PD

Correlation with Modality and Membrane Transport Characteristics

Methods:

- Reviewed data on 264 patients (61% CAPD)
- PET testing with 4.25% D & 24 hour urine for PO_4 clearance

Results:

- PO_4 Cl_P correlated best with Cr Cl_P than Urea Cl_P
- Hyperphosphatemia at 1 year (PO_4 > 5.5 mg/dl) found in 30% patients
- PO_4 levels negatively correlated with RKF and PO_4 Cl_K

Bernardo et al. CJASN 6:591-597, 2011

PO_4 REMOVAL BY PD

Correlation with Modality and Membrane Transport Characteristics

	CAPD	APD
Peritoneal Kt/V		
High	1.47 ± 0.3	1.99 ± 0.4
High Average	1.74 ± 0.51	1.56 ± 0.5
Low Average	1.66 ± 0.2	1.46 ± 0.4
Low	1.58 ± 0.3	1.44 ± 0.3
Peritoneal PO_4 Cl		
High	46.9 ± 12.6	48.1 ± 13.0
High Average	39.3 ± 10.4	39.6 ± 9.3
Low Average	35.9 ± 7.8	31.6 ± 6.6
Low	33.9 ± 15.2	24.5 ± 9.0

Bernardo et al. CJASN 6:591-597, 2011

PO_4 REMOVAL BY PD

Correlation with Modality and Membrane Transport Characteristics

Variable	High	H Average	L Average	Low	*P*
Peritoneal Kt/V	1.87 ± 0.5	1.63 ± 0.5	1.58 ± 0.4	1.51 ± 0.4	0.016
Peritoneal Cr Cl (L/W/1.73m^2)	49.3 ± 12.2	41.8 ±13.9	37.1 ± 8.8	34.3 ± 12.2	0.005
Peritoneal PO_4 Cl (L/W/1.73m^2)	47.4 ± 12.6	39.4 ± 9.9	34.0 ± 7.6	31.4 ± 14.3	<0.0001

Bernardo et al. CJASN 6:591-597, 2011

PO_4 REMOVAL IN PD IS RELATED TO TRANSPORT TYPE

Phosphate clearance is…

… about 90% of creatinine clearance (i.e. 4 hour PO4 D/P = 0.53 v 0.59)

… reduced by 25% in lower v higher transporters

N	RRF	Kt/V	D/P_{cr}	CrC	PO_4 C	Serum PO_4	PO_4 excr
11	0	2.46	0.49	51.6 L	4.2 ml/min	6.0 mg/dl	331 mg
13	0	2.46	0.68	72.2 L	6.2 ml/min	4.7 mg/dl	422 mg

PET results distributed equally

Am J Kidney Dis. 36: 1020, 2000.

PO4 CLEARANCE BY PD MODALITY

CAPD vs NIPD *Twardowski ASAIO Trans 36:M584-8, 1990*

- CAPD 8 L vs NIPD 26 cycles with 31 L
- Compared to CAPD – NIPD PO4 clearance were 17% lower while NIPD urea clearance was 31% higher

- CAPD vs CCPD *Gallar et al Nephrologia 20:355, 2000.*
  - Studies tend to show no significant difference with CAPD vs CCPD
  - Unless you do a mid day exchange
    - CCPD+MDE> CCPD > CAPD (61 vs 45 vs 41 L/week)

BOTTOM LINE PO_4 and PD

- At times Kt/V will be OK but PO_4 elevated
- In this case – YES restrict PO_4 in Diet, use binders, but remember you may be able to adjust PD dialysis Rx also!!
- If on PD, consider a wet day, consider length of dwell time, consider an increase in instilled volume, review UF volume.
- Although KDOQI no longer recommends tracking Creatinine Clearance – remember PO_4 removal correlates well with it.

Priorities

- Fix Phos
  - Limit intake
  - Block absorption
  - Remove effectively by dialysis
- Allow Ca^{++} flexibility
  - Low Ca^{++} may contribute to PTH stimulation, low BP, cramps, arrhythmia
  - High Ca^{++} may contribute to vascular calcification, BP stability, less cramps
- PTH
  - Fix Phos aggressively and Ca^{++} within reason
  - Want at least small amount of Vit D around for its other effects
  - Calcimimetics after low dose Vit D

PD and Phosphorus Removal

- Removal of the same magnitude as with conventional HD
- Maximize daily P removal:
  - Maintain residual renal function
  - All measures that maximize creatinine clearances will maximize P removal:
    - Increase fill volume
    - Continuously wet abdomen in anuric subjects
    - Mid-day exchange for the long dwell in APD patients
- Consider increasing UF and remember pathway for water removal (pores) is important.

CONCLUSIONS

- Phosphorus needs to be controlled
- PO_4 probably acts more like a middle molecule than a small solute
- Serum PO_4 hard to normalize with conventional dialytic therapies.
  - Remember: Diet, Binders, VDRA's,
- When rounding in a PD unit:
  - Remember relationship to dwell time and PO4 diffusion rates, in general longer dwells and 24 hours worth of PD dwell help
- When rounding in an HD unit consider:
  - More frequent Therapies
    - (PD and SDHD, Daily Nocturnal HD)