Phosphate Removal in Hemodialysis, Kinetics, and Modalities

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How to evaluate phosphate control in patients on dialysis

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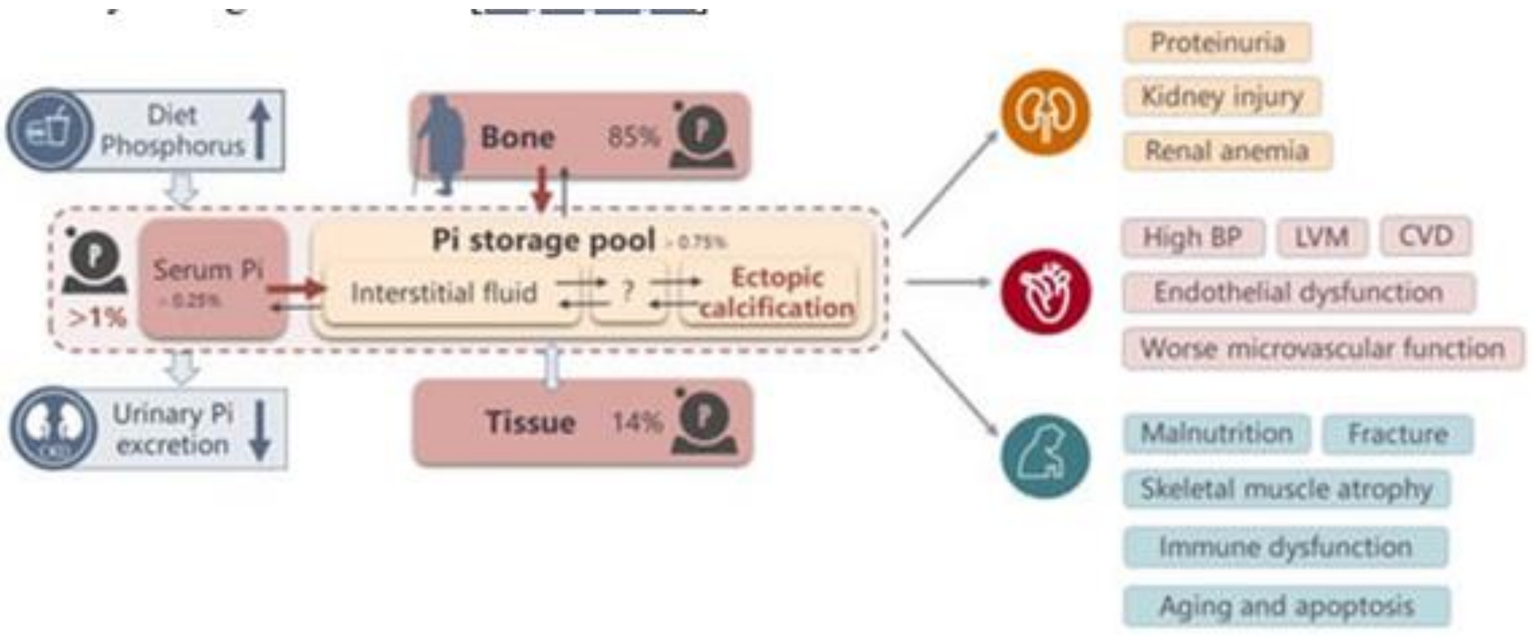

Figure 5. Reasons for phosphorus overload and harm of phosphorus overload. Note: Phosphorus balance can easily be disequilibrated by a persistent high-phosphorus diet, renal function decline, bone disease in the young population, CKD patients, and the elderly, and can finally result in phosphorus overload. Phosphorus overload leads to a serious of side effects including hyperphosphatemia, vascular calcification, a worse microvascular function, and so on. These are also the indirect evidence of phosphorus overload.

Wang M, Nutrients (15) 5; 2023

- ✓KDOQI guidelines recommend monitoring serum phosphate levels every month, this gives an incomplete picture of phosphate control.
- ✓Fujimoto et al and Shimazaki et al both found a 0.3 mg/dL higher predialysis serum phosphorus at the beginning of the week than prior to the midweek dialysis session.
- ✓ In the HEMO dataset, there was no significant difference between them.

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✓ Time out of range percentage:

✓Rolling averages over the last 6 months:

✓Trend:

✓Residual standard deviation (SD):

✓ Area under the curve (time spent out of range during a 6-month period):

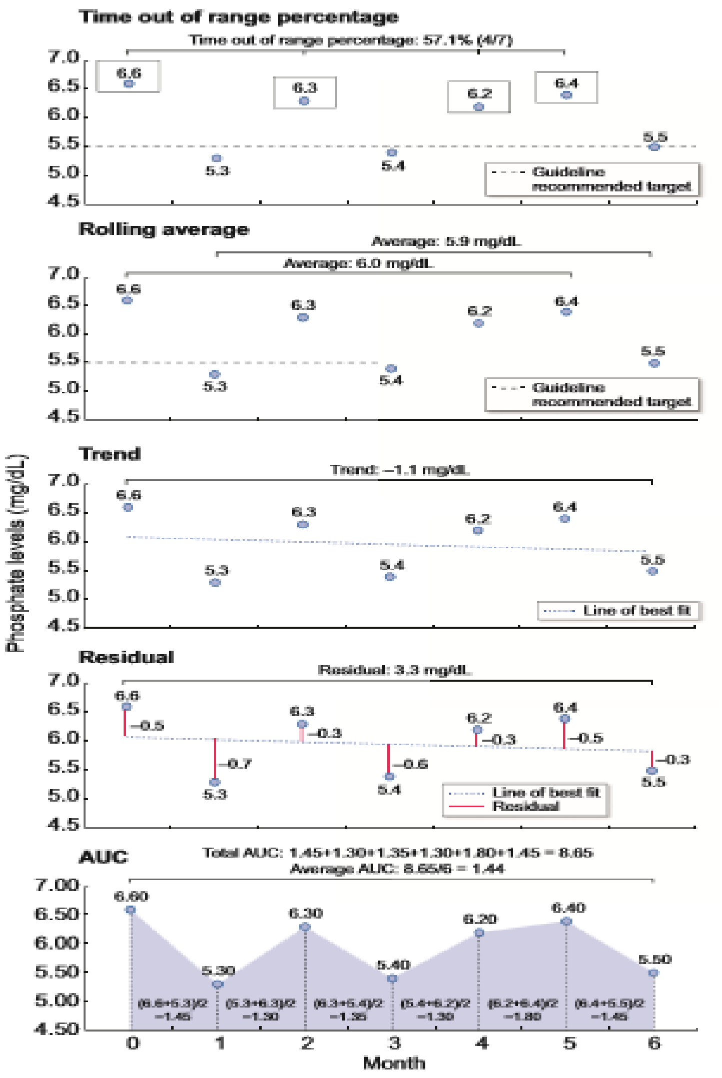

FIGURE 1: The calculation with the five listed methods with patient's past 7 months' phosphate levels. AUC, area under the curve.

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- ✓Phosphorus is the sixth most abundant element in the human body and plays a key role in cellular metabolism and tissue structure .
- ✓Most body phosphorus (85%) is stored in the bones and teeth. The remainder (14%) is stored in soft tissues.
- ✓Only 1% of the body’s total phosphorus stores are found in the ECF, including serum that directly accessible for HD.

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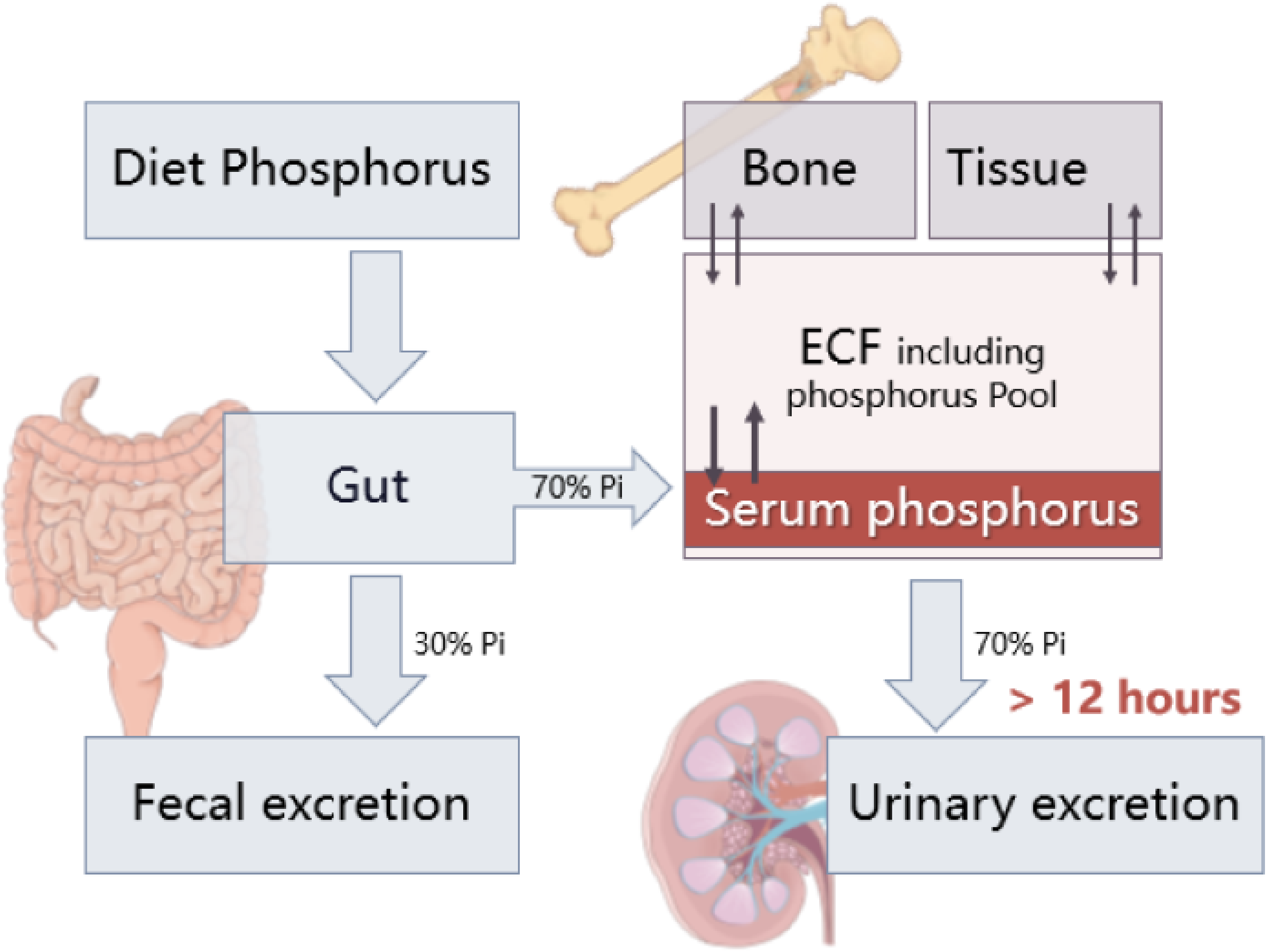

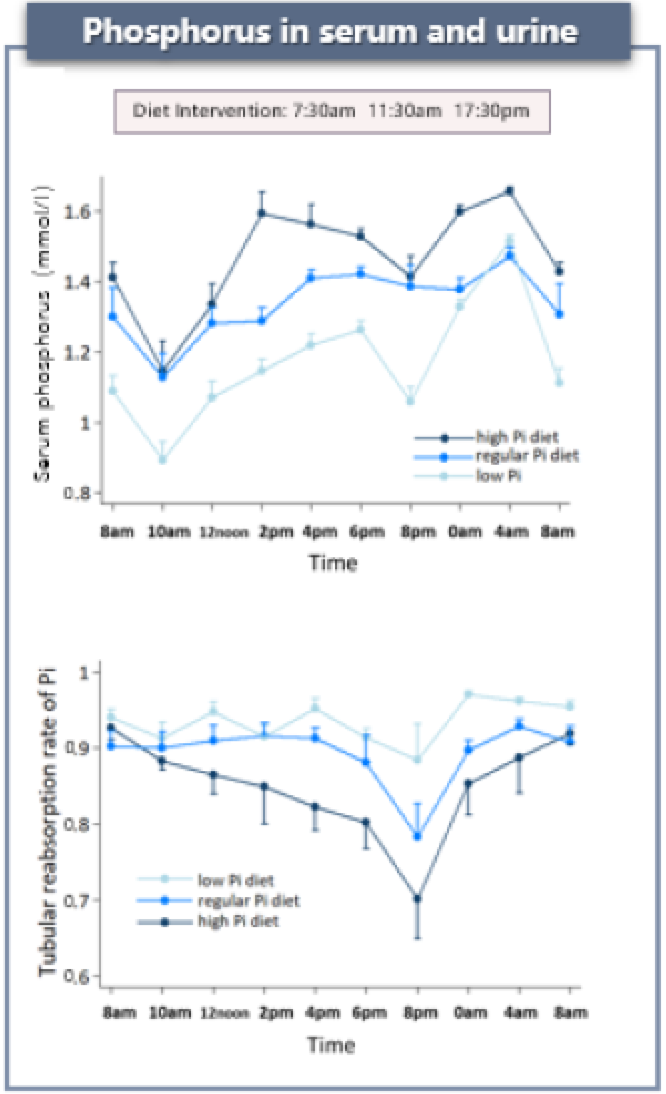

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Blood Purification

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Phosphate Elimination in Modalities of Hemodialysis and Peritoneal Dialysis

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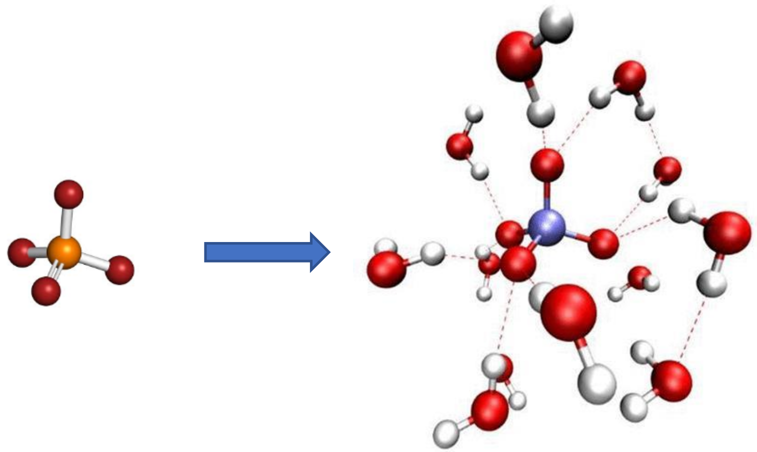
- ✓ The molecular weights of urea, phosphate anion, and creatinine are 60, 95, and 113 Da, respectively. Thus, phosphorus removal from an aqueous solution across a dialysis membrane should be somewhere between that of urea and creatinine.

- ✓Then we can imagine inorganic phosphorus acts like a small molecular weight uremic toxin with a distribution volume that is assumed to be equal to TBW.

Blood Purif 2010;29:137–14

✓However due to its hydrophilic nature, the molecular weight of phosphate is considerably increased.

✓Hence, the elimination characteristics of phosphate in HD is much more similar to those of typical middle molecules.



Blood Purif 2010;29:137–14

- ✓ While urea is removed from both plasma and RBCs water during dialysis, phosphorus is removed primarily from the plasma space.

- ✓ This markedly reduces phosphorus clearance relative to urea for any level of whole blood flow rate, specially in patients with high levels of hematocrit.

Blood Purif 2010;29:137–14

Seminars in Dialysis

PTH, PHOSPHATE AND VITAMIN D: CURRENT ISSUES AND CONCERNS

Removal of Phosphorus by Hemodialysis

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Seminars in Dialysis—28(6); 2015: 620–623

- ✓ During hemodialysis given 3/week, phosphorus removal is in the range of 800–1200 mg/session or 2.4–3.6 g/week.
- ✓On the other hand, phosphorus intake commonly ranges from 0.8 to 2.0 g/day, or 6–14 g/week.
- ✓In the absence of phosphorus binder ingestion, the percent of ingested phosphorus absorbed can range from 50% to 80% on average.
- ✓Then with a usual diet and conventional three times per week dialysis schedules, the use of phosphorus binders is almost universally required unless the patients have very substantial amounts of residual renal function.

Dogirdas JT, Seminars in Dialysis—Vol 28, No 6: 2015 pp. 620–623

- ✓Also the percent phosphate absorption is depends on the chemical form of phosphorus in the foods.
- ✓Phosphorus bound to phytate in vegetables is poorly absorbed, phosphorus associated with meat or cheese is more readily absorbed.
- ✓Phosphorus derived from food or beverage additives is absorbed to a very high degree.

Dogirdas JT, Seminars in Dialysis—Vol 28, No 6: 2015 pp. 620–623

Phosphate Kinetics during HD

- ✓ During HD, BUN concentrations continuously decline and, following a short rebound period immediately after termination of the treatment, steadily return to predialysis values during the interdialytic interval.
- ✓ Intradialytic plasma Pi kinetics shows a characteristic 2-phase pattern. In the first phase, serum phosphate levels, after an initial relatively steep decline, reach a plateau after about 2–2.5 h into dialysis.

Dogirdas JT, Seminars in Dialysis—Vol 28, No 6: 2015 pp. 620–623

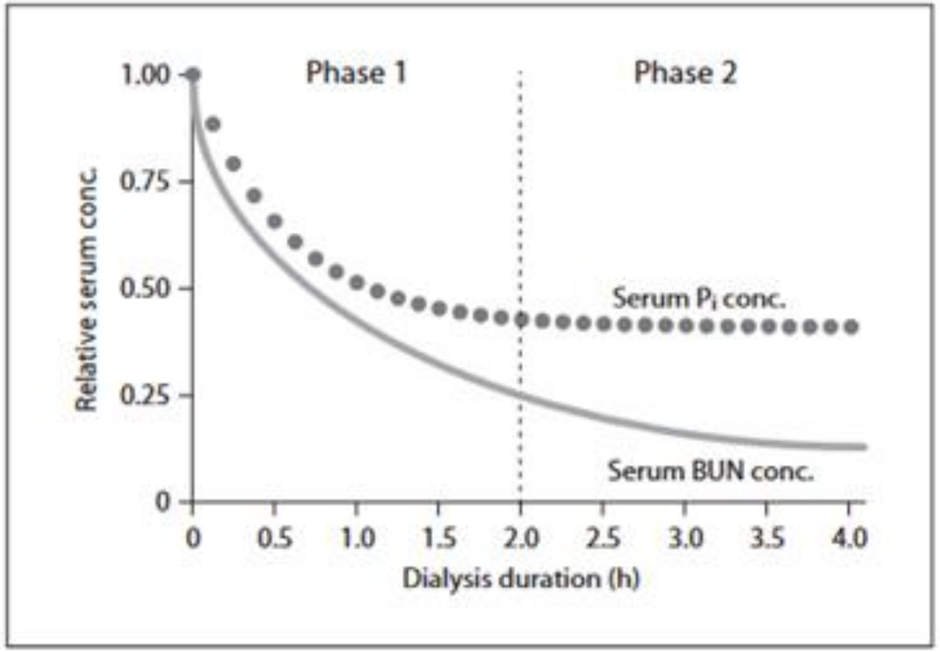


Fig. 1. Comparison of intradialytic phosphate and blood urea nitrogen (BUN) kinetics. Serum P_i concentration sharply drops during the first phase of dialysis (phase 1) and, after reduction of serum P_i to about 40% of predialysis levels, stabilizes throughout the rest of the treatment (phase 2). In contrast, BUN levels steadily decline during dialysis without reaching a plateau.

Blood Purif 2010;29:137–14

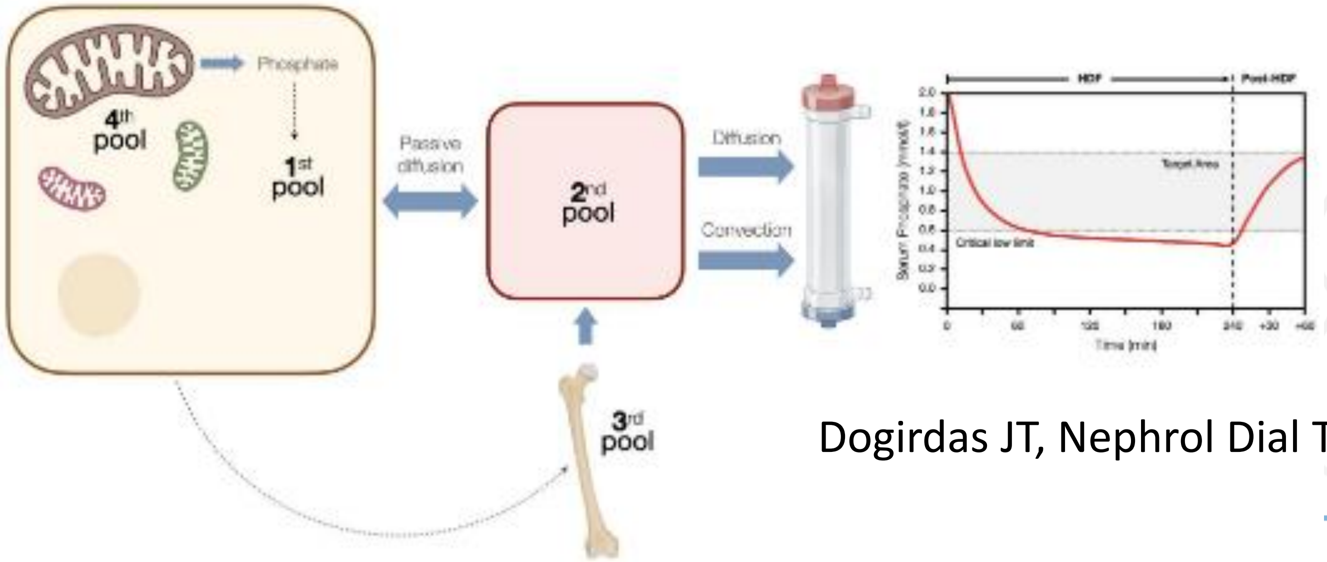
- ✓Yet in a minority, there is a more gradual, sustained fall in serum phosphorus, suggesting ready availability of nearby phosphorus stores.

- ✓It may be that the latter patients have a higher degree of interstitial mineral deposition, and it may also be possible that this interstitial store of phosphorus may be amenable to removal by intensive dialysis.

Dogirdas JT, Nephrol Dial Transplant (2016) 0: 1–9

✓Because of the complexities of controlling phosphorus in dialysis patients, some sort of mathematical modeling to serve as a guide might be useful.

✓Spalding et al. suggessted a four-pool model for phosphate. Intracellular (1st pool) and extracellular (2nd pool) compartments, the bone matrix (3rd pool), 4th pool is phosphate derived from mitochondrial (ATP).



Dogirdas JT, Nephrol Dial Transplant (2016) 0: 1–9

- ✓Leypoldt et al. suggested two – pool model.
- ✓They approached the idea of modeling the plateau effect of serum phosphorus during dialysis by assuming that phosphorus was stored in a distal compartment of infinite size.

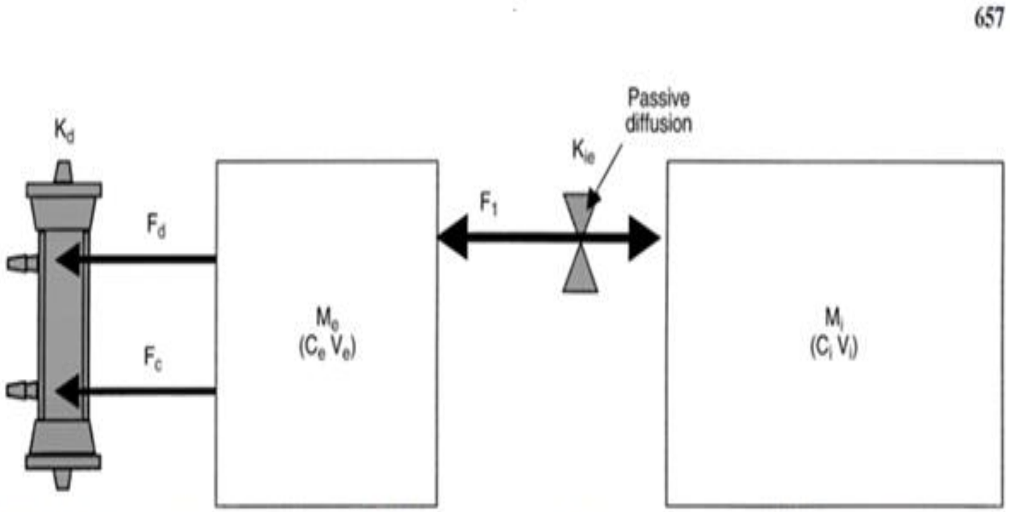


Fig. 1. Model A: Schematic representation of two-pool kinetics. Abbreviations are: M_e, extracellular mass of solute; C_e, extracellular concentration of solute; V_e, extracellular volume; M_i, intracellular mass of solute; C_i, intracellular concentration of solute; V_i, intracellular volume; F_1, intercompartmental flux; F_d, diffusive flux across dialyzer membrane; F_c, convective flux across dialyser membrane; K_d, dialyzer clearance; K_{ie}, cell membrane mass transfer coefficient.

Dogirdas JT, Nephrol Dial Transplant (2016) 0: 1–9

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Nephrology Dialysis Transplantation

Original Article

A two-pool kinetic model predicts phosphate concentrations during and shortly following a conventional (three times weekly) hemodialysis session

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The

✓None of them didn’t have ability to explain phosphor removal in dialysis completely.

✓Daugirdas had modified a two-pool model by:

(1) Low values of serum phosphorus increases clearance of phosphorus between distal storage compartment and proximal space (ECF).

(2) the size of the distal compartment is increased only to twice the value of the TBW.

Dogirdas JT, Nephrol Dial Transplant (2016) 0: 1–9

Table 2. Modeling parameters based on HEMO Study patients at 4 months of follow-up ($n = 415$)

Number of pools	Size of the distal pool	Size of proximal pool		Kc (mL/min/35L V) dynamically adjusted during the dialysis treatment		
Both genders	Both genders	Men	Women	Men		Women
				P < 3.0 mg/dL (0.97 mmol/L)	P ≥ 3.0 mg/dL (0.97 mmol/L)	Any range of P
2	3.0 V	0.26 V	0.32 V	686-200	86	As for men, but multiplied by 0.83

V = postdialysis two-pool urea distribution volume; P = intradialysis serum phosphorus.

Dogirdas JT, Nephrol Dial Transplant (2016) 0: 1–9

- ✓This modified two-pool model can predict serum phosphorus concentrations in patients undergoing conventional three times per week hemodialysis regimens.

- ✓It is unknown where the storage pool of phosphorus lies. Preliminary data suggest that intradialytic phosphorus release is not related to an active bone interface.

Dogirdas JT, Nephrol Dial Transplant (2016) 0: 1–9

- ✓A higher value for Kc may be result in a higher postdialysis serum phosphorus, as it allows more ‘refilling’ of phosphorus from the distal pool during dialysis.

- ✓At very low serum phosphorus levels, additional pools of phosphorus are apparently mobilized in an attempt to prevent severe hypophosphatemia.

Dogirdas JT, Nephrol Dial Transplant (2016) 0: 1–9

Factors that affect on phosphate removal in hemodialysis:

1. K0A for phosphorus that is 0.4 times the K0A for urea
2. High efficient membrane (but not flux)
3. Negative charge of some membranes
4. Type of membranes (cellolosic vs. synthetics)
5. High QD (but not QB)
6. Heparin
7. acidifying bicarbonate-based dialysate with citrate instead of acetate
8. Physical activity before or during dialysis

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Phosphate removal in different dialysis modalities:

- ✓ Almost none of the patients in the frequent "daily" dialysis were able to dispense with phosphorus binders. It may be due to:

1. Decreased attention by patients to dietary restriction.
2. total weekly dialysis time was only marginally increased.

- ✓ Patients frequent nocturnal dialysis with total weekly dialysis time greater than 30 hours per week not only can dispense with phosphorus binders; in many, addition of phosphorus to the dialysate is required to prevent hypophosphatemia.

Dogirdas JT, Nephrol Dial Transplant (2016) 0: 1–9

Convective therapies

- ✓Increased phosphate control by convective techniques has been reported. In one study, although urea and creatinine clearance was similar with HDF and HD, phosphate clearance was higher on HDF.

- ✓Despite the beneficial effect on phosphate removal, patients undergoing convective therapy still require phosphate binders, although at possibly a lower dose.

Huang Z et al, Companion to Brenner and Rector's The Kidney, 2nd ed:2006. p.481.

- ✓The traditional postdilution mode and predilution mode can be applied in this therapy.
- ✓ Postdilution HDF has been shown to be more effective than predilution HDF.
- ✓ Mixed dilution may be of special advantage in patients with high predialysis hematocrit and an increased risk of filter clotting with postdilution HDF due to hemoconcentration.

Huang Z et al, Companion to Brenner and Rector's The Kidney, 2nd ed:2006. p.481.

Table 1 Ranges of phosphate removal (grams per week) by different dialysis strategies

Conventional diffusive hemodialysis, 4 hours	2.3–2.6 g
Extended diffusive hemodialysis, ≥5 hours	3.0–3.6 g
Nocturnal hemodialysis, ~8 hours	4.5–4.9 g
Endogenous hemofiltration with reinfusion, 4 hours	1.8–2.4 g
Postdilution hemodiafiltration, 4 hours	3.0–3.3 g
Predilution hemofiltration (exchange volumes 1.2 × body weight)	0.9–1.5 g
Peritoneal dialysis (CAPD, 2 L × 4/day)	2.0–2.2 g

Abbreviation: CAPD, continuous ambulatory peritoneal dialysis.

International Journal of Nephrology and Renovascular Disease 2013:6

	IHD	SLED	CVVH*	p value
Number of patients (M/F)	8 (6/2)	8 (7/1)	10 (6/4)	
Age, years	53.9 ± 17.7	66.5 ± 8.0	74.7 ± 5.5	0.003
Pre-dialysis weight, kg	69.9 ± 9.9	76.9 ± 19.6	71.4 ± 8.0	NS
Net UF, liters/session	3.4 ± 0.4	1.9 ± 1.6	2.7 ± 1.8	NS
Phosphate, mmol/l				
Pre-dialysis	1.65 ± 0.45	1.71 ± 0.42	1.52 ± 0.61	NS
ΔPi	0.81 ± 0.42	0.55 ± 0.23	0.29 ± 0.48	0.043
BUN, mg/dl				
Pre-dialysis	143.6 ± 42.0	171.0 ± 89.6	123.8 ± 93.3	NS
ΔBUN	98.8 ± 31.5	77.0 ± 48.3	25.3 ± 47.8	0.005
Calcium, mg/dl				
Pre-dialysis	9.6 ± 0.6	8.7 ± 1.5	8.7 ± 0.8	NS
ΔCalcium	–1.0 ± 1.2	–0.7 ± 0.8	0.4 ± 1.1	NS

IHD = Intermittent hemodialysis; SLED = slow low-efficiency dialysis; CVVH = continuous venovenous hemofiltration; UF = ultrafiltrate. The CVVH session was 24 h. Δ = Difference value before and after dialysis.

Blood Purif 2010;29:137–14

- ✓In summary, the main factor affecting serum phosphorus levels during dialysis is intake and absorption, with residual kidney function also playing a substantial role.
- ✓Conventional dialysis treatment, e.g., 9–14 hours per week, even with very high- efficiency dialyzers, removes only a fraction of absorbed phosphorus, such that continued ingestion of phosphorus binders is needed.
- ✓The best way to assure phosphorus removal by dialysis is to increase weekly dialysis time, about 18–30 hours appears to obviate the need for phosphorus binders.
- ✓The benefits of HDF are not completely established.

Dogirdas JT, Seminars in Dialysis—Vol 28, No 6: 2015 pp. 620–623