Achieving Equilibrium in ESRD Patients

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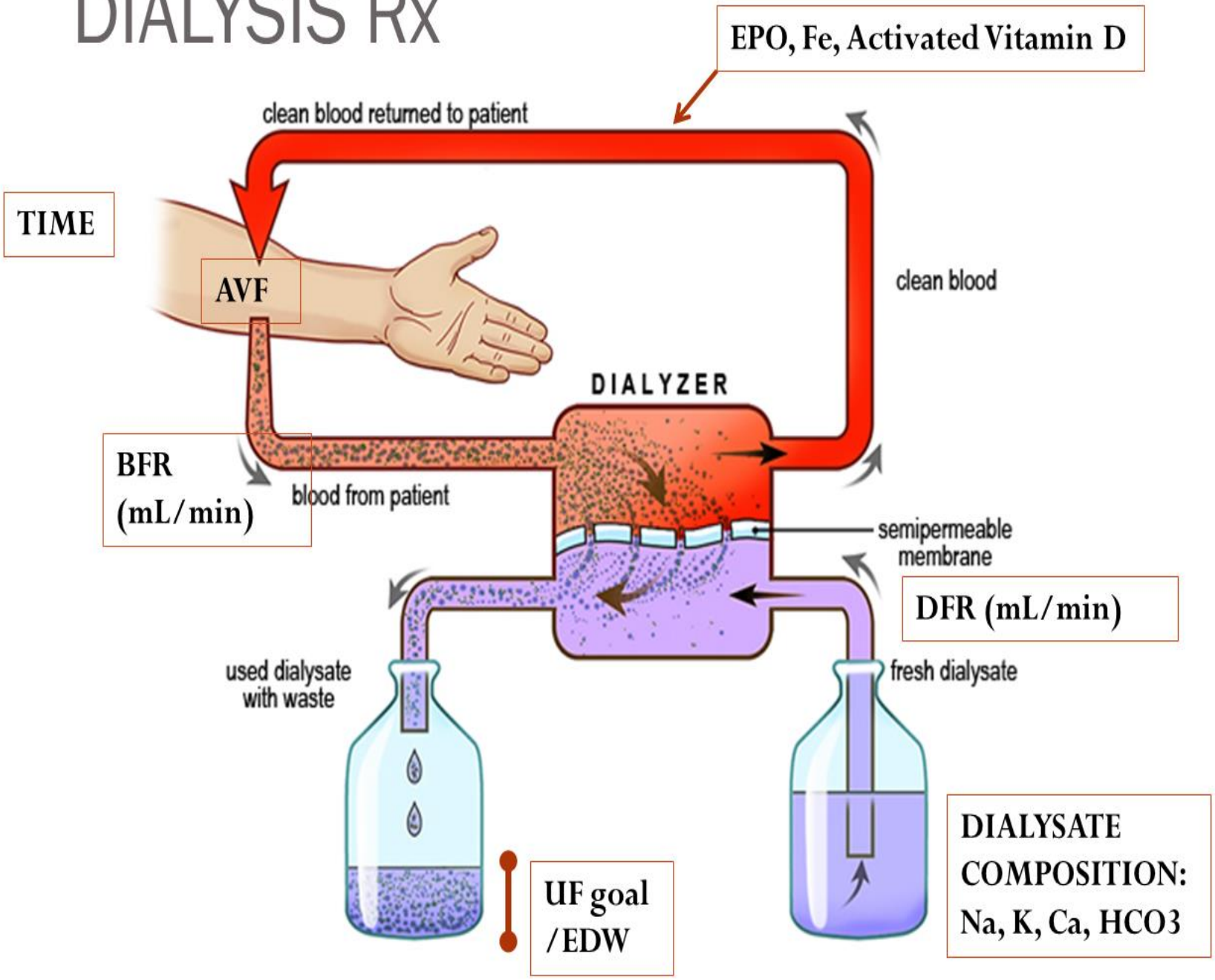
-BRRH Grand Rounds: April 18th, 2017

Outline

- Dialysis prescription

- Adequacy
- Estimated Dry Weight (EDW)
- Electrolytes / Acid-Base
- Anemia
- Bone Mineral Disease (BMD)

DIALYSIS Rx


EPO, Fe, Activated Vitamin D
clean blood returned to patient
TIME
AVF
clean blood
DIALYZER
BFR
(mL/min)
blood from patient
semipermeable
membrane
DFR (mL/min)
used dialysate
with waste
fresh dialysate
UF goal
/EDW
DIALYSATE
COMPOSITION:
Na, K, Ca, HCO3

Dialysis Adequacy

- Effective removal of uremic solutes
  - Small, water soluble
    - Urea "BUN"
  - Small, protein bound
    - Indoles
    - Phenols
  - Middle molecules
    - B2 microglobulin

- Note: "adequate dialysis" =/= "doing well on dialysis"

BUN

- Advantages
  - Easily measurable- index of nitrogenous waste products from protein consumption
- Disadvantages
  - Studies suggest difficult to measure uremic solutes may be more important
  - BUN can be different than expected due to different clinical states

Urea Reduction Ratio (URR)

$$URR = \frac{U_{pre} - U_{post}}{U_{pre}} \times 100\%$$

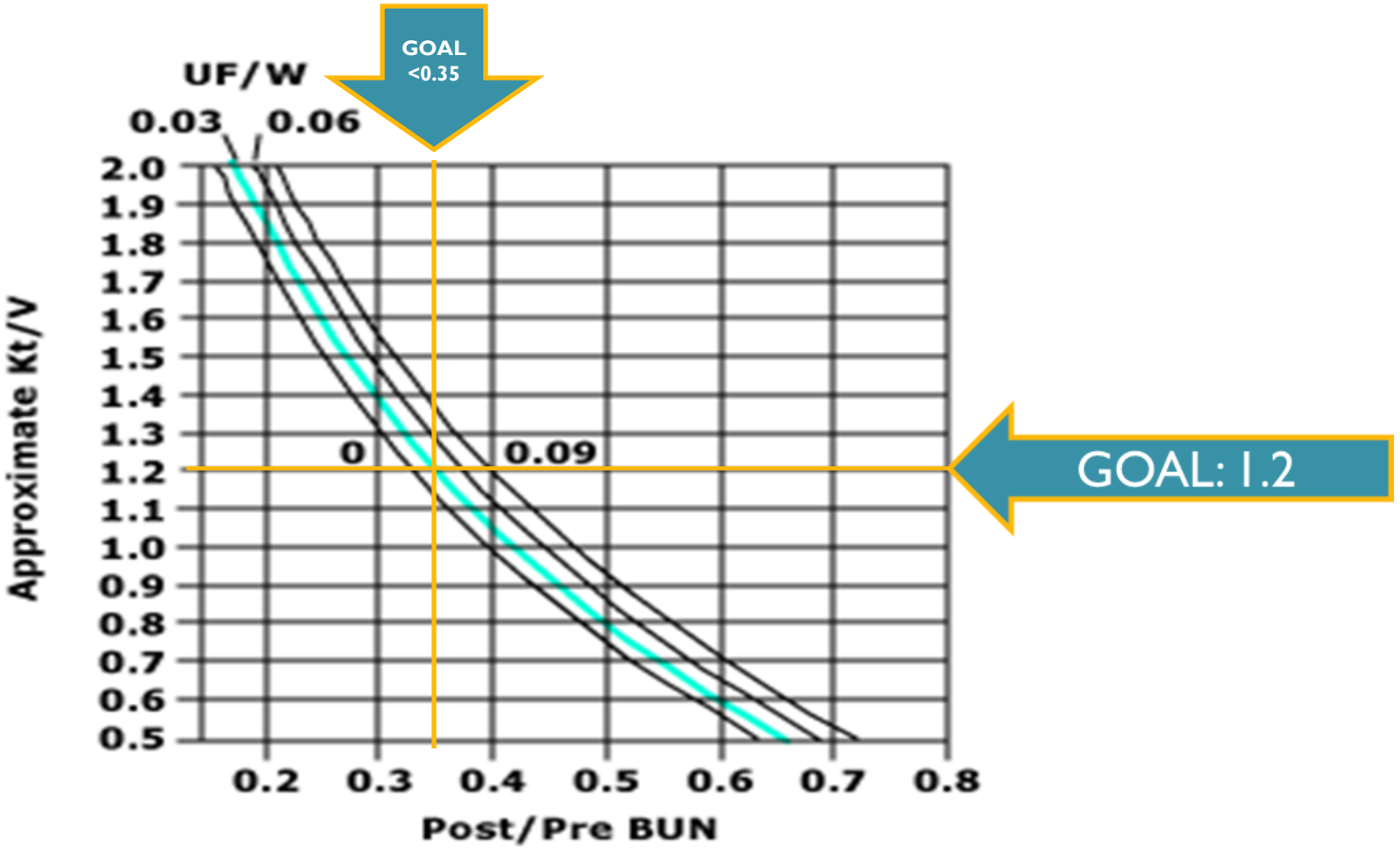
- Simple
- Goal: 65% or more
- Doesn't take into account urea generation or UF

Kt/V = Fractional Urea Clearance

- K = dialyzer clearance of urea (mL/min)
- t = time of dialysis tx (min)
- V = volume of distribution (mL) = TBW

- WARNING: gory math details ahead!
- HD pt- mass 70 kg (154 lb) , HD t=4 hours, dialyzer urea clearance 215 ml/min.
- Kt/V = [215 x 240] / [70000 x 0.6] = 1.23

Correlation b/t URR and Kt/V

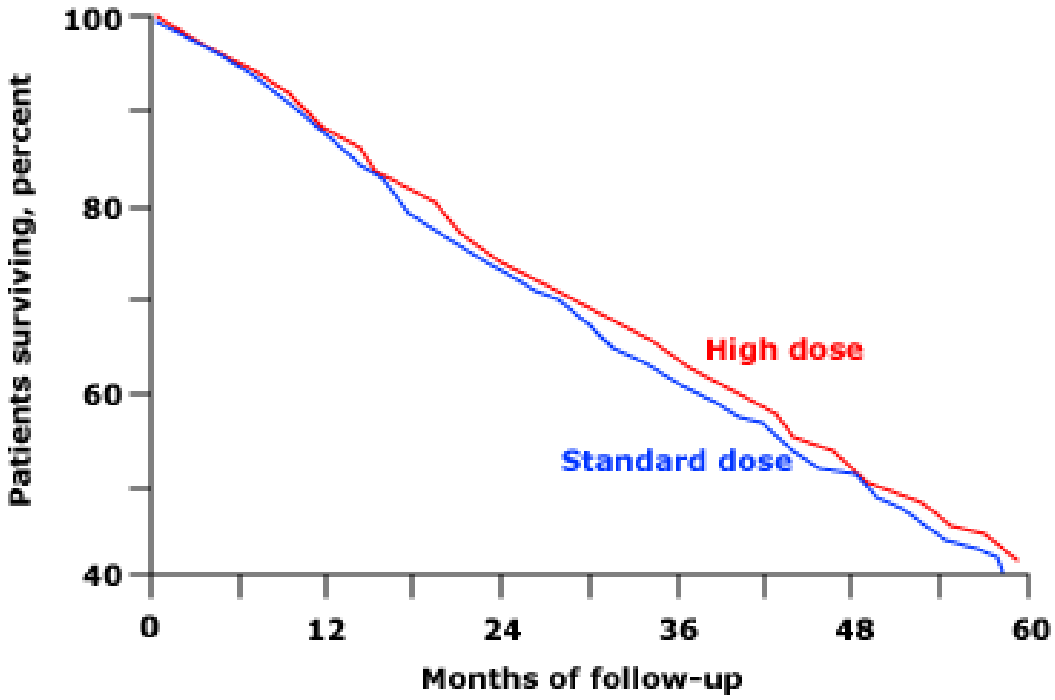


Limitations

- Can be artificially elevated by an elevated "Kt" or a diminished "V"
- Assumes urea removal is similar to other uremic toxins/ middle molecules
- BUN "rebound"

So if decent Kt/V is good, is a lot more even better?

- HEMO TRIAL (NEJM 2002)
- Kt/V
  - 1.32 (SD)
  - 1.71 (HD)
  - RR 0.96



How to manage inadequate Kt/V

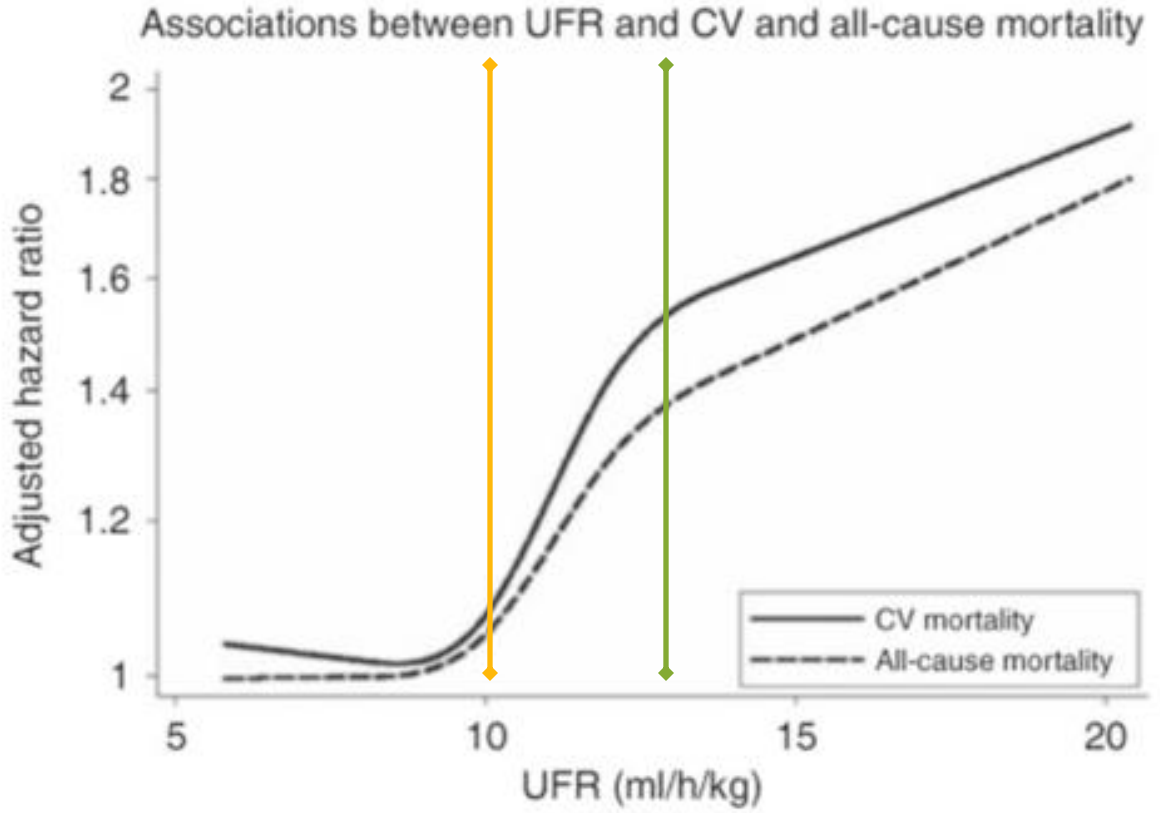
- *More time
- Bigger dialyzer (higher flux)
- Increase BFR
  - AVF/AVG instead of CVC
  - Larger gauge needles
- Ensure no recirculation
- Preserve RRF

Fluid/Volume Balance

- Patients weighed at beginning (B) and end (E) of each treatment
- B→E: UF (Liters) = Weight lost (kg)
  - Parameter we set, usually aiming for EDW
- E→B: Interdialytic weight gain (IDWG)
  - Driven by patient salt > fluid intake

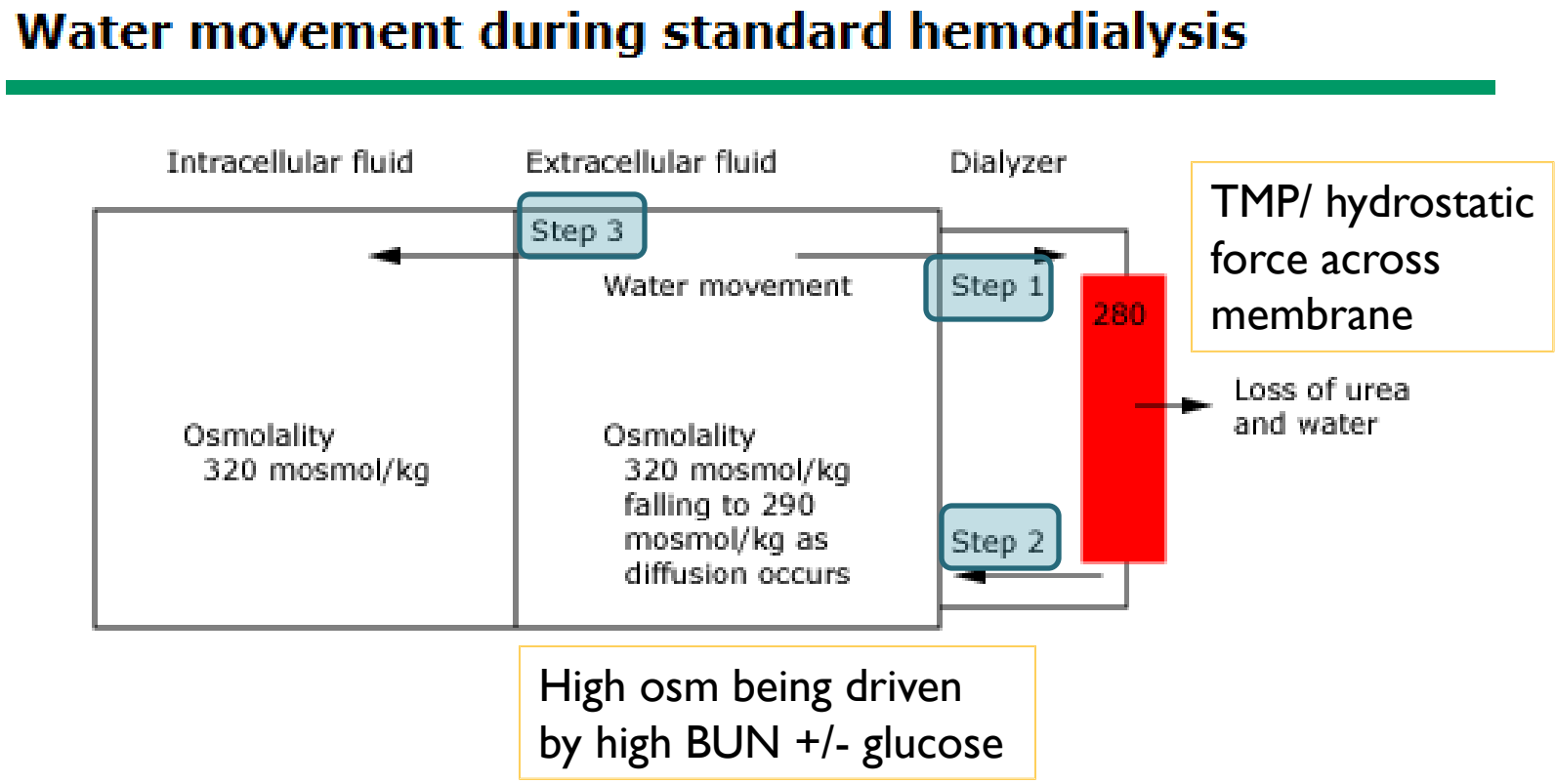
High IDWG is bad → High UFR

- Major dialysis orgs advise max rate 13mL/h/kg



Flythe. KI, 2011.

Overaggressive clearance can be harmful, too.



Consequences of over/underaggressive ultrafiltration

Too much UF (*<EDW)	Too little UF (>EDW)
Syncope	Volume Overload
Presyncope	Hypertension
Chest Pain	Edema
Cramping	CHF
Hypotension	LVH
General organ hypoperfusion	

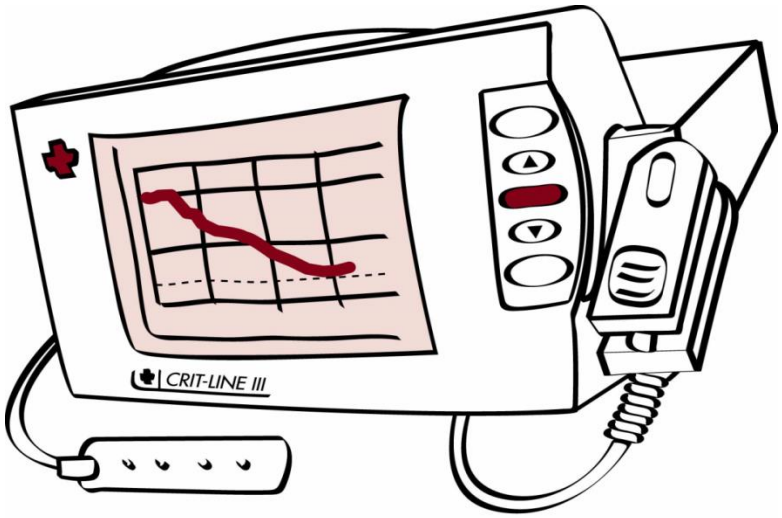
*Patients can be simultaneously volume overloaded and overaggressively ultrafiltrated!

Estimated Dry Weight (EDW)

- Rough definition: Normal seated BP at end of HD treatment without orthostatic hypotension or signs of volume overload
- Difficult to measure
- Relies on clinical judgment / "trial and error"
- Multiple alternative techniques being developed

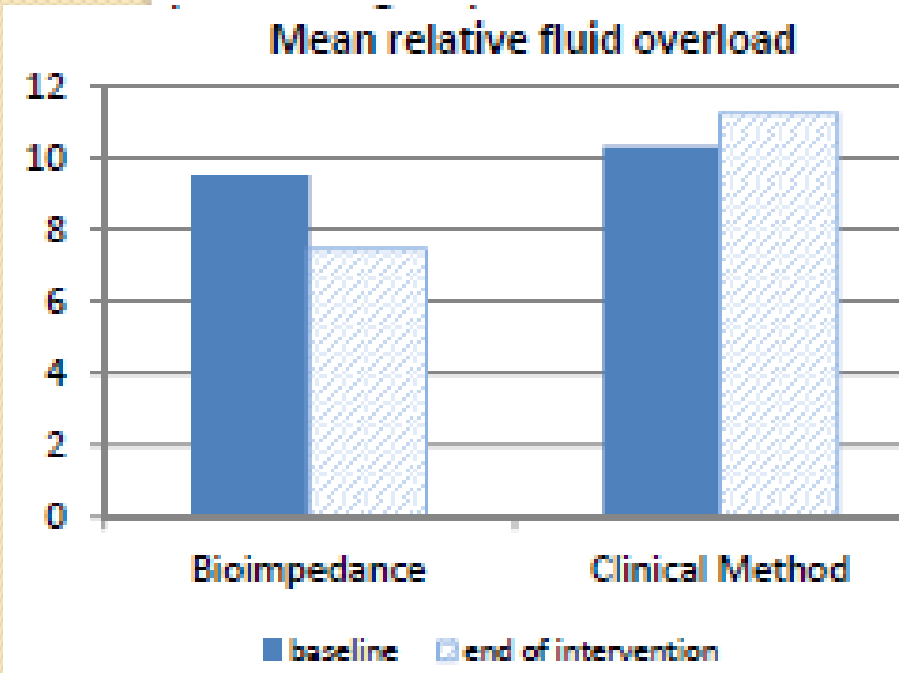
CritLine

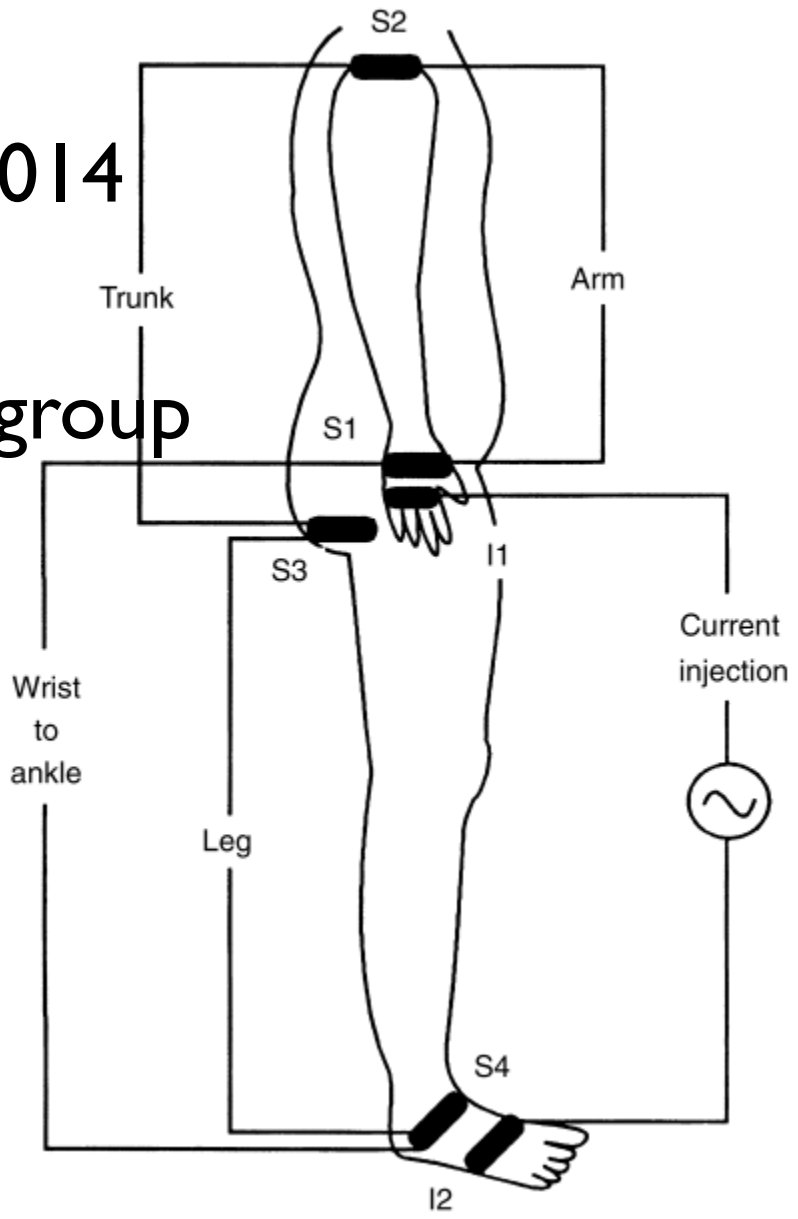
- Cuvette attached to dialyzer estimates hematocrit
- Hematocrit increases with removal of blood volume
- Slope of curve >5% suggests overaggressive UF



Bioimpedence

- Onofriescu, AJKD 2014
- Mortality HR 0.112
- Less BP meds in BI group





Other Methods

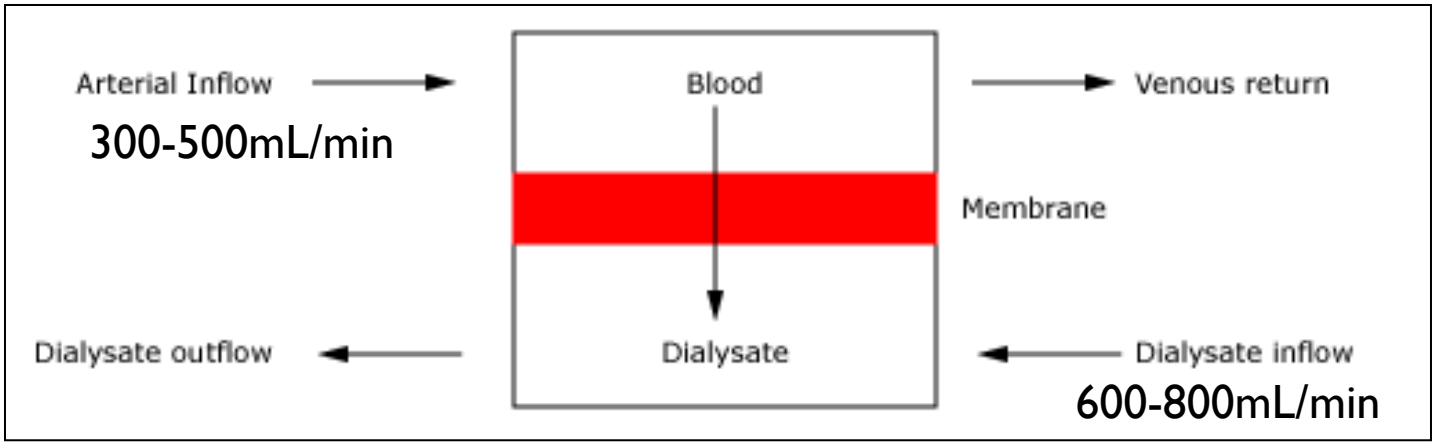
- Plasma ANP
  - More elevated in hypertensive pts predialysis
  - Lower at end of HD if BP was dialysis-sensitive
  - Absolute values not helpful to predict EDW

- IVC Diameter
  - "standardized" measurements postdialysis often included many hypertensive or overloaded pts

Mehta, JASN 1999

Dialysis Clearance

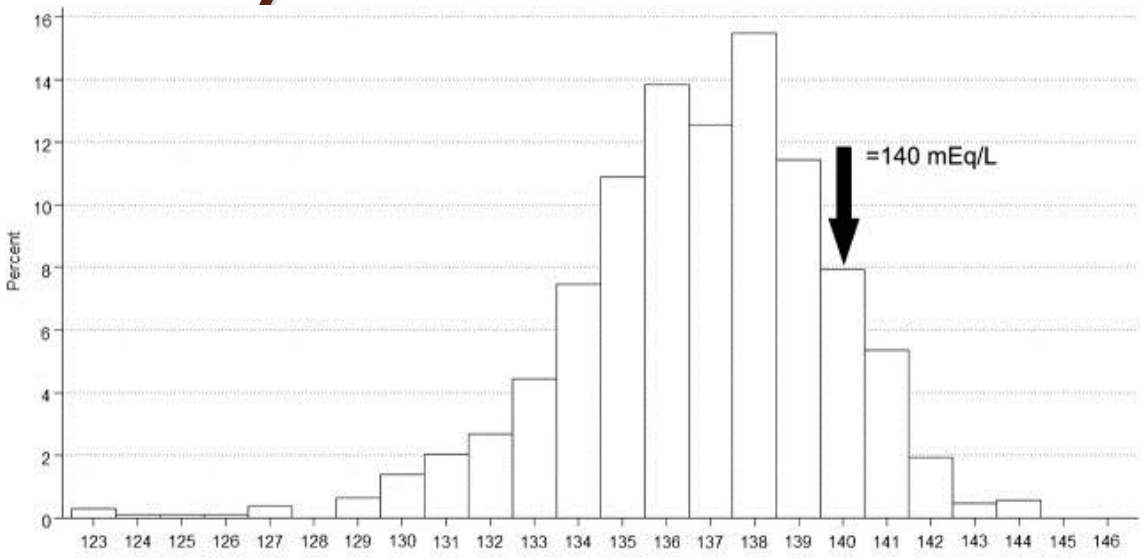
- DIFFUSION
  - Higher → lower concentrations
  - Bidirectional
- CONVECTION
  - Solvent drag
  - Effective for middle molecules



Dialysate Composition

Electrolyte	Concentration (meq/liter)
Sodium	134-140
Potassium	0-4
Bicarbonate	34-40
Calcium	2-3 (1 meq/L = 4 mg/dL)

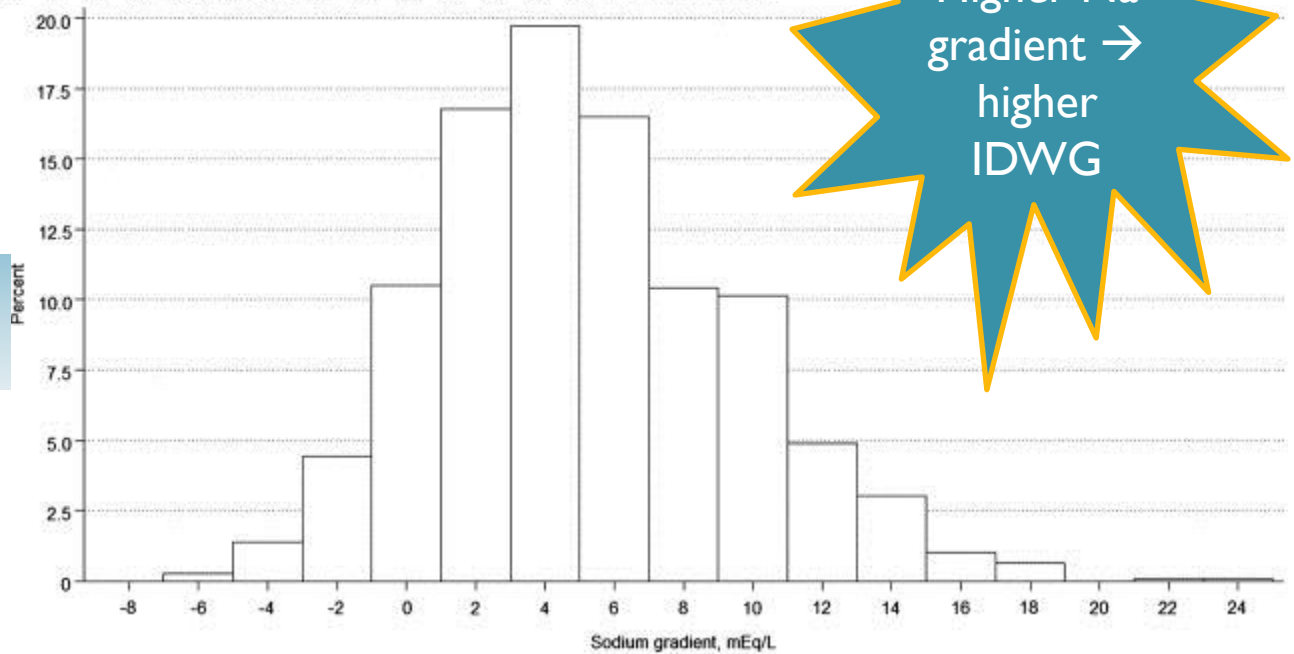
Dialysate Sodium



Sodium level at start of HD (n=1084)

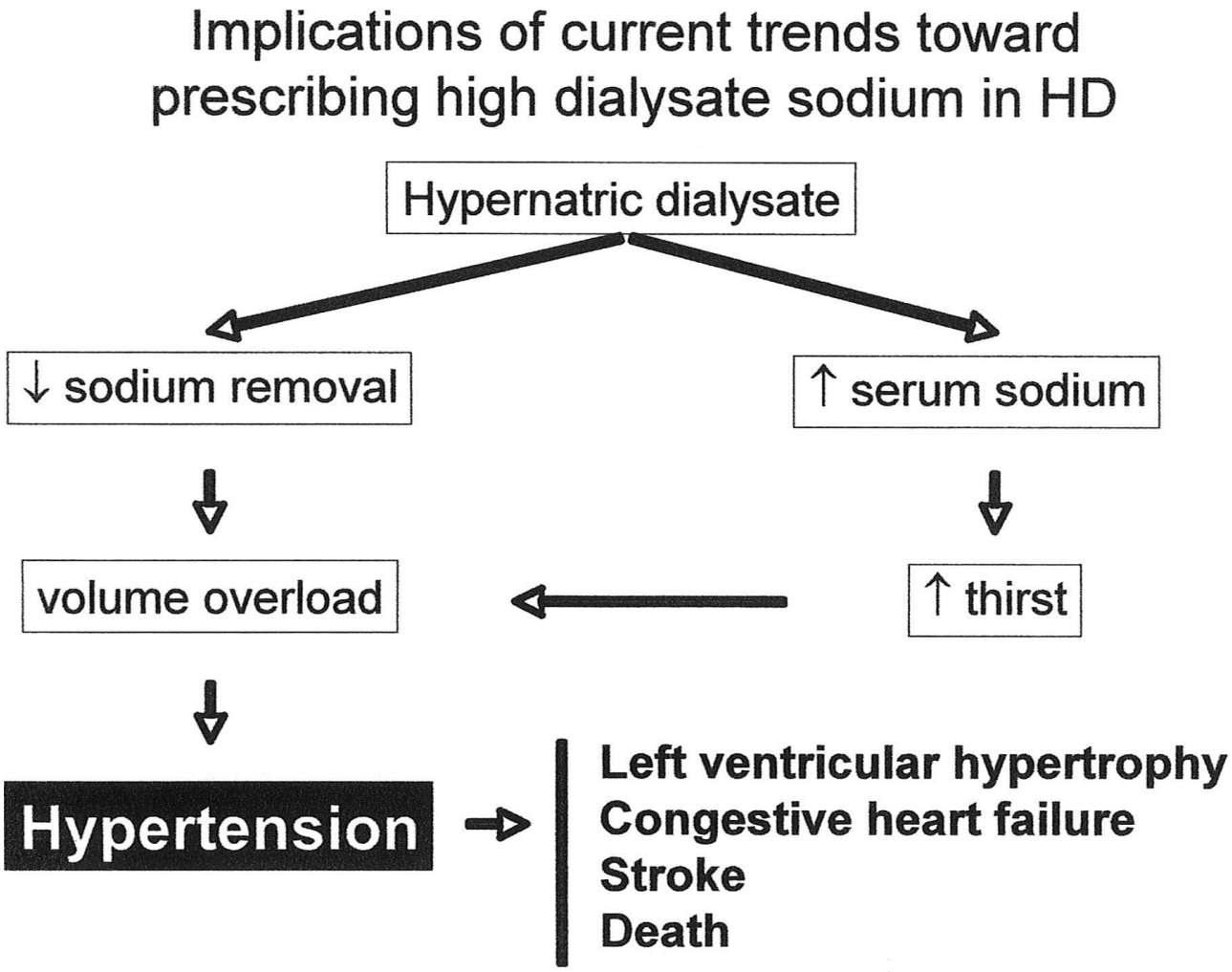
Higher Na gradient → higher IDWG

Sodium gradient = D.Na – S.Na



Munoz NDT 2011

Dialysate Sodium

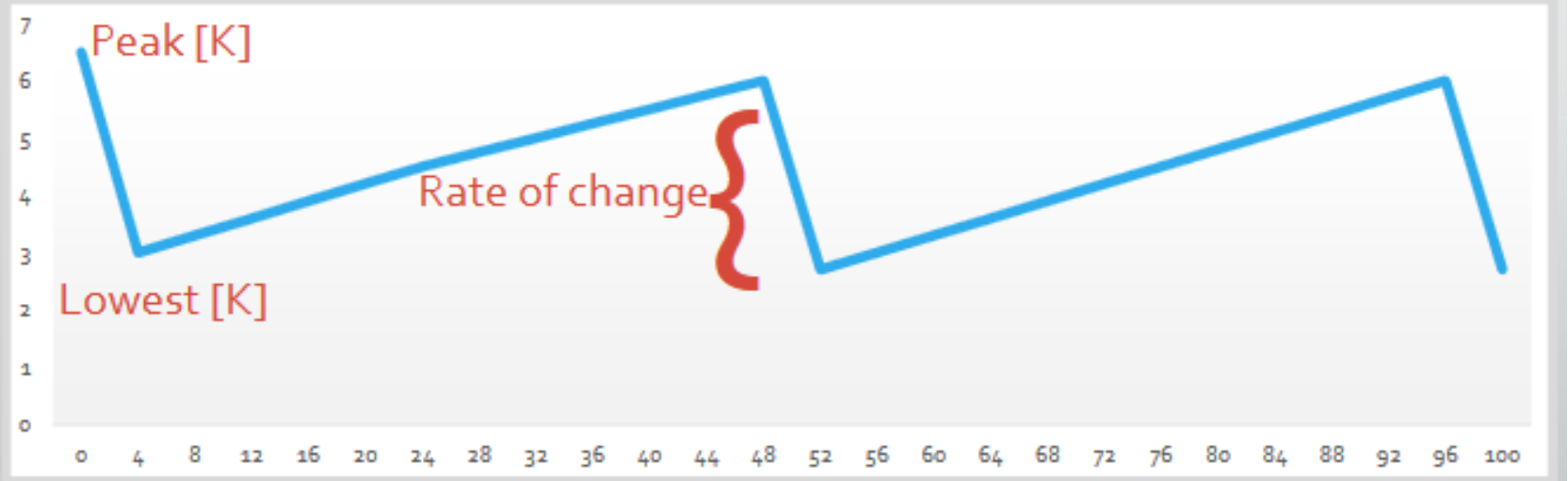


Santos CJASN 2008

Dialysate Potassium

- Generally 2-3meq/L

- Emergently can use 0K bath
  - Need to check frequent blood gas Ks
  - Not available at BRRH



Dialysate Potassium

- Predialysis hyperkalemia
- Postdialysis hypokalemia
- →SCD?

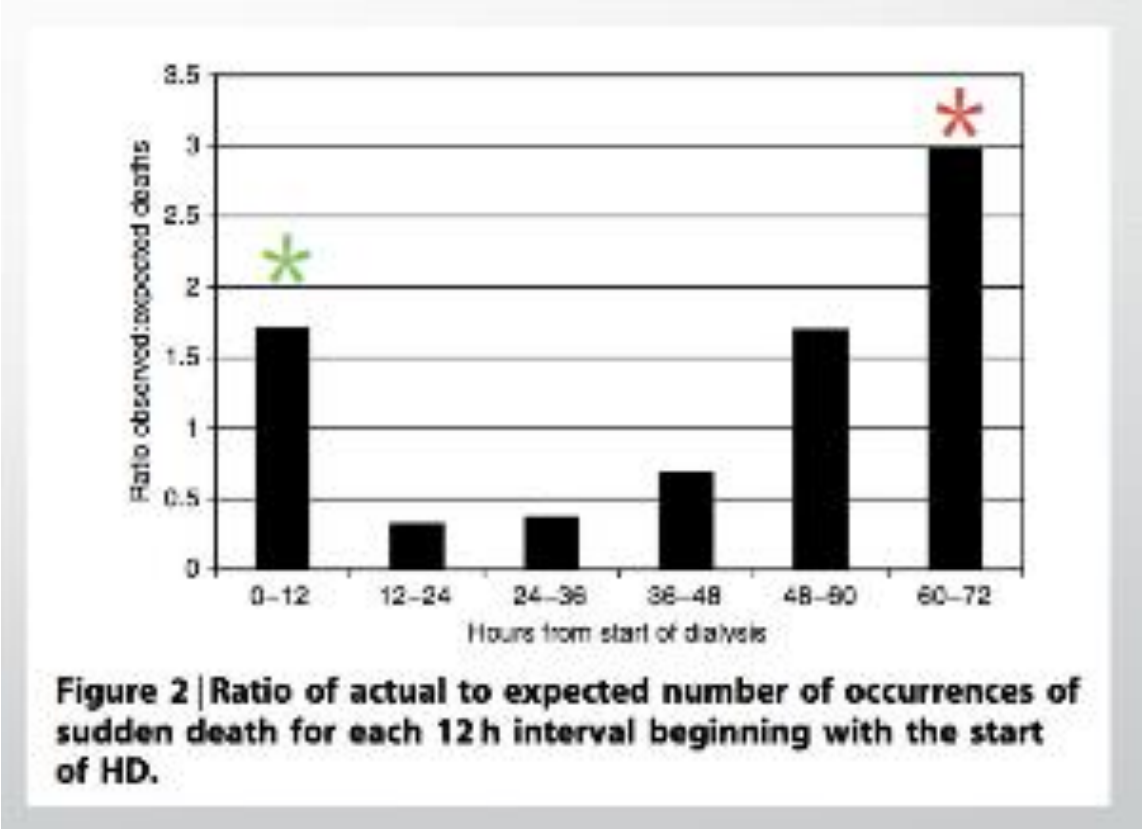


Figure 2 | Ratio of actual to expected number of occurrences of sudden death for each 12 h interval beginning with the start of HD.

Bleyer KI 2006

Dialysate Bicarbonate

- Primary buffer
- 34-40meq/L

- Pts mildly acidotic at start of tx

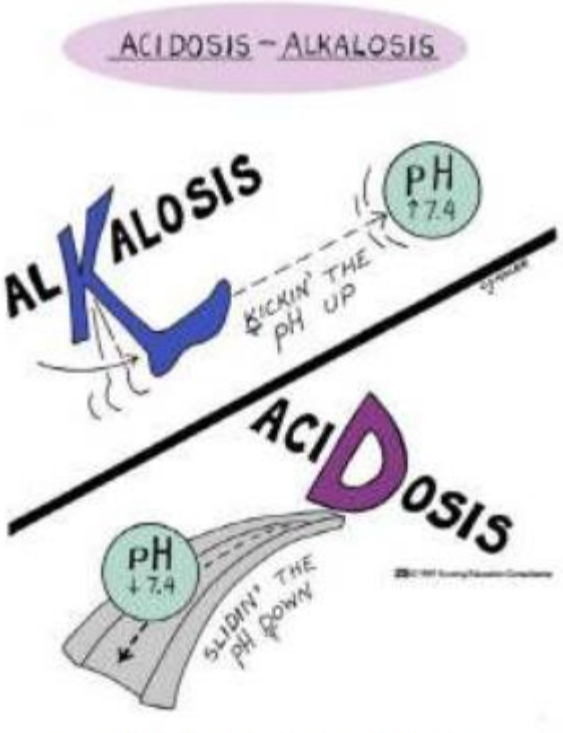


Image taken from Nursing Consultants, Inc.
http://www.nursinged.com/index.html

Dialysate Calcium

- 2-3 meq/L (usually 2.5meq/L)
- Low Ca baths associated with increased risk of hypotension
  - Decreased cardiac contractility
- High Ca baths can calcium load
  - Caution with binder, vitamin D use!
  - Increased [Ca x P]
  - May be needed following parathyroidectomy

Anemia in ESRD

- Kidneys produce 90% of circulating EPO
- EPO production declines as CKD advances
- Less EPO → apoptosis of erythroid cell progenitors
- Iron deficiency

Clinical Manifestations

- Fatigue
- Cognitive impairment
- Decreased libido
- Decreased exercise tolerance
- DOE
- Increased CV risk

Iron Deficiency

- Causes
  - Decreased GI absorption
  - Occult GIB
  - Phlebotomy
  - Dialysis effects
  - ESAs exhaust iron stores

- Indications to treat: Tsat < 20-30%, HgB variable

Erythropoetin Stimulating Agents (ESAs)

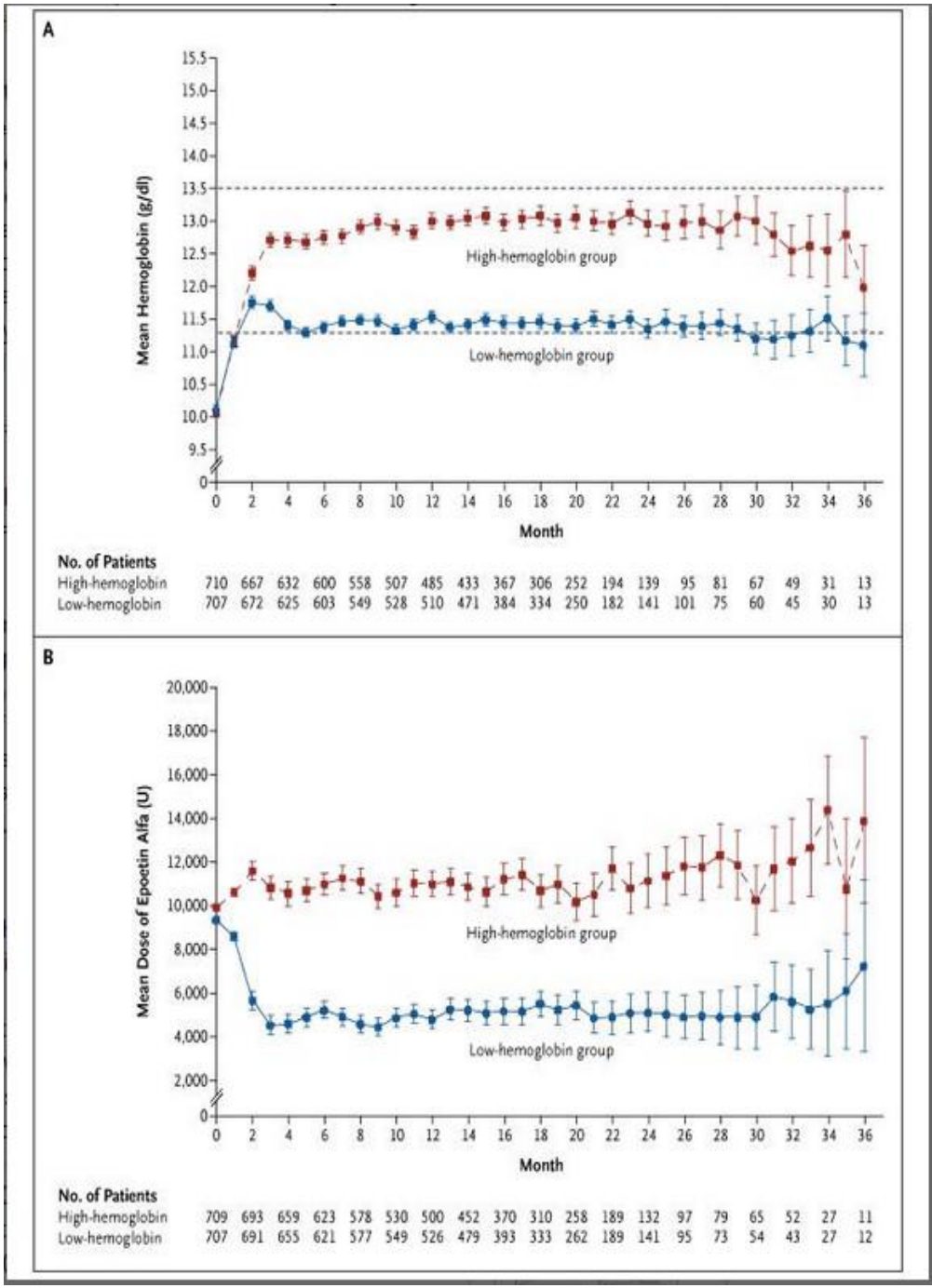
- Epogen/Procrit
- Darbopoetin/Aranesp

- SC or IV* administration
- Goal HgB ~ 10-11 g/dL

- Benefits
  - Improved M&M
  - Less transfusions
  - Improved QOL and exercise tolerance

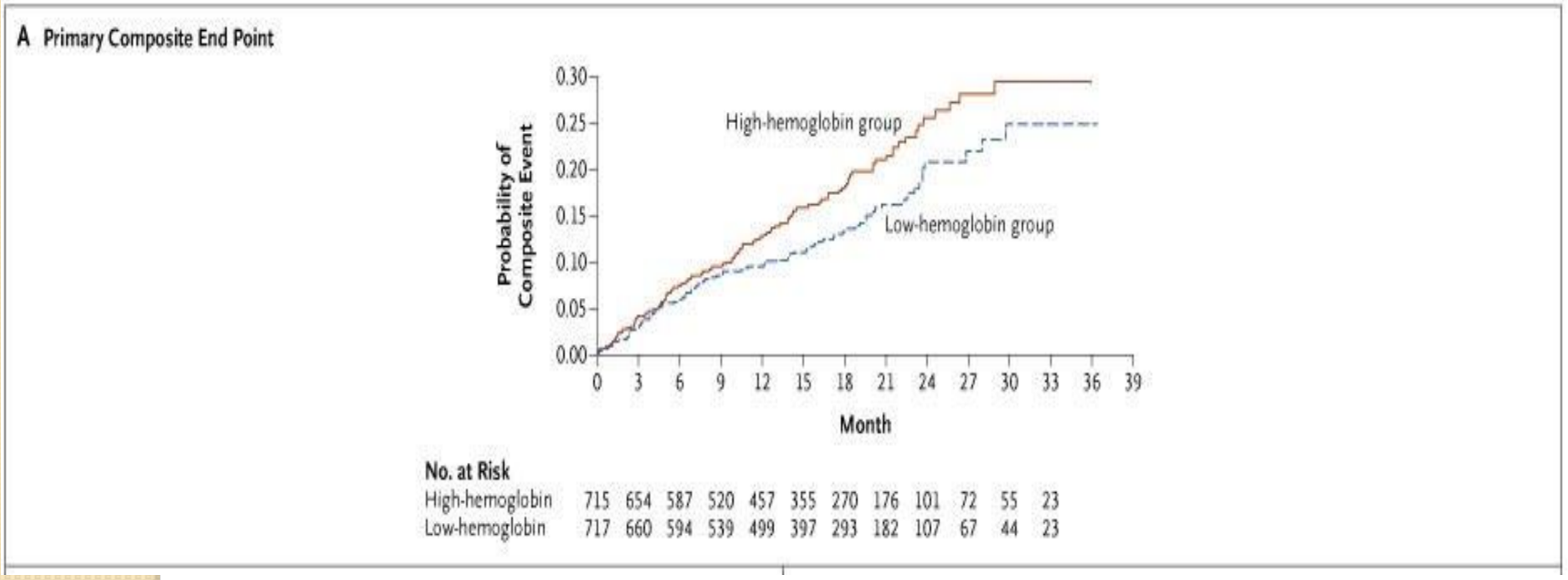
Target HgB

- CHOIR Trial (NEJM 2006)
- ~1400 CKD (non HD) pts
- Goal HgB
  11.3 vs 13.5



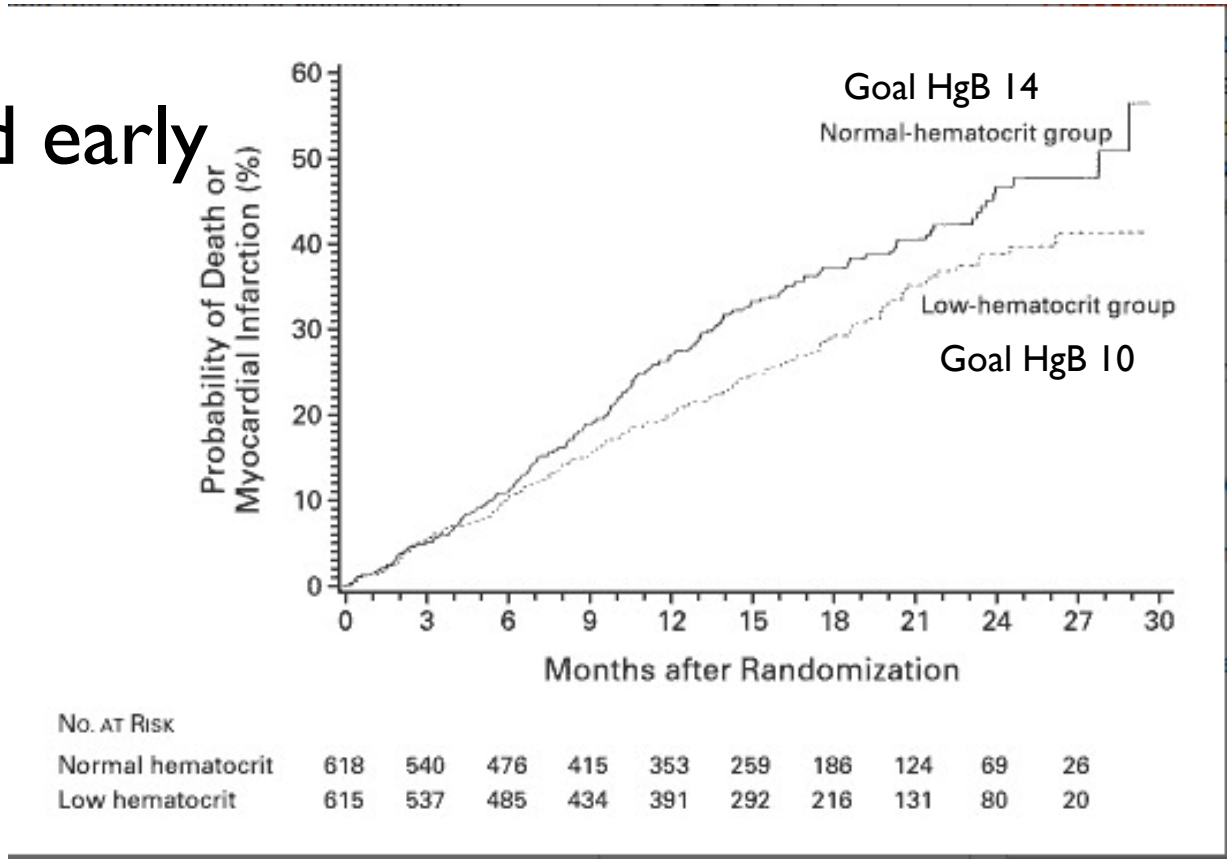
CHOIR Trial: Results

- Composite endpoint- death, myocardial infarction, hospitalization for congestive heart failure without renal replacement therapy, or stroke



What about HD patients?

- Normal Hematocrit Trial (NHT)- 1998
- All patients with heart disease (CHF, CAD)
- Stopped early

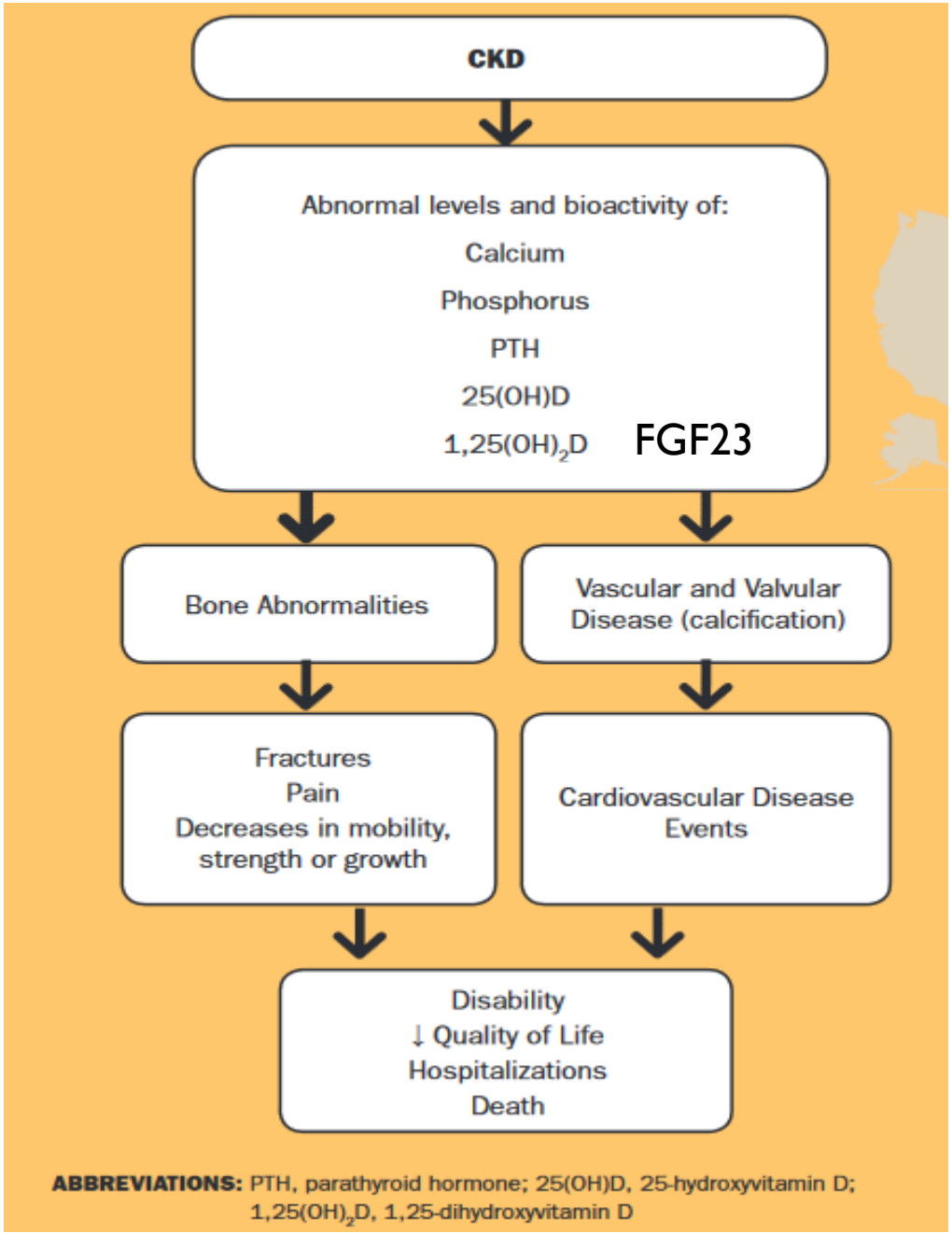


ESA Adverse Effects

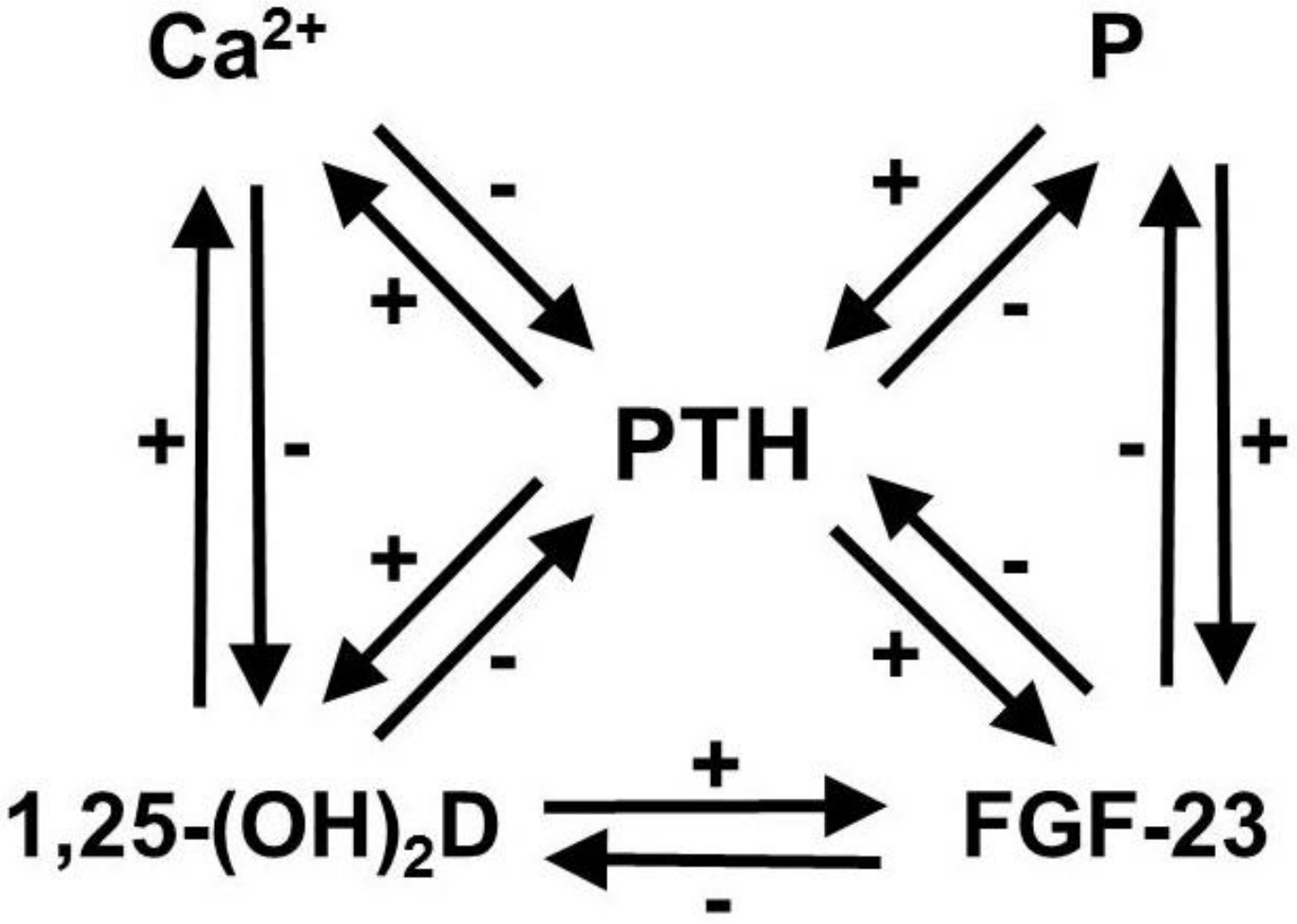
- When aiming for normal HgB
  - Increased mortality
  - CV events
  - Malignancy
  - Access thrombosis
    - NHT 39% vs 29% in normal HgB group
- When aiming for any HgB
  - Hypertension
    - Vasoconstriction – EPO receptors in blood vessels

CKD-MBD

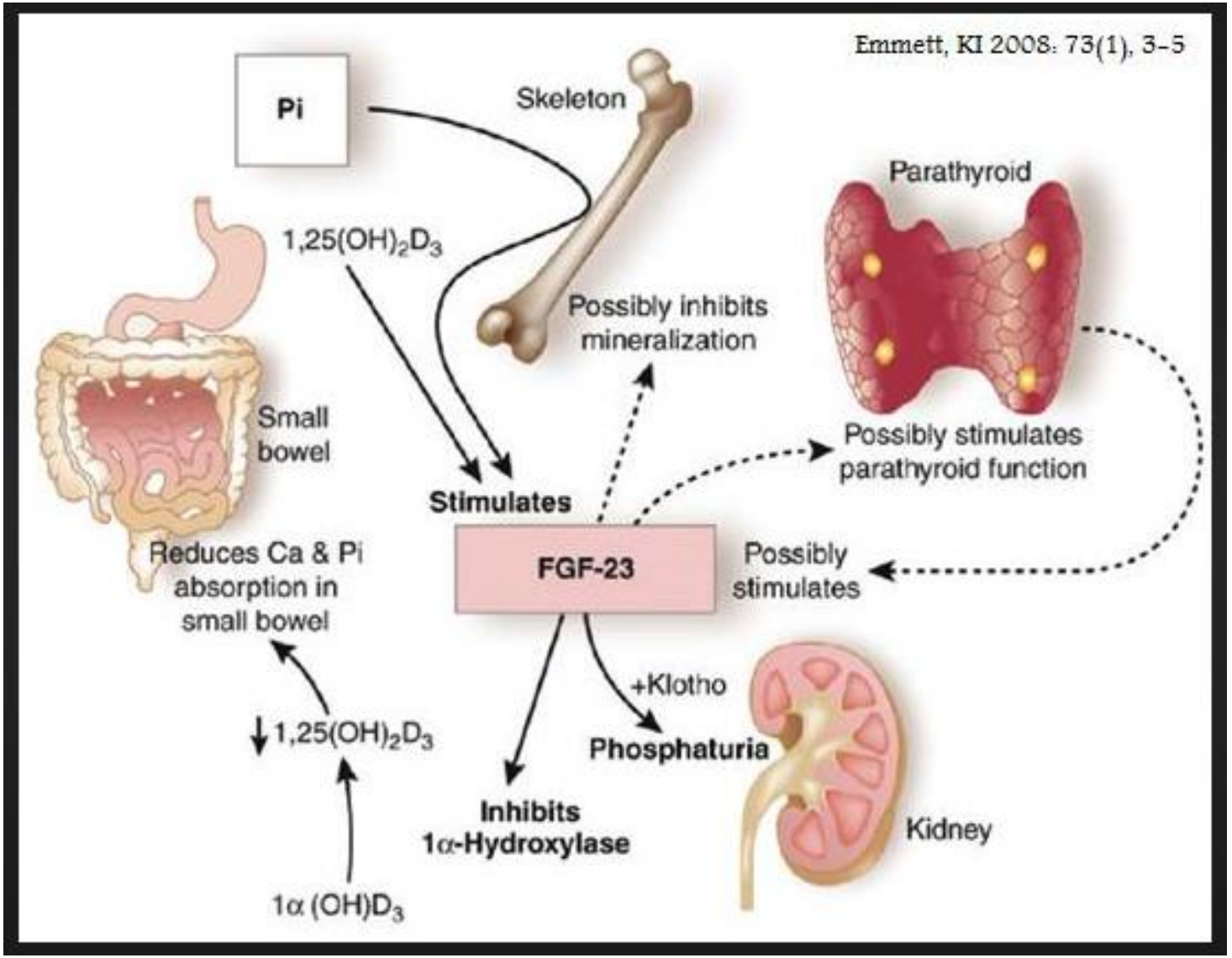
- nkf


CKD
Abnormal levels and bioactivity of:
Calcium
Phosphorus
PTH
25(OH)D
1,25(OH)2D
FGF23
Bone Abnormalities
Vascular and Valvular Disease (calcification)
Fractures
Pain
Decreases in mobility, strength or growth
Cardiovascular Disease Events
Disability
↓ Quality of Life
Hospitalizations
Death
ABBREVIATIONS: PTH, parathyroid hormone; 25(OH)D, 25-hydroxyvitamin D; 1,25(OH)2D, 1,25-dihydroxyvitamin D

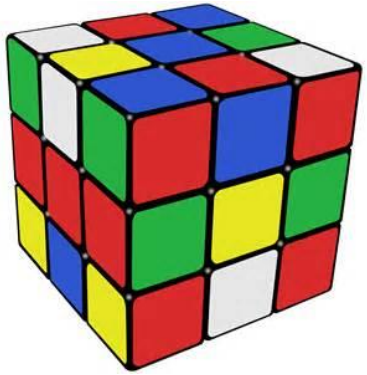
Mechanism…



Mechanism…


Emmett, KI 2008: 73(1), 3–5
Pi
Skeleton
Parathyroid
1,25(OH)2D3
Possibly inhibits mineralization
Small bowel
Stimulates
Possibly stimulates parathyroid function
Reduces Ca & Pi absorption in small bowel
FGF-23
Possibly stimulates
+Klotho
↓1,25(OH)2D3
Phosphaturia
Inhibits 1α-Hydroxylase
Kidney
1α (OH)D3

Treatment



- Very difficult
- Medications will simultaneously improve and worsen various lab values

- Goals:
  - Ca 8.5-10.2
  - Ph 3.5-5.5
  - [Ca x P] < 55
  - PTH < 500-600
  - VitD > 30

Medication Options

	Calcium	Phosphorous	PTH
Phos Binders (calcium based)	↑	↓	↓↔
Phos Binders (non calcium based)	↔	↓	↓↔
Activated Vitamin D	↑	↑	↓
Cinacalcet	↓	↓	↓

*In addition to low phos diet!

Summary

- ESRD patients suffer from a large number of hemodynamic, chemical, hematologic, and musculoskeletal abnormalities.
- Optimization of the dialysis prescription can help mitigate many of these issues

Thank You!

- Dr Ira Lazar, Dr John Panos, Dr Eric Lazar, and/or myself are always around to answer questions and be of assistance.
- Email: marc.richards@gmail.com
- Cute picture of kids: