Nutrition Support for Critically Ill Patients with Renal Dysfunction

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Exceptional People. Extraordinary Results.

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Disclosures

- I have no commercial relationships relevant to the topic being presented.
  - Nestlé HealthCare Nutrition, Inc. provided supplement products for a Physician-Sponsored Clinical trial for which I was the PI
  - Baxter advisory committee on premixed PN products
- I am not a nephrologist.

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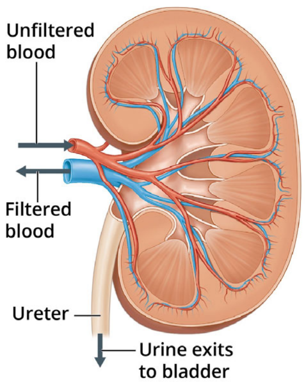
Learning Objectives

- Discuss the effects of renal replacement therapy on energy and protein requirements of critically ill patients.
- Evaluate electrolyte derangements seen with renal dysfunction and different modes of renal replacement.
- Identify micronutrient deficiencies common to critically ill patients on renal replacement therapy and discuss potential mitigation strategies.

Background

- Why is renal dysfunction in the ICU important?
- How is renal dysfunction managed in the ICU?

The Kidney



- Maintains acid-base balance
- Maintains electrolyte levels
- Eliminates some drugs
- Regulates volume status
- Clears nitrogenous waste
- Synthesizes/metabolizes hormones

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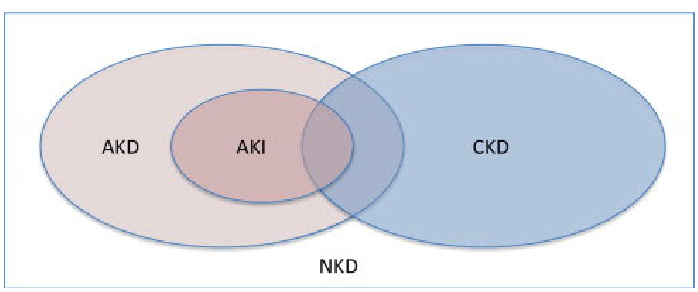
Background

- Renal dysfunction is common in the ICU
  - Approximately 50% of ICU patients
  - Rarely primary reason for ICU admission]
- Renal dysfunction may be acute, chronic, or acute on chronic



Acute Kidney Injury and CKD: Chicken or Egg? Bedford, Michael et al. American Journal of Kidney Diseases, Volume 59, Issue 4, 485 - 491

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Acute Kidney Injury (AKI)

- 2012 KDIGO criteria
  - Abrupt decrease in kidney function occurring over ≤ 7 days
  - Defined by increased creatinine or decreased urine output

Stage	Serum creatinine	Urine output
1	1.5 - 1.9 x baseline OR ≥ 0.3 mg/dL increase	< 0.5 mL/kg/h for 6 - 12 hours
2	2.0 - 2.9 x baseline	< 0.5 mL/kg/h for ≥ 12 hours
3	3.0 x baseline OR Increase in serum creatinine to ≥ 4.0 mg/dL OR Initiation of renal replacement therapy	< 0.3 mL/kg/h for ≥ 24 hours OR Anuria for ≥ 12 hours

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Chronic Kidney Disease (CKD)

- 2024 KDIGO
  - Persistent alterations in kidney function or structure lasting > 3 months
  - Classified by cause, GFR, and markers of kidney damage

GFR Category	GFR (mL/min per 1.73 m^2)	Comment
G1	> 90	Kidney damage with normal kidney function
G2	60 - 89	Kidney damage with mild loss of kidney function
G3a	45 - 59	Mild to moderate loss of kidney function
G3b	30 - 44	Moderate to severe loss of kidney function
G4	15 - 29	Severe loss of kidney function
G5	< 15	Kidney failure

Albuminuria Category	ACR (mg/g)	Comment
A1	< 3	Normal to mildly increased
A2	3 - 300	Moderately increased
A3	> 300	Severely increased

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Additional forms of Kidney Dysfunction

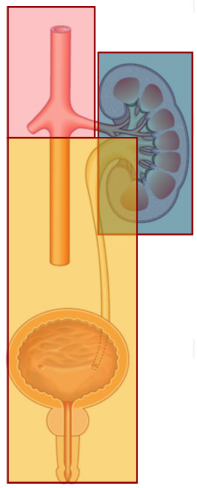
- Acute on Chronic
  - Acute decline in kidney function in a patient with baseline CKD
- Acute Kidney Disease and Disorders
  - Not meting criteria for AKI or CKD but at risk
- End Stage Renal Disease
  - eGFR < 15 ml/min
  - Often requiring chronic renal replacement therapy (RRT)

Incidence of Renal Dysfunction in the ICU

- AKI-EPI study
  - Multicenter, international cross-sectional study
  - 1800 patients, 97 ICUs, 33 countries

  - 57% of patients developed AKI within the 1 week study period
  - 39% of patients developed stage 2 or 3 AKI
  - 13.5% of patients needed RRT
    - 23.5% of AKI patients
- CKD
  - Upward of 30%
  - Predisposes patients to AKI on CKD

Common Causes of Renal Dysfunction



Causes of acute kidney injury.
Source : Davidsons Essentials of Medicine, 2e

PRE-RENAL

Impaired perfusion:
- Cardiac failure
- Sepsis
- Blood loss
- Dehydration
- Vascular occlusion

RENAL

Glomerulonephritis
Small-vessel vasculitis
Acute tubular necrosis
- Drugs
- Toxins
- Prolonged hypotension

Interstitial nephritis
- Drugs
- Toxins
- Inflammatory disease
- Infection

POST-RENAL

Urinary calculi
Retroperitoneal fibrosis
Benign prostatic enlargement
Prostate cancer
Cervical cancer
Urethral stricture/valves
Meatal stenosis/phimosis

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Renal Dysfunction Affects Outcomes in ICU

KI REPORTS KIReports.org — CLINICAL RESEARCH

Impact of Acute Kidney Injury and CKD on Adverse Outcomes in Critically Ill Septic Patients

Check for updates

Javier A. Neyra[1,2,3,8], Federica Mescia[2,4,8], Xilong Li[5], Beverley Adams-Huet[2,5], Lenar Yessayan[6], Jerry Yee[7], Robert D. Toto[3,5] and Orson W. Moe[2,3]; for the Acute Kidney Injury in Critical Illness Study Group

- Single-center, retrospective cohort study
- 2632 adult patients admitted to ICU with severe sepsis
- Classified patients according to baseline CKD and incident AKI
  - No-CKD, eGFR $\geq$ 60, eGFR 15-59
  - No-AKI, AKI stage 1, AKI stage $\geq$2
- Evaluated 90-day mortality and incident/progression to CKD

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Renal Dysfunction Affects Outcomes in ICU

- 46% of patients had CKD; 57% of patients had AKI
- Adjusted hazard ratios (95% CI) for 90-day mortality relative to no-CKD /no-AKI
  - 1.5 (1.1-2.0) in no-CKD/AKI stage 1
  - 2.4 (1.9-3.1) in no-CKD/AKI stage ≥ 2
  - 1.1 (0.8-1.4) in CKD/no-AKI
  - 1.2 (0.9-1.6) in CKD/AKI stage 1
  - 2.2 (1.7-2.9) in CKD/AKI stage ≥ 2

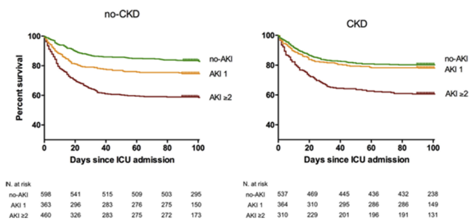

Figure 2. Ninety-day mortality across chronic kidney disease (CKD)/acute kidney injury (AKI) groups. For the purpose of clarity, the no-CKD and CKD groups are represented on the left and right chart, respectively. no-CKD: baseline eGFR ≥60; CKD: baseline eGFR <60; no-AKI: no AKI occurrence; AKI 1: KDIGO-sCr stage 1 AKI; AKI ≥2: KDIGO-sCr stage 2 or higher. ICU, intensive care unit; KDIGO, Kidney Disease: Improving Global Outcomes; sCr, serum creatinine.

Renal Dysfunction Affects Outcomes in ICU

- Patients with AKI requiring RRT have hospital mortality rates ranging from 40-50%
  - 2.3 fold increase in mortality after controlling for many confounders
- Even stage 1 AKI is linked to decreased survival at 10 years compared to increased risk of mortality associated with CKD requiring ICU admission which is often limited to 6 months following discharge
- Duration of AKI influences survival
  - AKI improved within 7 days had a 10% mortality rate at 1 year compared to 60% mortality rate in age adjusted patients with prolonged renal recovery

Knowledge Check

- Renal dysfunction…
  a) Is a common reason for ICU admission
  b) Requires ICU admission
  c) Is a frequent consequence of critical illness
  d) Necessitates dialysis

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Background

- Why is renal dysfunction in the ICU important?
- How is renal dysfunction managed in the ICU?

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How is renal dysfunction managed in the ICU

- Supportive care
  - Treating shock states
  - Avoiding nephrotoxic agents
  - Restricting sodium, fluid, potassium, phosphorus, (nitrogen?)
- Renal replacement therapy (RRT)
  - Hemodialysis
  - Peritoneal dialysis
  - Continuous renal replacement therapy
    - More common in ICU given tenuous hemodynamics and inability to tolerate large volume shifts

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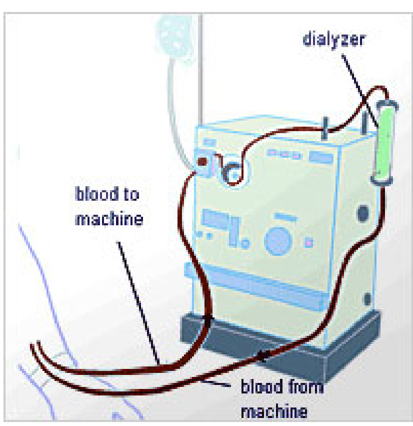
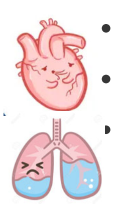
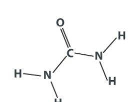
RRT can assume many functions of the kidney





- Maintains acid-base balance
- Maintains electrolyte levels
- Eliminates some drugs
- Regulates volume status
- Clears nitrogenous waste



- RRT cannot
  - Synthesize/metabolize hormones

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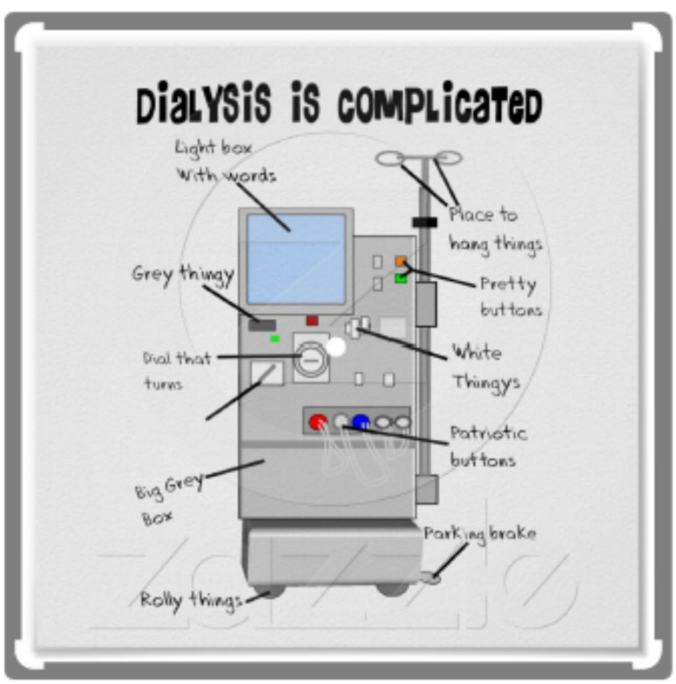
Goals of RRT

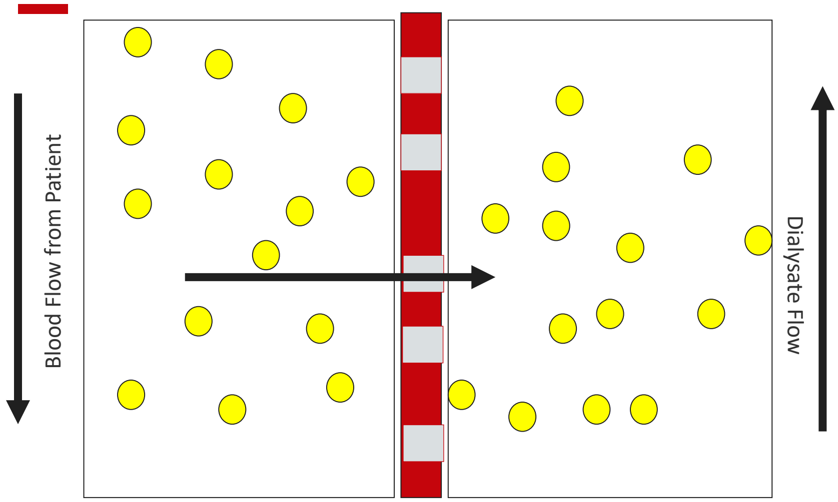
- Remove uremic waste products
- Correct metabolic acidosis
- Correct electrolyte disturbances
- Remove excess salt and water

(First three) → Clearance

Remove excess salt and water → UF



Principle: Diffusion

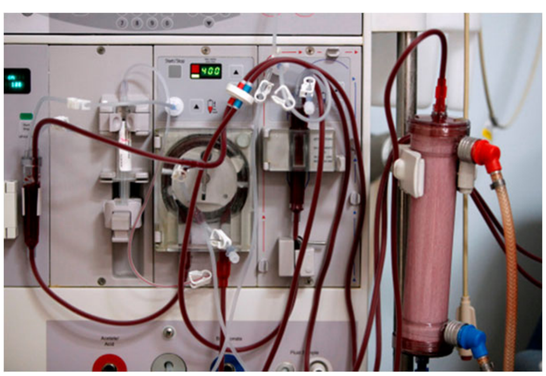


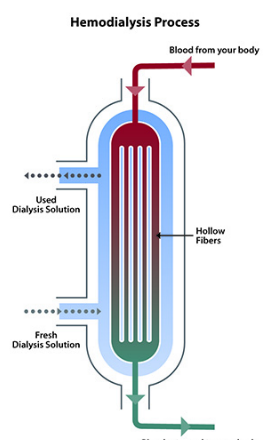
- Concentration difference
- Dialysate and blood flow rates
- Dialyzer Surface
- Pore size

Counter-current flow forming natural concentration gradient

Courtesy of Dr. Tripti Singh

Hemodialysis: Diffusion Based





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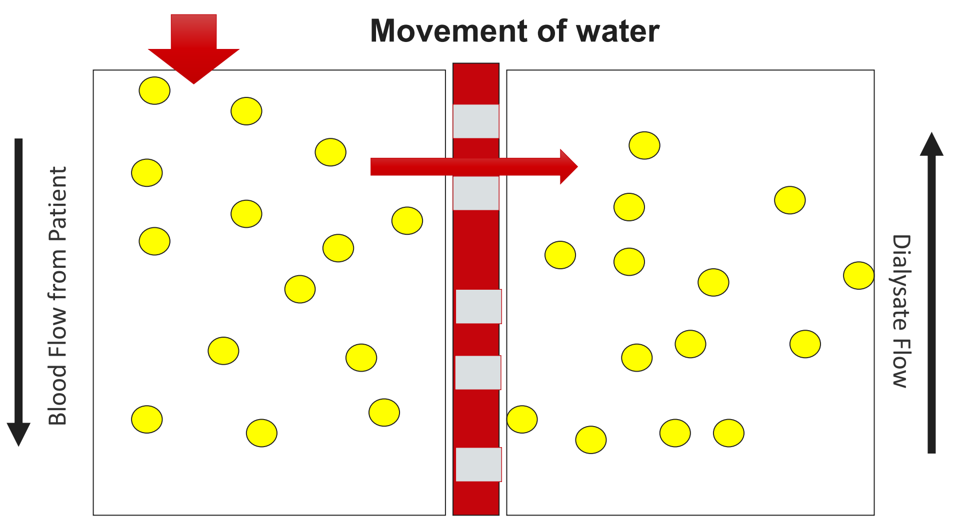
Clearance by Diffusion

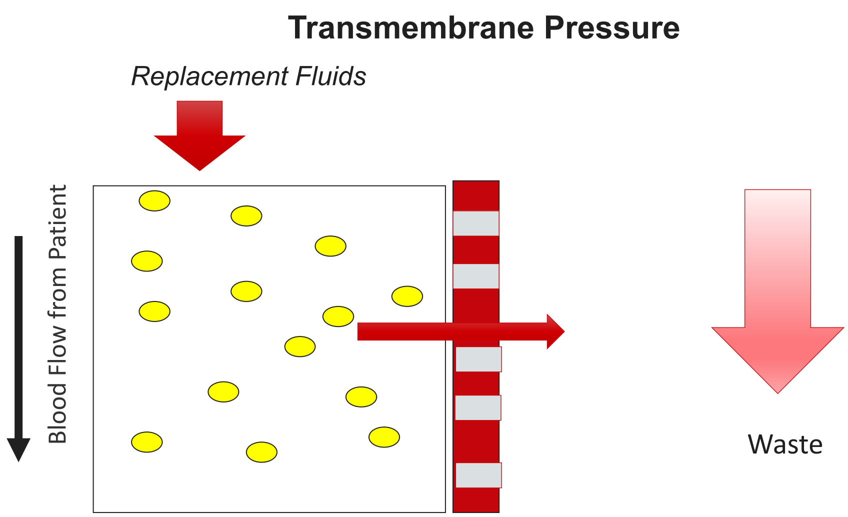
- Low molecular weight like K+ or H+
  - *flow dependent*
- High molecular weight like phosphates and cytokines
  - *contact time, surface area, pore size*

Principle: Convection



Courtesy of Dr. Tripti Singh

Principle: Convection

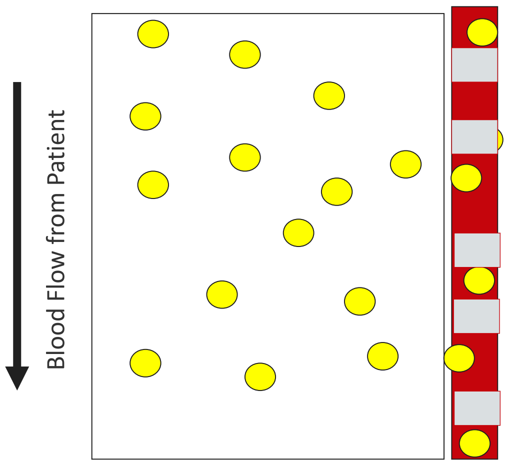


Courtesy of Dr. Tripti Singh

Principle: Ultrafiltration

- Refers to movement of solvent
- Any molecules small enough will carried with solvent, i.e., solvent drag
- Convective movement

Principle: Adsorption



- Stuck on membrane

Courtesy of Dr. Tripti Singh

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Types of RRT

- Intermittent
  - IHD
  - PIRRT/SLED
- Continuous
  - CRRT
    - CVVH
    - CVVHD
    - CVVHDF
    - SCUF
  - PD

IHD: Intermittent Hemodialysis
PIRRT: Prolonged Intermittent Renal replacement therapy
PD: Peritoneal Dialysis
CVVH: Continuous venovenous hemofiltration
CVVHD: Continuous venvenous dialysis
CVVHDF: Continuous venovenous dialfiltration
SCUF: Slow continuous ultrafiltration
SLED: Sustained low efficiency dialysis

Courtesy of Dr. Tripti Singh

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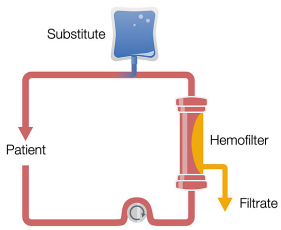
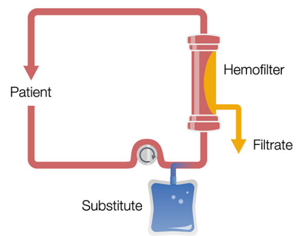
CVVH

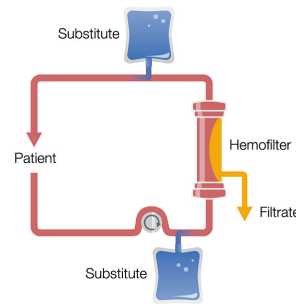
- Convection based therapy



Post- replacement fluid



Pre- replacement fluid



Pre and post- replacement fluid

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Courtesy of Dr. Tripti Singh

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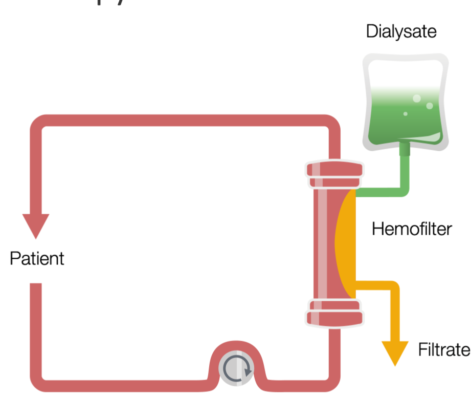
CVVHD

- Diffusion based therapy



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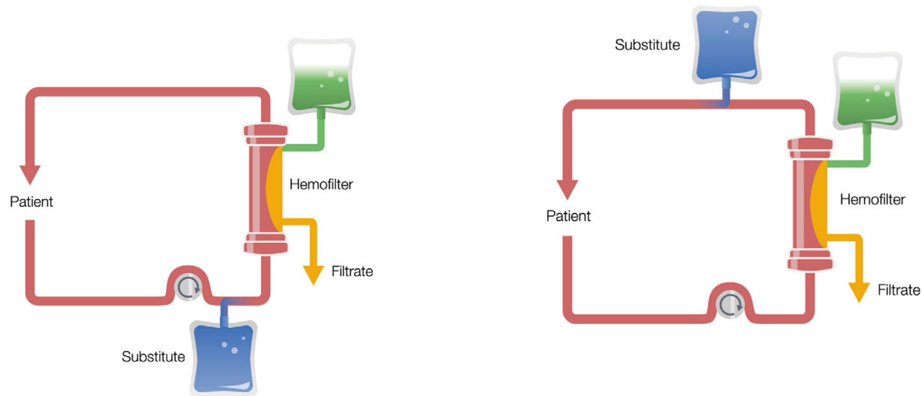
CVVHDF

- Combines both diffusion and convection therapies



Post- replacement fluid

Pre- replacement fluid

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Knowledge Check

- Which of the following is a principle of hemodialysis?
  - a) Diffusion
  - b) Convection
  - c) Adsorption
  - d) Ultrafiltration
  - e) All of the above

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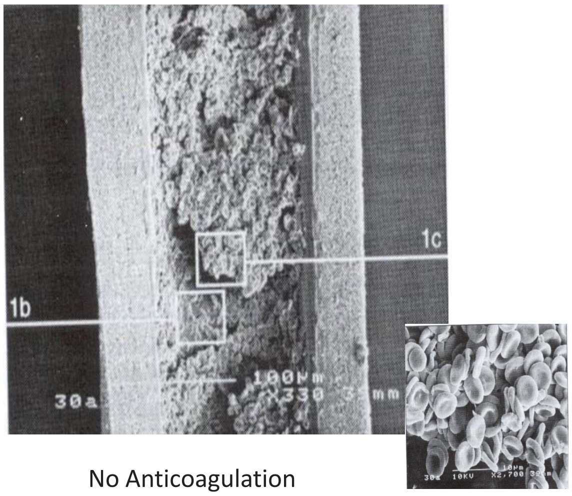
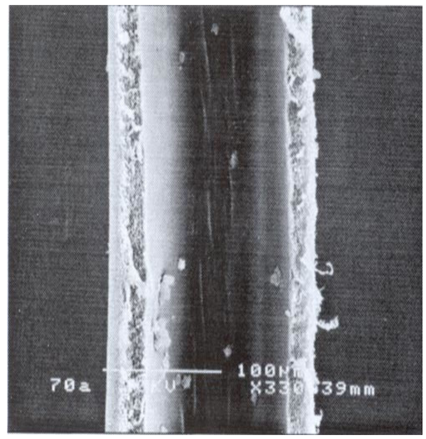
Anticoagulation



No Anticoagulation



Citrate Anticoagulation

Courtesy of Dr. Tripti Singh

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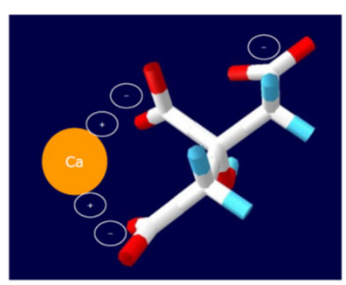
Citrate Anticoagulation

- Chelates Ca^{2+} in extracorporeal circuit
- Prevents activation of Ca^{2+} dependent pro-coagulants
- Anticoagulant effect measured by $iCa^{2}+$
- Anticoagulation reversed by $Ca^{2}+$ infusion



Courtesy of Dr. Tripti Singh

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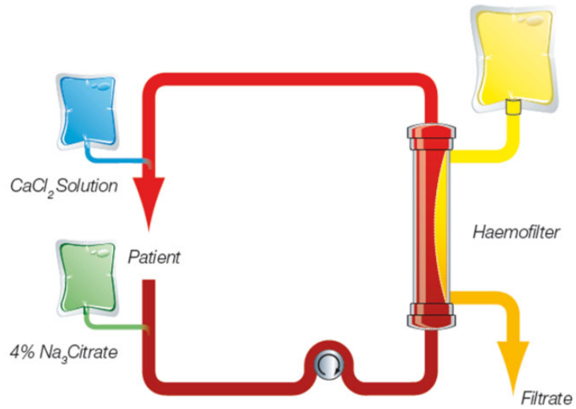
Citrate Anticoagulation in CRRT



Courtesy of Dr. Tripti Singh

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Metabolic Consequence of Citrate

- Metabolic alkalosis
  - Citrate overdose
- Metabolic acidosis
  - Citrate toxicity in setting of severe liver disease or hypoperfusion
- Hypernatremia
  - Hyperosmolar citrate solutions
- Hypocalcemia and hypercalcemia
  - Inappropriate calcium supplementation
- Hypomagnesemia

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CRRT

- Indications
  - Hemodynamic instability
  - Continuous solute control
  - Continuous volume control
  - Increased ICP
  - Slow correct of severe dysnatremias
  - High risk of osmotic disequilibrium
- Disadvantages
  - ICU level care
  - Cost
  - Slow removal of toxins
  - Patient immobility
  - Anticoagulation
  - Hypothermia
  - Drug clearance
  - **Nutritional loss**

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Learning Objectives

- Discuss the effects of renal replacement therapy on energy and protein requirements of critically ill patients.
- Evaluate electrolyte derangements seen with renal dysfunction and different modes of renal replacement.
- Identify micronutrient deficiencies common to critically ill patients on renal replacement therapy and discuss potential mitigation strategies.

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Metabolic Changes in AKI

- Protein catabolism
  - Altered metabolism of individual AA
  - Altered metabolism of exogenously administered AA
- Carbohydrate metabolism
  - Hyperglycemia
  - Peripheral insulin resistance
  - Hepatic gluconeogenesis
    - cannot be suppressed by exogenous nutrient intake
- Lipid metabolism
  - Hypertriglyceridemia due to suppressed lipolysis
  - Fat clearance is delayed after EN or PN

Energy Requirements with Renal Dysfunction in ICU

- Energy requirements for patients with AKI are similar to those without renal impairment
  - 2 studies
    - Measured EE is 30% high in AKI patients compared to control group
      - Only when AKI was associated with sepsis
      - No altered EE in non-sepsis AKI group
    - REE in patients with sepsis and AKI was similar to patients with sepsis and no AKI
  - Study comparing REE vs. Harris-Benedict equation in 124 AKI patients in ICU
    - 62% hypercatabolic, 14% hypometabolic
- Energy requirements for patients with CKD do not change with initiation of RRT
- Energy requirements for patients with AKI or CKD that require continuous RRT are increased

Metabolic Changes due to Hemodialysis

- Continuous RRT usually used in critically ill
- High filtration rates
  - Results in significant influences on electrolyte and nutrient balance
  - Particularly if losses are not replaced
    - AA loss is approximately 0.2 g/L filtrate
    - Water soluble vitamins are lost
  - Excess intake through dialysate fluid can also cause problems
    - Hyperlactatemia
    - Metabolic alkalosis
    - Significant dextrose load

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Metabolic Changes due to Hemodialysis

- Loss of water soluble molecules with low molecular weight
  - AA
  - Water soluble vitamins
  - L-carnitine, etc
- Activation of protein catabolism through
  - Loss of substrates (AA)
  - Release of cytokines (TNF-a, etc)
  - Blood loss
- Electrolyte disorders due to high fluid turnover
  - Hypophosphatemia
  - Hypomagnesaemia
  - Hyponatremia
- Loss of heat (loss of energy)

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Energy Needs

- Recommend indirect calorimetry when available
- Predictive equations tend to underestimate energy needs
- Critically ill
  - AKI ± RRT
    - 20-30 kcal/kg/day (KDIGO 2012)
    - 25-30 kcal/kg/day (ASPEN/SCCM 2016)

    - 20-25 kcal/kg/day catabolic phase
    - 25-30 kcal/kg/day anabolic phase

  - CKD ± RRT
    - 30-35 kcal/kg/day (KDIGO, ESPEN, ISRNM)

    - Providing < 12 kcal/kg/day is associated with worse clinical outcomes, including mortality

Remember to account for exogenous sources

- CRRT
  - Can contribute 500-1300 kcal/day
    - Dextrose in dialysate (3.4 kcal/g)
    - Citrate anticoagulation (3 kcal/g)
    - Lactate as a buffering agent in dialysate (3.62 kcal/g)
  - Dextrose free dialysate
- Lipid in propofol (1.1 kcal/ml)
- Dextrose containing fluids

Protein Requirements with Renal Dysfunction

- It depends…
  - Stage of kidney disease
  - Chronicity
  - Modality of RRT
  - Underlying comorbidities
  - Nutritional status
  - Presence of acute illness

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Protein Requirements with Renal Dysfunction in the Community

- CKD stage 3-5; not on RRT
  - KDOQI 2020 guidelines recommend 0.55-0.6 g/kg/day
  - Add diabetes
    - Recommend 0.6-0.8 g/kg/day
- Rationale
  - Decrease renal hyperfiltration and azotemia
- But…
  - Evidence suggests protein intake of 0.8 to >1 g/kg/day is not associated with increased risk of kidney failure or death in patients with CKD stage 3 and may have little effect on slowing progression of CKD
  - Protein restriction may worsen Protein Energy Wasting

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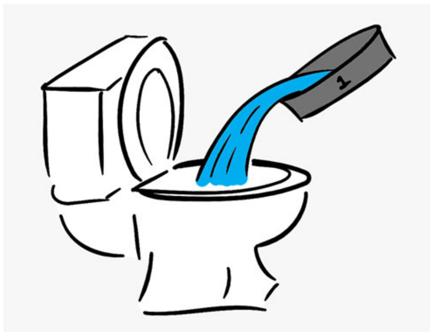
Protein Requirements with Renal Dysfunction in the Hospital

- AKI
  - Non-catabolic: 0.8 – 1 g/kg/day
  - Catabolic: 1.2 – 2 g/kg/day
  - + RRT: 1.0-1.5 g/kg/day
  - + CRRT: 1.5- 2.5 g/kg/day
- CKD
  - Non-catabolic: 0.6 – 0.8 g/kg/day
  - Catabolic: 1 g/kg/day
  - + RRT: 1.0-1.4 g/kg/day
  - + CRRT: 1.5-2.5 g/kg/day

Protein Losses with RRT

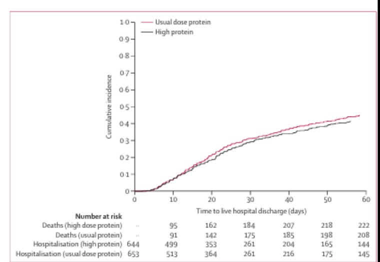
- iHD 10-13 g per session
- CRRT 5-20 g per day



EFFORT Protein Trial

- Pragmatic, registry-based, single-blinded, randomized trial
- 85 ICUs in 16 countries
- Mechanically ventilated adults prescribed high-dose protein (≥2.2 g/kg/day) versus usual dose protein (≤ 1.2 g/kg/day) started within 96 h of ICU admission and continued for up to 28 days or until transitioned to PO or death
- Primary outcome: time to discharge alive up to 60 days after ICU admission
- Secondary outcome: 60 day mortality

EFFORT Protein Trial



Number at risk							
Deaths (high dose protein)	..	95	162	184	207	218	222
Deaths (usual protein)	..	91	142	175	185	198	208
Hospitalisation (high protein)	644	499	353	261	204	165	144
Hospitalisation (usual dose protein)	653	513	364	261	216	175	145

Figure 4: Time-to-discharge-alive from hospital by treatment group
The figure shows the cumulative incidence of time-to-discharge-alive from hospital (primary outcome) by treatment group. Overall estimate of treatment effect: HR 0·91, 95% CI 0·77–1·07; p=0·27.

- 1329 patients randomized; 1301 patients included
- Protein given: 1.6 ± 0.5 vs 0.9 ± 0.3 g/kg/day
- Energy given: 14.7 ± 6.9 vs 13.2 ± 6.4 kcal/kg/day
- 60 day discharge alive
  - 46.1% (95% CI 42.0-50.1%) in high-dose vs. 50.2 %(46.0-54.3%)
  - Hazard ratio 0.91 (95% CI 0.77-1.07, p = 0.27)
- 60 day mortality
  - 34.6% in high-dose vs. 32.1% (RR 1.08, 95% CI 0.92-1.26)
  - Subgroup effect with higher protein provision being harmful in patients with AKI and high organ failure scores at baseline.

The effect of higher protein dosing in critically ill patients with high nutritional risk (EFFORT Protein): an international, multicentre, pragmatic, registry-based randomised trial
Heyland, Daren K et al. The Lancet, Volume 401, Issue 10376, 568 - 576

RESEARCH — Open Access

The impact of higher protein dosing on outcomes in critically ill patients with acute kidney injury: a post hoc analysis of the EFFORT protein trial

Christian Stoppe[1,2*†], Jayshil J. Patel[3†], Alex Zarbock[4], Zheng-Yii Lee[2,5], Todd W. Rice[6], Bruno Mafrici[7], Rebecca Wehner[8], Man Hung Manuel Chan[9], Peter Chi Keung Lai[9], Kristen MacEachern[10], Pavlos Myrianthefs[11], Evdoxia Tsigou[11], Luis Ortiz-Reyes[12,13], Xuran Jiang[12,13], Andrew G. Day[13], M. Shahnaz Hasan[5], Patrick Meybohm[1], Lu Ke[14] and Daren K. Heyland[12,13*]

- Post-hoc analysis looking at different subgroups of critically ill patients with AKI within 7 days of ICU admission
- Of 1329 patients, 312 developed AKI (163 in high-dose protein, 149 in usual protein dose)

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Post hoc EFFORT Protein trial

- Of 1329 patients, 312 developed AKI (163 in high-dose protein, 149 in usual protein dose)
- 1.5 $\pm$ 0.5 versus 0.9 $\pm$ 0.3 g/kg/d
- Protein dose did not significant affect the duration of RRT post randomization
- Incidence of new RRT after randomization was the same
- Serum BUN was higher in AKI patients in high-protein arm
- Time to discharge alive was longer among AKI patients in high-protein group and consistent across AKI stage 1-3
  - HR 0.5, 95% CI 0.4-0.8, p = 0.001

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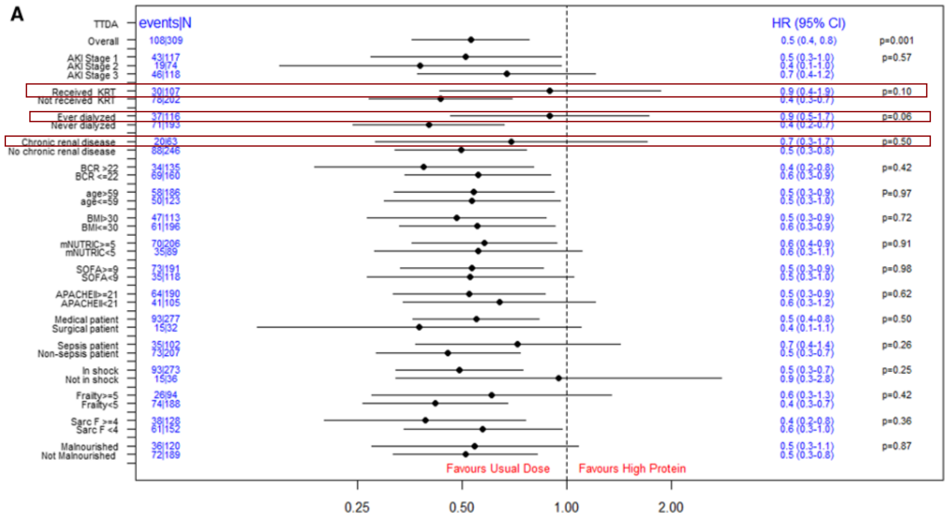
Time to Discharge Alive



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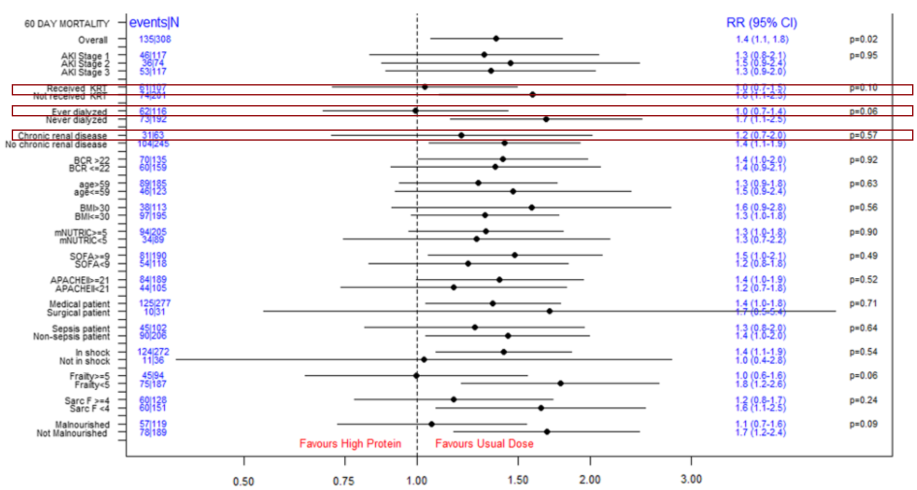
60-Day Mortality



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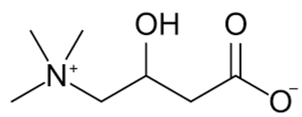
Brief Word on Carnitine

- High prevalence of carnitine deficiency in patients on RRT
- Carnitine is important for fatty acid metabolism, cell membrane stabilization, cellular repair
- Recent Cochrane review
  - Carnitine supplementation in the treatment of dialysis-related carnitine deficiency is not currently supported



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Knowledge Check

- Which of the following is true about macronutrients in renal dysfunction?
  a) Carbohydrate needs are substantially increased with AKI
  b) Protein is lost with renal replacement therapy
  c) Protein dosing should always be restricted in hospitalized patients with AKI
  d) Exogenous energy sources do not need to considered when prescribing nutrition support to ICU patients with renal dysfunction

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Learning Objectives

- Discuss the effects of renal replacement therapy on energy and protein requirements of critically ill patients.
- Evaluate electrolyte derangements seen with renal dysfunction and different modes of renal replacement.
- Identify micronutrient deficiencies common to critically ill patients on renal replacement therapy and discuss potential mitigation strategies.

Electrolyte Derangements seen with Kidney Failure

- Sodium
  - <2300 mg/day in CKD $\pm$ iHD/PD
- Potassium
  - < 40 mg/kg/day (or < 1 mEq/kg/day) if serum level is elevated in CKD $\pm$ iHD/PD
  - Low potassium diet 2000-3000 mg/day
- Magnesium
  - Dietary Reference Intake
- Phosphate
  - 800-1000 mg/day in CKD $\pm$ iHD/PD
  - Phosphate binders if persistently high
- Calcium
  - 1.5 g/day in CKD
  - <2 g/day in CKD + iHD/PD
- Metabolic acidosis
  - Supplement if bicarbonate <22 mmol/L

Renal Specific Enteral Formulas

- Reduced
  - Sodium
  - Potassium
  - Magnesium
  - Phosphorus
  - Water
- Useful when on iHD
- Unnecessary when on CRRT

Electrolyte Control with RRT

- Dialysate
  - Sodium 135-145 mEq/L
  - Potassium 0-4 mEq/L
  - (Calcium 2.5-3.5 mEq/L)*
  - Magnesium 0.5-0.75 mEq/L
  - Chloride 98-124 mEq/L
  - Bicarbonate 30-40 mEq/L
  - Dextrose 11 mEq/L
- Replacement Fluid
  - Sodium 140 mEq/L
  - Potassium 0-4 mEq/L
  - Calcium 3.0 mEq/L
  - Magnesium 1.0 mEq/L
  - Bicarbonate 35 mEq/L

*calcium free-dialysate is used with citrate anticoagulation

Potassium

Dialysate/Replacement Fluid
Refeeding Syndrome
Residual Renal Function
Medications

AKI/CKD
Tissue Catabolism
Potassium Intake
Medications

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Electrolyte Abnormalities with CRRT

- Citrate Anticoagulation
  - Sequesters magnesium with calcium
  - Risk for hypomagnesemia and hypocalcemia
  - Post-filter magnesium and calcium infusions
- Phosphorus
  - Traditionally not in dialysate
  - Rapidly removed with RRT (CRRT >>>>iHD)
  - Aggressive supplementation needed if phosphorus free dialysate
  - Provider needs to be aware when CRRT is initiated, discontinued or interrupted

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Knowledge Check

- What electrolyte(s) need to be added post-filter if citrate anticoagulation is used?
  a) Calcium
  b) Magnesium
  c) Phosphorus
  d) Potassium

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Learning Objectives

- Discuss the effects of renal replacement therapy on energy and protein requirements of critically ill patients.
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Micronutrient Deficiencies

- Due to
  - Inadequate dietary intake
  - Impaired absorption
  - Altered metabolism and utilization
  - Increased losses
- Fah et al. Study of 106 patients:
  - Micronutrient deficiency present in 90% exposed to CRRT
  - Micronutrient deficiency present in 61% no exposed to CRRT
- Systemic inflammation makes laboratory assessment less reliable

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Micronutrient Deficiencies with Renal Dysfunction

- CKD stage 3-5
  - Water soluble vitamin supplementation
  - Avoid excessive fat-soluble vitamins
  - Avoid vitamin C $\geq$ 500 mg/day
- ICU patients
  - Not on RRT
    - standard multivitamin preparations unless deficiencies identified
  - RRT, particularly CRRT
    - Additional supplementation may be needed
    - Losses into effluent
    - Adsorption by dialysis tubing and membranes

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Micronutrient Deficiencies with RRT

- Dependent on
  - RRT modality
    - CRRT has highest solute removal
    - Convection based RRT >>> diffusion based RRT
  - RRT dose
  - RRT duration
    - Particularly > 7-10 days of CRRT

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Micronutrient Deficiencies with RRT

- Found in Effluent
  - Thiamine
  - Pyridoxine
  - Folic acid
  - Ascorbic acid
  - Chromium
  - Copper
  - Manganese
  - Selenium
  - Zinc
- Not in Effluent
  - Fat-soluble vitamins (ADEK)

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Thiamine (B_1)

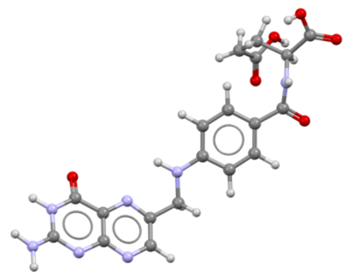
- Deficient in 20% of ICU patients (higher in CRRT patients)
  - Total body store ~25-30 g
- Testing
  - Whole blood thiamine diphosphate- affected by intake and inflammation
  - Thiamine pyrophosphate- less available but not affected by acute phase response
- Recommendations on CRRT: 100 mg/day of thiamine
  - Lose 4 mg/day with CRRT; 1.1 mg per iHD session
  - Only 2-4 mg/L in high protein renal enteral formulas
  - Only 6 mg/dose of standard PN multivitamin

Pyridoxine (B_6)

- Prevalence
  - Deficiency 24-26% om ESRD patients on iHD
  - Study of 106 ICU patients, deficiency in 69.2 patients after 20 days on CRRT
- Testing
  - Plasma pyridoxal 5-phosphate level
  - Red cell pyridoxal 5-phosphate level – more reliable in inflammation
- Recommendations on CRRT: 100 mg/day
  - Pyridoxine loss 0.02 mg/day (13.6%) after 3 days of CRRT
  - High protein renal enteral formula 8 mg/L
  - PN multivitamin 6 mg/dose

Folate (B_9)

- Prevalence: 2-19% deficiency among critically ill
- Testing
  - Serum folate- need to be fasting
  - Red blood cell folate- reduced in patients with a vitamin B12 deficiency
  - Plasma homocysteine level- affected by age, renal function, other B vitamin deficiencies
- Recommendations on CRRT: 1 mg/day folate
  - Lose 0.3 mg/day of folic acid
  - Recommended for iHD or CRRT
  - High protein renal enteral formulas contain 0.75-1 mg/L
  - PN multivitamin 0.6 mg/dose



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Vitamin C (Ascorbic Acid)

- Present in 80% critically ill receiving CRRT
- Testing:
  - Plasma vitamin C levels decrease during acute phase response
- Recommendations in CRRT: 250 mg/day
  - 75-100 mg/day for iHD;
  - Lose 68-93 mg/day
  - High –protein renal enteral formulas 90-100 mg/L
  - PN multivitamins 200 mg/dose
- Excess of 200 mg/day limited due to increased risk for oxalate crystal
  - But 2g/day may be needed to maintain stores on CRRT and high doses in the short term do not pose an increased risk for oxalate crystal production

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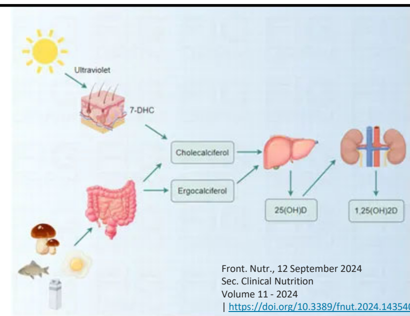
Vitamin D



Front. Nutr., 12 September 2024
Sec. Clinical Nutrition
Volume 11 - 2024
| https://doi.org/10.3389/fnut.2024.1435403

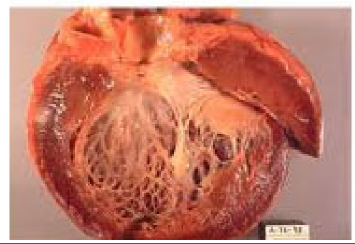
- Prevalence: ~70-85% in CKD;
  - Decreased 25D in AKI;
    - Decreased intake
    - Sequestered with inflammation
  - Decreased conversion of 25D to 1,25D by the damaged kidney
- Recommendations in CRRT: Supplement if deficient (100-125 mcg/day)
  - High protein renal enteral formulas provide 10-30 mcg/L
  - PN multivitamins contain 5 mcg of either ergocalciferol (D_2) or cholecalciferol (D_3) per dose
- Deficient patients should be supplemented to achieve 25D ≥ 30 ng/ml
  - Ergocalciferol, cholecalciferol
  - Calcifediol (25D itself)
  - Vitamin D analogs (1,25D; does not require activation from the kidney)

Copper

- Prevalence: 60% CRRT patients have copper deficiency
- Monitor level especially if on CRRT > 2 weeks
  - Levels increase during inflammation as ceruloplasmin, its transport protein, is a positive acute phase reactant
  - Normal serum copper in the setting of inflammation does not rule out deficiency
- Recommendations in CRRT: 3 mg/day to maintain serum levels if on CRRT ≥ 2 weeks
  - High protein renal formulas provide ~2 mg/L
  - PN trace element formulations contain 0.3 mg/dose cupric sulfate

Selenium

- Patients on chronic RRT have lower serum selenium than controls
- Testing:
  - RBC selenium- not affected by acute phase response
  - Serum selenium- decreases with acute phase response
- Recommendations in CRRT: supplement 50-200 mg/day
  - 68-84% of selenium depleted during CRRT
  - High protein renal formulas provide 60-100 mg/L
  - PN trace elements 60 mg/dose as selenious acid



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Knowledge Check

- Which micronutrient deficiency can be reliably diagnosed in patients on CRRT?
  a) Vitamin C
  b) Folate
  c) Copper

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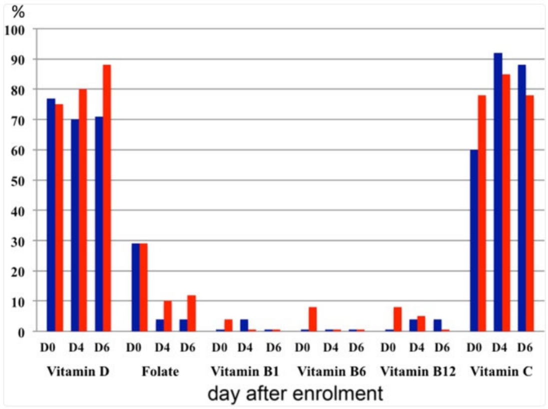
Micronutrient Deficiency is Common in Critically Ill



Proportion of patients with plasma concentrations of vitamins below the reference range. CRRT patients in blue; severe AKI patients who were not treated with CRRT in red.

Ostermann, M., Summers, J., Lei, K. *et al.* Micronutrients in critically ill patients with severe acute kidney injury – a prospective study. *Sci Rep* **10**, 1505 (2020).

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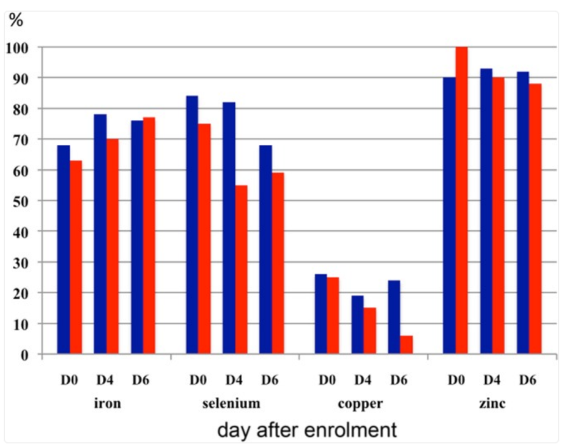
Micronutrient Deficiency is Common in Critically Ill



Proportion of patients with plasma concentrations of trace elements below the reference range. CRRT patients in blue; severe AKI patients who were not treated with CRRT in red.

Ostermann, M., Summers, J., Lei, K. *et al.* Micronutrients in critically ill patients with severe acute kidney injury – a prospective study. *Sci Rep* **10**, 1505 (2020).

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Original article

Micronutrient deficie

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REVIEW

What do we know about micronutrients in critically ill patients? A narrative review

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Final Thoughts

- AKI is common among critically ill patients
- There is ongoing debate surrounding optimal energy and protein provision to critically ill patients
- Micronutrient deficiencies are common among critically ill patients

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CRRT

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Final Thoughts

- Give
  - Increased protein
  - Thiamine 100 mg/day
  - Pyridoxine 100 mg/day
  - Folate 1 mg/day
  - Vitamin C 250 mg/day
  - Vitamin D 100-125 mcg/day
    - If deficient
  - Copper 3 mg/day
    - If on CRRT > 2 weeks
  - Selenium 50-200 mcg/day
- Lose
  - Protein 5-20 g/day
  - Thiamine 4 mg/day
  - Pyridoxine 0.02 mg/day
  - Folate 0.3 mg/day
  - Vitamin C 68-93 mg/day

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A Cautionary Tale

- 65 yo male admitted following heart transplant and LVAD explant
- Complicated by heart failure requiring redo transplant
- CRRT 2/11-3/22, 5/12-5/15, 6/19-7/4, 7/31-9/29, 10/3- 11/16, 11/30-1/9, 1/26-2/15
- ~221/371 days on CRRT

	Latest Reference Range & Units	12/27/22 05:18	01/02/23 05:57
CHROMIUM (ARUP)	<=5.0 ug/L	**28.8 (H)**	**23.1 (H)**

(H): Data is abnormally high
******toxicity may result from receiving prolonged IVF and dialysis***

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Thank you

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