# Innovations in Caring for Patients with Electrolyte Disorders
# Part I

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- None

# Objectives

Understand the critical determinants of serum sodium during renal replacement therapy.

Understand the application of a variety of techniques to achieve controlled correction of serum sodium

# Nephrology Consult

## History

A 54-year-old female with:

- Nausea, decreased oral intake for few weeks
- Decreased urine output for few days
- Confusion, decreased responsiveness, and generalized weakness x 1week

## Physical Exam

- T 37.1, BP 140/80, HR 106, RR 21, pulse ox 94% on RA, W 50 Kg
- Gen: Appeared older than her stated age, malnourished
- ENT: Oral mucosa moist, no JVD
- Lungs: Bilateral lower lung crackles. Heart: RRR
- Neuro: Generalized weakness, she was unable to ambulate with no focal deficits
- Psych: Alert but confused

# Nephrology Consult

**Initial Laboratory Data**

**Na 96** | K 5.6 | Cl 64 | $HCO_3$ 16
BUN 51 | Cr 9.9
Glu 107 | AG 16

PH 7.36 | $PCO_2$ 27.9 | $HCO_3$ 15 | $PO_2$ 57.5

# Nephrology Consult

**Assessment and Plan**

Acute kidney injury

- Hyperkalemia
- Acidosis
- Hypoxemia with clinical evidence of fluid overload

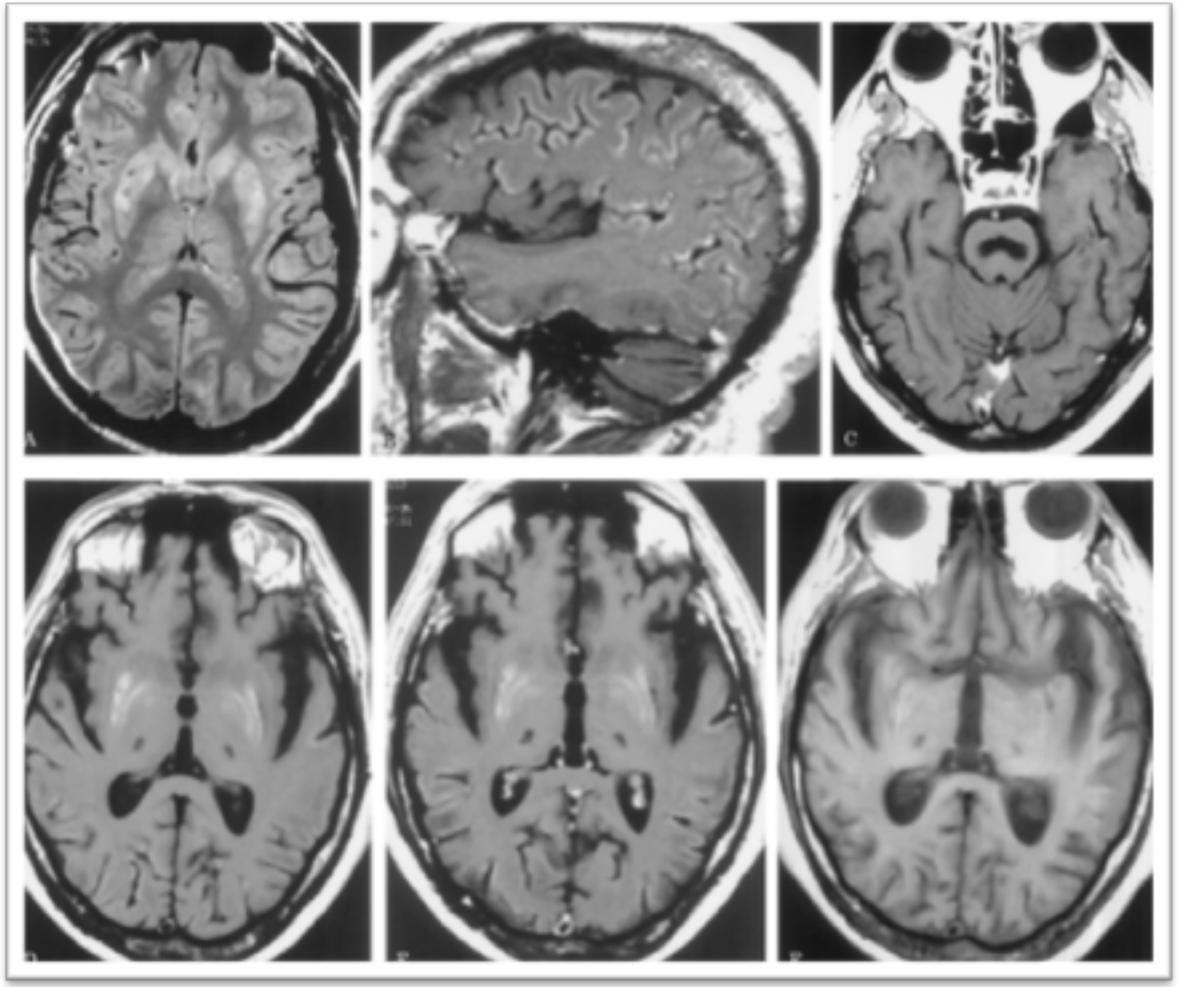
Patient with several indications for RRT initiation

Severe hyponatremia

# Hyponatremia

- May coexist with AKI, CKD or ESRD.[1]
- Inappropriate RRT prescription in patients with co-existing hyponatremia may result in rapid correction of $Na^+$ , producing permanent neurologic sequelae (osmotic demyelination syndrome).
- Rates of correction with RRT may far exceed corrections caused by hypertonic infusions or renal free water loss.

24 hrs
**SNa**: 100 → 116 mM
13 days later: Quadriparesis, Areflexia[2]




1. Kovesdy CP, *NDT.* 2012

2.Calakos: Neurology. 2000:55(7):1048-1051

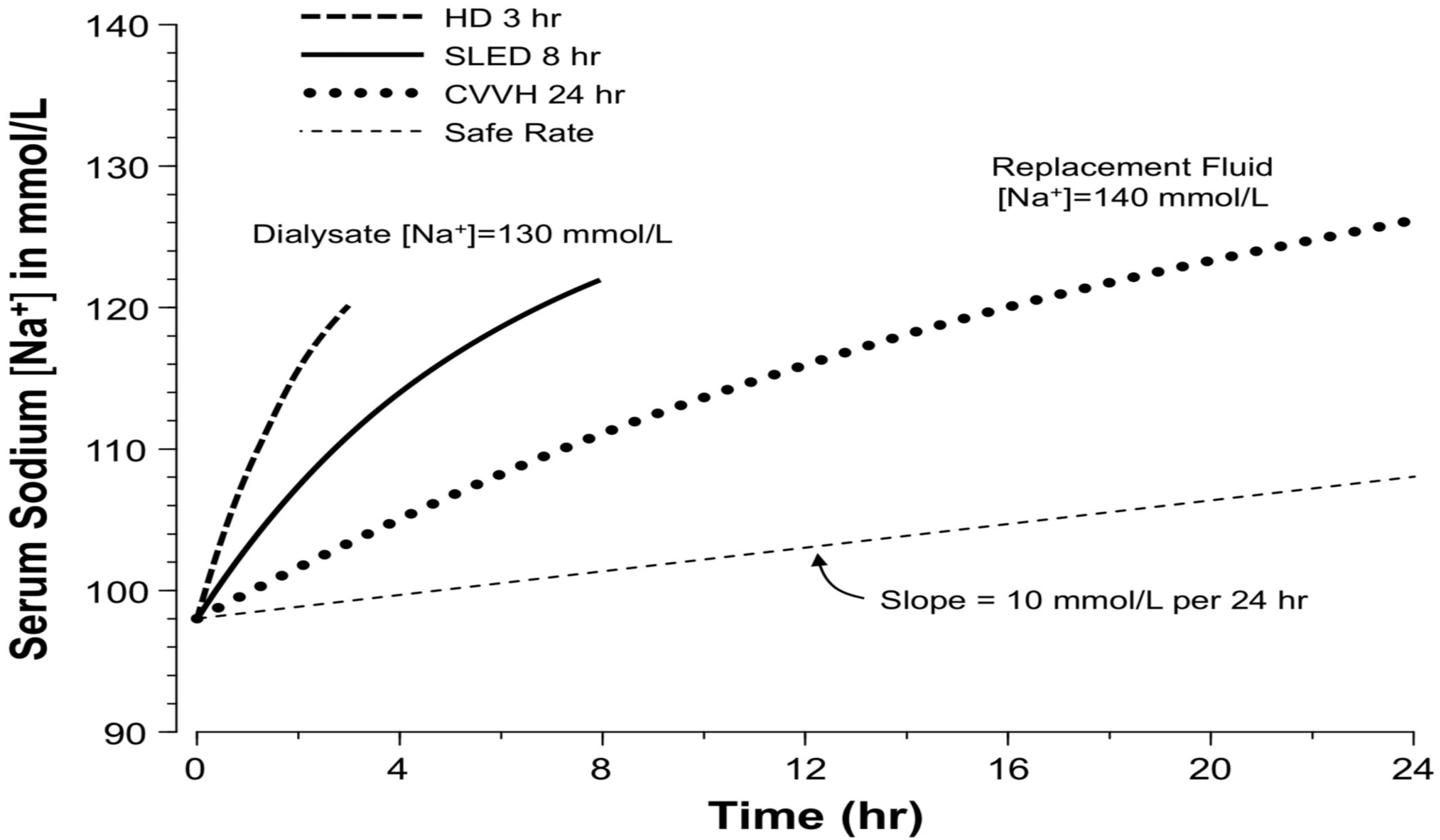
# Recommended Rate of correction of chronic hyponatremia

- 2013 American Expert Panel Recommendations
  - Serum sodium correction limit of 10–12 mEq/L in any 24-hour for patients at average risk of ODS
  - Serum sodium correction limit of 8 mEq/L in any 24-hour period for patients at high risk of ODS (alcohol use, malnutrition, serum Na< 105 and liver disease)

- The guidelines do not address the unique situation where hyponatremia and dialysis requiring kidney disease coexist

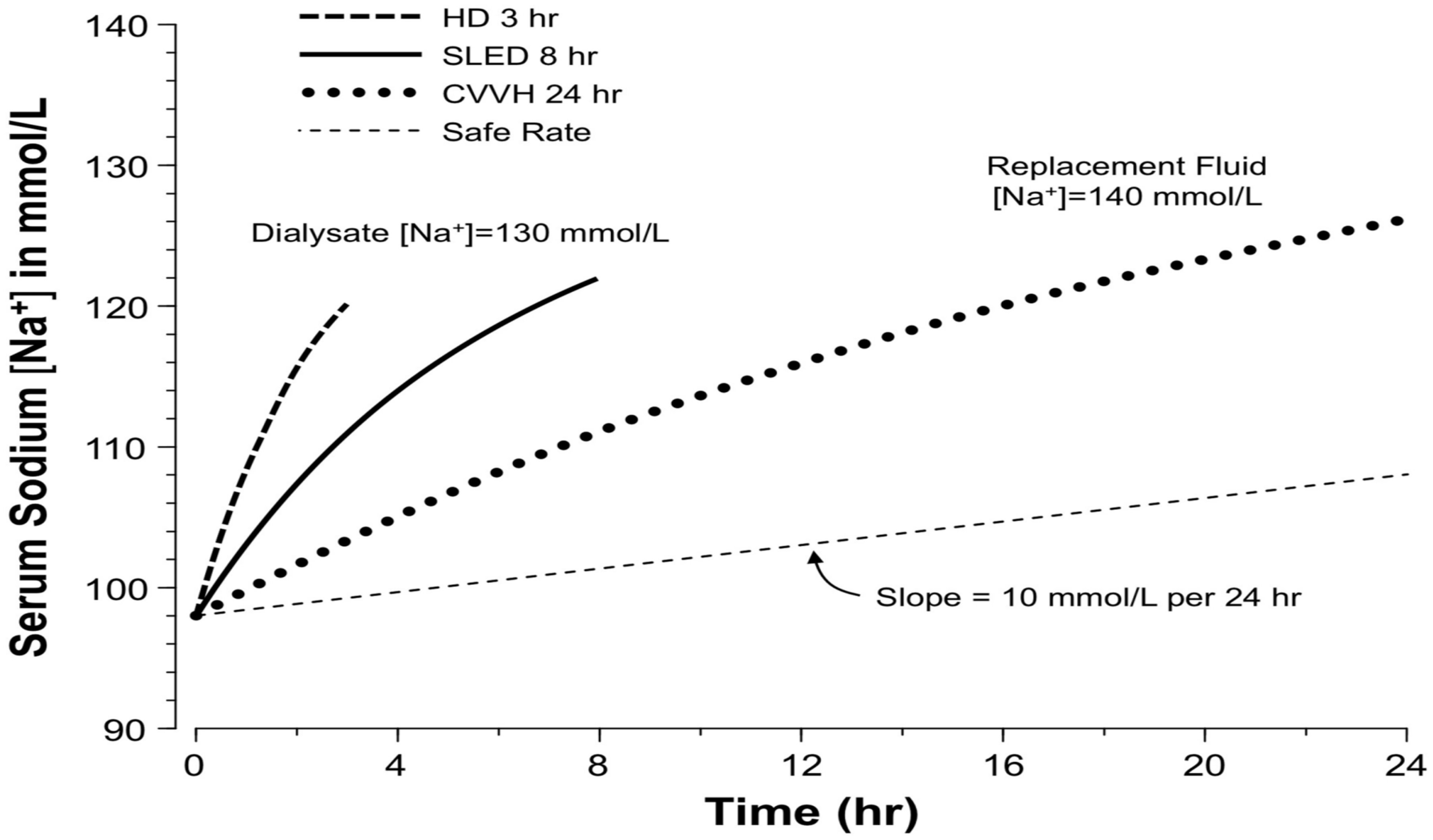
# Which of the following RRT prescriptions would increase serum sodium changes > 10 mEq/L

A. Hemodialysis: 3 hours, dialysate Na 130 mEq/L, Qb 200 ml/min, Qd 400 ml/min
B. SLED: 8 hours, dialysate Na 130 mEq/L, Qb 200 ml/min, Qd 100ml/min
C. CVVH: 24 hours, RF Na 140 mEq/L, QRF (post) 1.2 L/hr, CRRT dose (30ml/kg/hr)
D. A and B
E. None of the Above
F. All of the Above




Yessayan L, Yee J, Frinak S, Szamosfalvi B. Treatment of severe hyponatremia in patients with kidney failure: role of continuous venovenous hemofiltration with low-sodium replacement fluid. Am J Kidney Dis. 2014

$$Na_{(t)} = Na_0 + \left(Na_{CRRT\,fluid} - Na_0\right) \times \left(1 - e^{\frac{-D \times t}{V}}\right)$$

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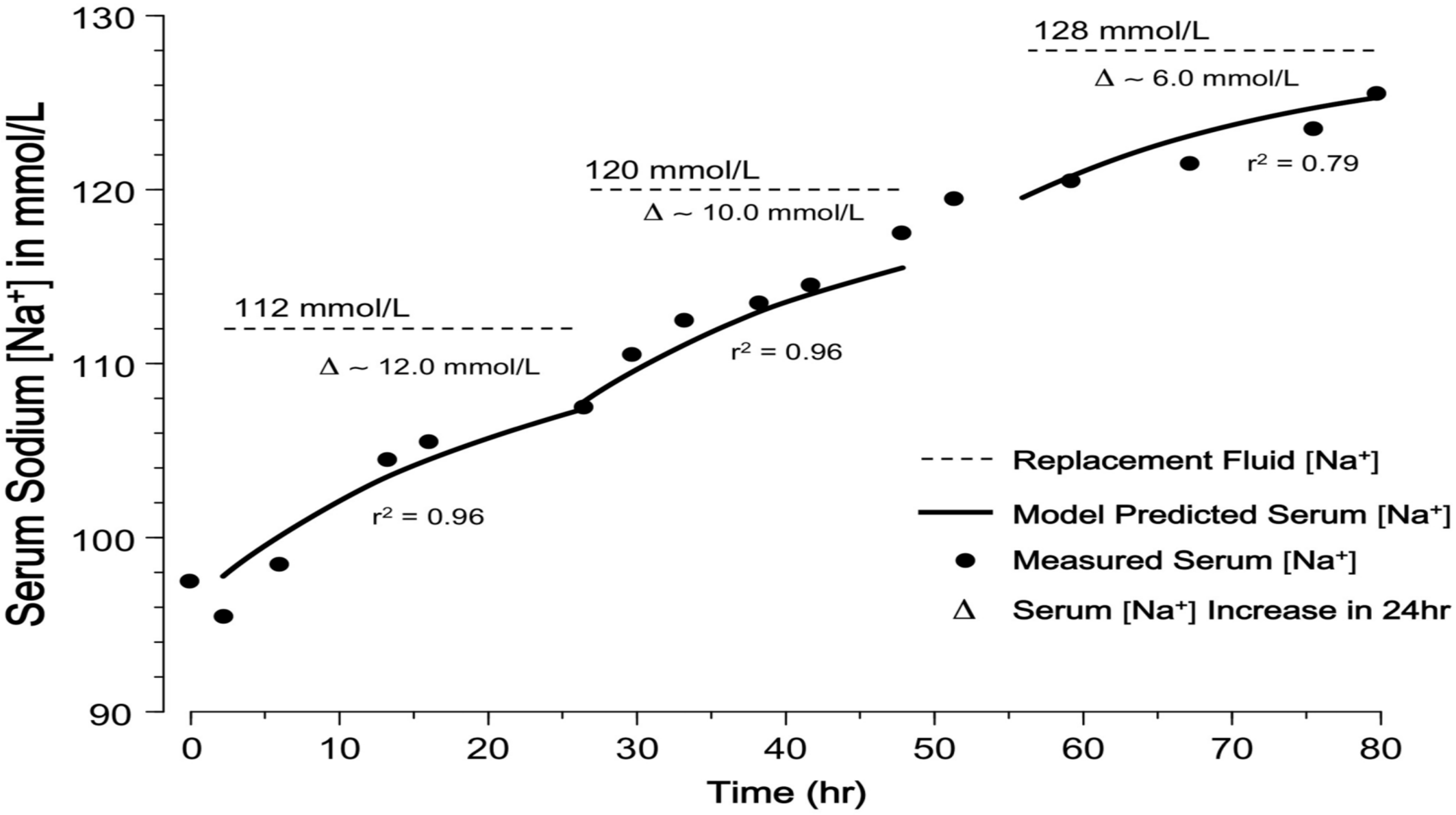
$$CRRTfluid\,[Na^+] = \frac{desired\,\Delta\,serum\,[Na^+]}{\left(1 - e^{-\frac{K\,X\,24\,h}{V}}\right)} + [Na^+]_i$$

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# Considerations When Managing Patients Who Require RRT With Concomitant Chronic Hyponatremia

# RRT Requiring Kidney Disease with Chronic Hyponatremia

$[Na^+]$ is 120−130 mEq/L

↓

**Intermittent hemodialysis**

Target KT/V ≤1.2

[dNa+] 130 mEq/L

$[Na^+]$ <120 mEq/L

↓

**CRRT**

Options

- CRRT with hypotonic CRRT fluids
- CRRT and 5% dextrose water
- CRRT ± dose adjustment

# Clearance

- Clearance (K): Volume of blood completely cleared from substance per unit time
- Expressed in units of volume . time $^{-1}$
- All things being equal, higher clearance will correct sodium faster

# Urea Clearance

**CRRT**

- ~ sum of dialysate, replacement fluids, (±ultrafiltration) (Adjusted for predilution if pre- replacement fluid used)

**Hemodialysis**

- Since dialysate rate > blood flow, can't be higher than blood flow
- Clearance ~ 250-300 ml/min (15-18 L/hr)
- Machines with online clearance technology (e.g. Kecn measured ionic dialysance)
- Clearance of a dialyzer for a set of QB and QD in countercurrent dialysis is available on the dialyzer brochure

# What Dialysance (D) Means

- Dialysance (D): Volume of blood completely equilibrated with dialysate per unit time
- Expressed in units of volume . time $^{-1}$
- Fresh dialysate contains sodium: use term dialysance
- Sodium and urea have similar solute transfer characteristics: (urea clearance= sodium dialysance)
  - Non protein bound
  - Molecular weight
  - Effective blood water flow

# Controlled Sodium Change by Applying Kinetic Principles

- Sodium and urea have similar solute transfer characteristics:
- Fixed-volume, single-pool sodium kinetic equation can be used
  - Applicable to daily clinical practice

$$[Na^+]_t = Na_0 + \left(Na_{CRRT\ fluid} - Na_0\right) \times \left(1 - e^{\frac{-D \times t}{V}}\right)$$

Yessayan et al. Management of dysnatremias with continuous renal replacement therapy. Semin Dial. 2021.

$$Na_{(t)} = Na_0 + \left(Na_{CRRT\ fluid} - Na_0\right) \times \left(1 - e^{\frac{-D \times t}{V}}\right)$$

| | |
|---|---|
| $Na_0$ | Initial serum sodium |
| $\boldsymbol{Na_{CRRT\ fluid}}$ | **CRRT Fluid sodium** |
| $V$ | Total body water |
| $t$ | Time on RRT |
| $\boldsymbol{D}$ | **Sodium dialysance ~ urea clearance** |

Yessayan L, et al. Am J Kidney Dis. 2014

$$Na_{(t)} = Na_0 + (Na_{CRRT\ fluid} - Na_0)\times\left(1 - e^{\frac{-D\times t}{V}}\right)$$

**Case #1.** Patient with $Na_0$ **100 meq/L** is prescribed a CVVH, replacement fluid rate 1.25 L/hr, CRRT fluid Na+ 140 mEq/L, body weight 50 kg (V 25 L). What is $[Na^+]_{24}$?

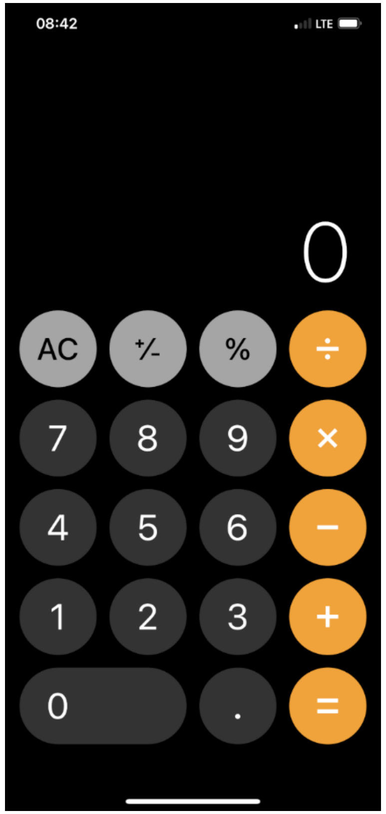
- Urea clearance ~ 1250 ml/h=1.25 L/h
- Assume sodium dialysance (D)=Urea clearance (K)
- Calculate $\frac{D\times t}{V}$ =(1.25 × 24)/25 = 1.2
- $e^{-1.2} = 0.3$ ***I will show you how to calculate***

$$Na_{(24)} = 100 + 40\times(1 - 0.3)$$

$$Na_{(24)} = 100 + 28 = 128$$

# How do I calculate $e^{-1.2}$ ?

1

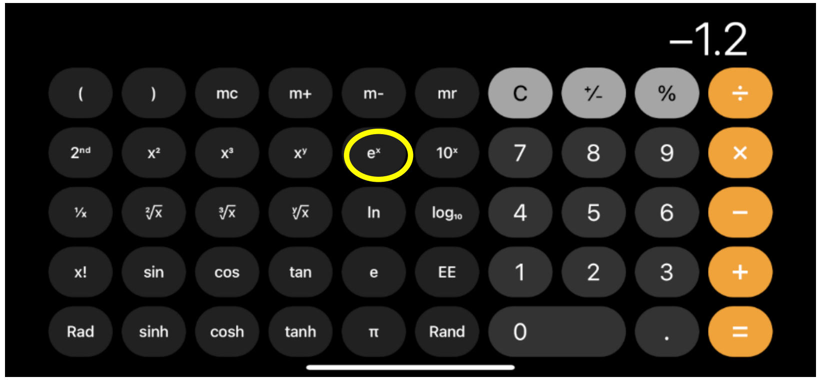



- Take the iphone out of your pocket
- Find the calculator icon
- Get to this screen!

2

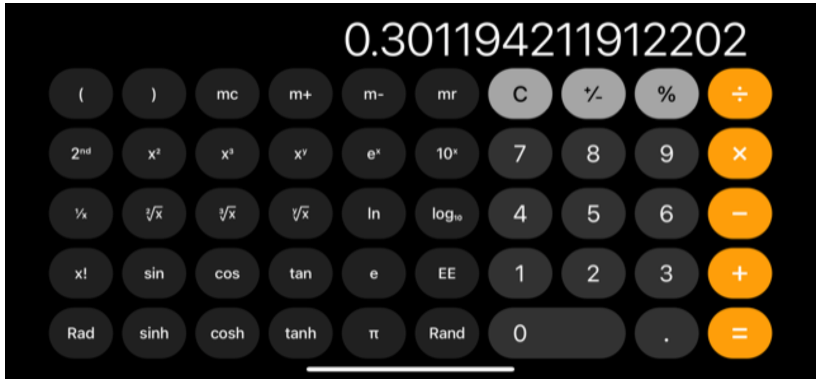

- Enter the KT/V value

3




- Rotate your screen 90 degrees
- Tap on $e^x$

4




- Celebrate you found your answer!

# Strategies to avoid overly rapid correction of chronic hyponatremia with CRRT:

I. **Diluting CRRT solutions based on kinetic principles**

II. Running separate dextrose water infusion

III. Regulating clearance (i.e. sodium dialysance)

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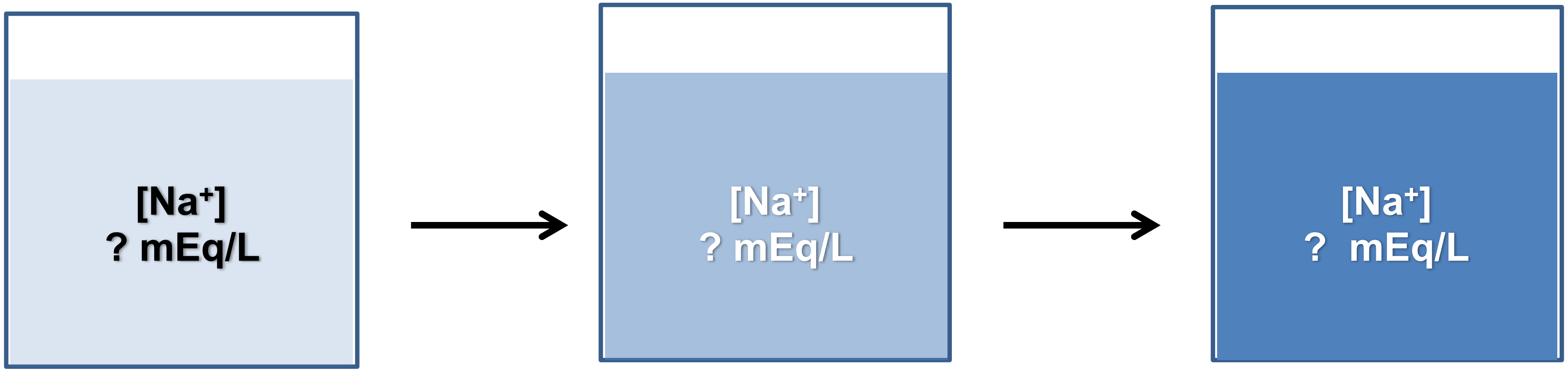
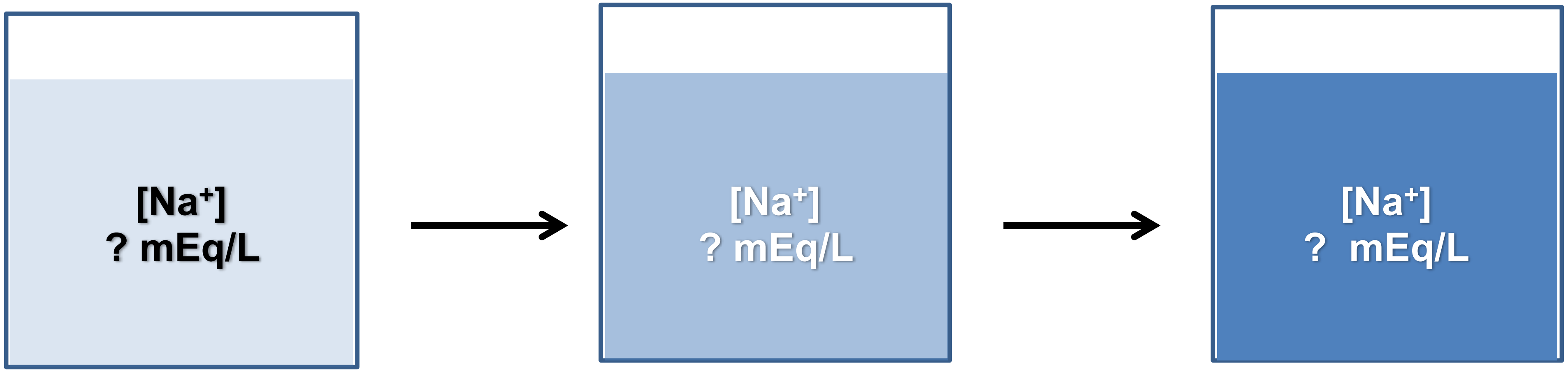
# CRRT with Hypotonic CRRT Fluid




- CRRT fluid bags with successively higher CRRT Na every 24 hours.
- Over-correction in 24 h avoided
- No readily available commercial hyponatric CRRT fluid bags

# CRRT with Hypotonic CRRT Fluid




- CRRT fluid bags with successively higher CRRT Na every 24 hours.
- To what concentration the CRRT bag must be diluted every 24 hours to achieve desired sodium for a particular patient and CRRT dose is estimated by an equation you don't need to memorize!
- https://kidneyguide.org/continuous-dialysis-calculators

# CRRT fluid $[Na^+]$ needed to maintain patient sodium within desired limits of correction

$$CRRT\,fluid\,[Na^+] = \frac{desired\,\Delta\,serum\,[Na^+]}{\left(1 - e^{-\frac{D \times t}{V}}\right)} + [Na^+]_i$$

Yessayan L, Yee J, Frinak S, Szamosfalvi B. Treatment of severe hyponatremia in patients with kidney failure: role of continuous venovenous hemofiltration with low-sodium replacement fluid. Am J Kidney Dis. 2014;64(2):305-310

**Case #2.** Patient with $Na_i$ **100 meq/L** is prescribed a CVVH, post filter replacement fluid rate 1.25 L/hr, body weight 50 kg (V 25 L). What CRRT fluid sodium is needed for desired serum [Na+] increase of 10 mEq/L in 24 h?

$$CRRT\,fluid\,[Na^+] = \frac{desired\,\Delta\,serum\,[Na^+]}{\left(1 - e^{-\frac{D\times t}{V}}\right)} + [Na^+]_i$$

$[Na^+]_i = 100$ $\quad$ $Desired\,\Delta\,serum\,[Na^+] = 10$ $\quad$ $D = 1.25\,\frac{L}{hr}$ $\quad$ $V = 25\,L$

$$\frac{D \times t}{V} = \frac{1.25 \times 24}{25} = 1.2$$

Yessayan L, Yee J, Frinak S, Szamosfalvi B. Treatment of severe hyponatremia in patients with kidney failure: role of continuous venovenous hemofiltration with low-sodium replacement fluid. Am J Kidney Dis. 2014;64(2):305-310

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$$\frac{D\times t}{V} = \frac{1.25\times 24}{25} = 1.2$$

$$e^{-1.2} = 0.3$$

$$CRRT\,fluid\,[Na^+] = \frac{10}{(1-0.3)} + 100 = 114\,mmol/L$$

Yessayan L, Yee J, Frinak S, Szamosfalvi B. Treatment of severe hyponatremia in patients with kidney failure: role of continuous venovenous hemofiltration with low-sodium replacement fluid. Am J Kidney Dis. 2014;64(2):305-310

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# Calculate dialysis dose or dialysate sodium to achieve target sodium

## Estimate the rate of serum sodium correction over 24 hours with changes in dialysis prescription.

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**BASELINE INFO**

INITIAL SODIUM

100 mmol/L

TARGET SODIUM

110 mmol/L

BODY FLUID ESTIMATE

25 liters

**SOLVE FOR DIALYSATE SODIUM**

SPECIFY EFFLUENT RATE

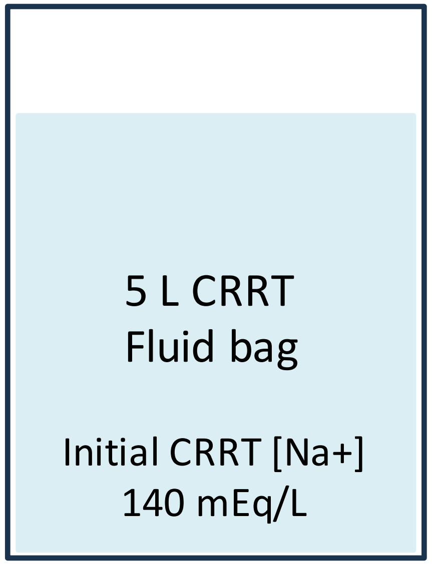
1.25 liters/hour

DIALYSATE SODIUM

**114 mmol/L**

# Methods of Dilution

*Add sterile water*




Exchange specified volume of CRRT fluid with an equal volume of sterile free water

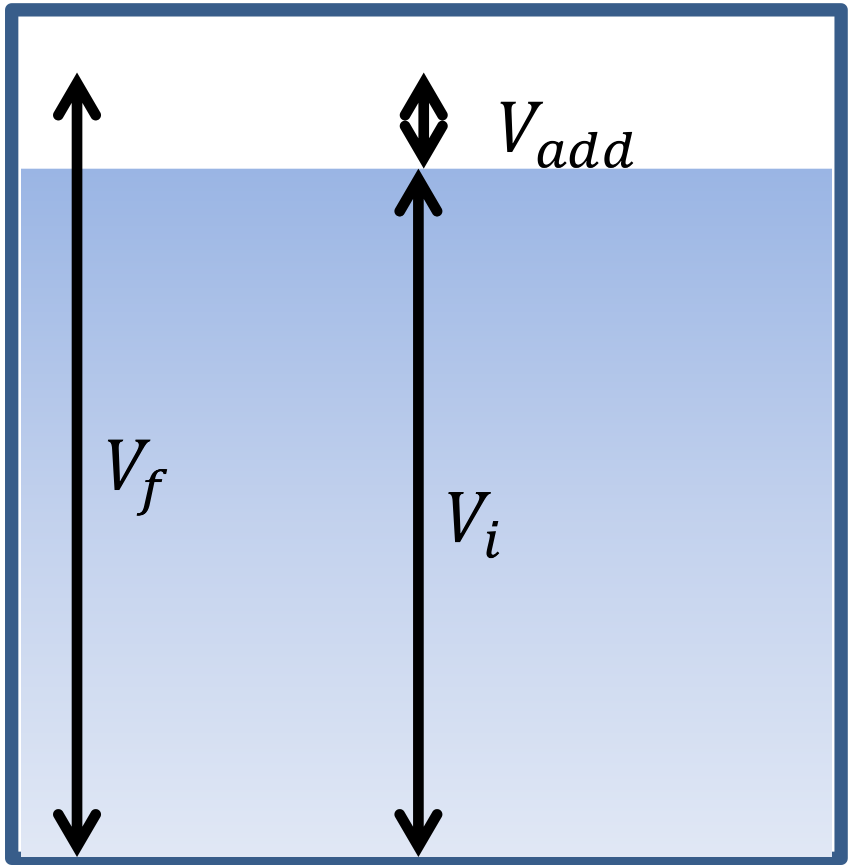
This method is useful when there is a concern for the commercial CRRT solution bag not having the extra space to accommodate the needed additional water volume (typically > 1 L)

$$Volume\ to\ add = \frac{initial\ CRRT[Na^{+}] \times CRRT\ initial\ volume}{desired\ CRRT[Na^{+}]} - CRRT\ initial\ volume$$

$$Volume\ to\ exchange = CRRT\ fluid\ volume - \frac{desired\ CRRT[Na^{+}] \times CRRT\ fluid\ volume}{initial\ CRRT[Na^{+}]}$$

# Addition of Sterile Free Water

$$V_{add} = \frac{CRRT\ [Na^{+}]_{i} \times V_{i}}{CRRT\ [Na^{+}]_{f}} - V_{i}$$



# Addition of Sterile Free Water

$$V_{add} = \frac{CRRT\ [Na^{+}]_{i} \times V_{i}}{CRRT\ [Na^{+}]_{f}} - V_{i}$$

5 L CRRT bag, CRRT Na+ 140 mEq/L and want to dilute to 120 mEq/L

$$V_{add} = \frac{140 \times 5}{120} - 5$$

$=0.833\ \mathrm{L}$

$833\ \mathrm{mL}$

Yessayan L et al. Am J Kidney Dis. 2014

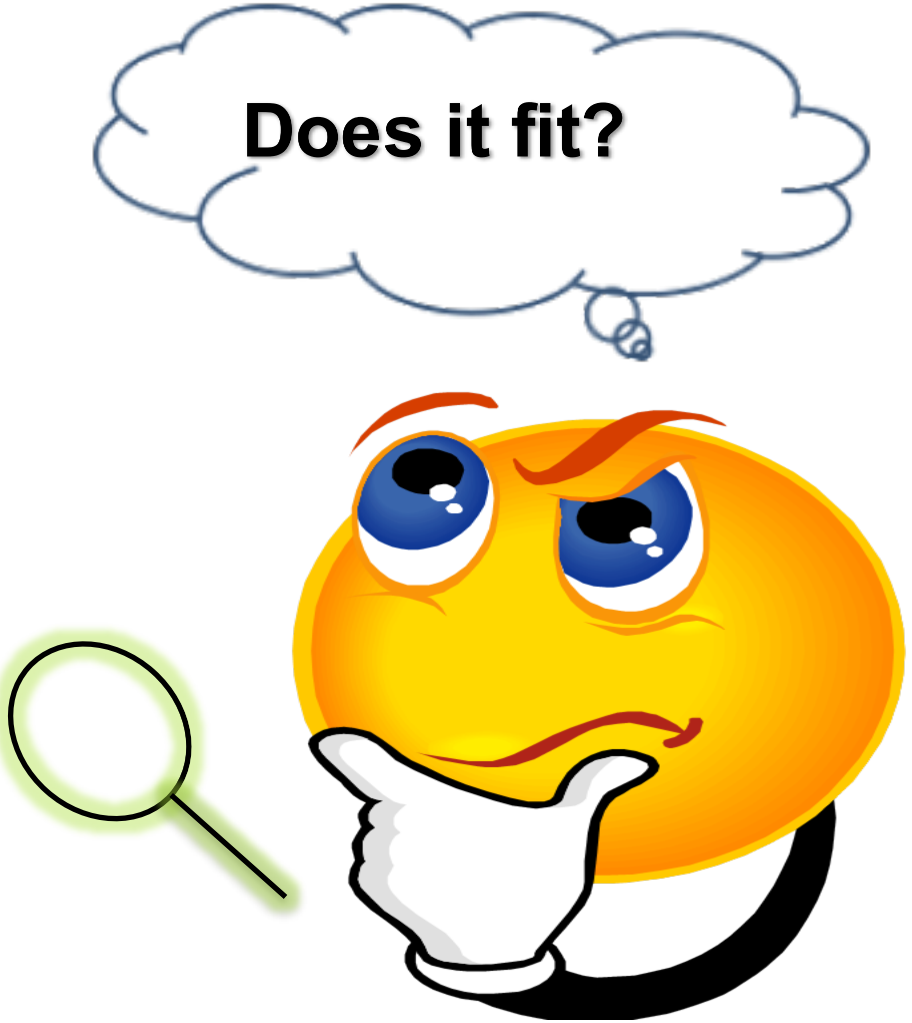
# Addition of Sterile Free Water

$$V_{add} = \frac{CRRT\ [Na^{+}]_{i} \times V_{i}}{CRRT\ [Na^{+}]_{f}} - V_{i}$$

5 L bag, 140 mEq/L and want to dilute to 100 mEq/L

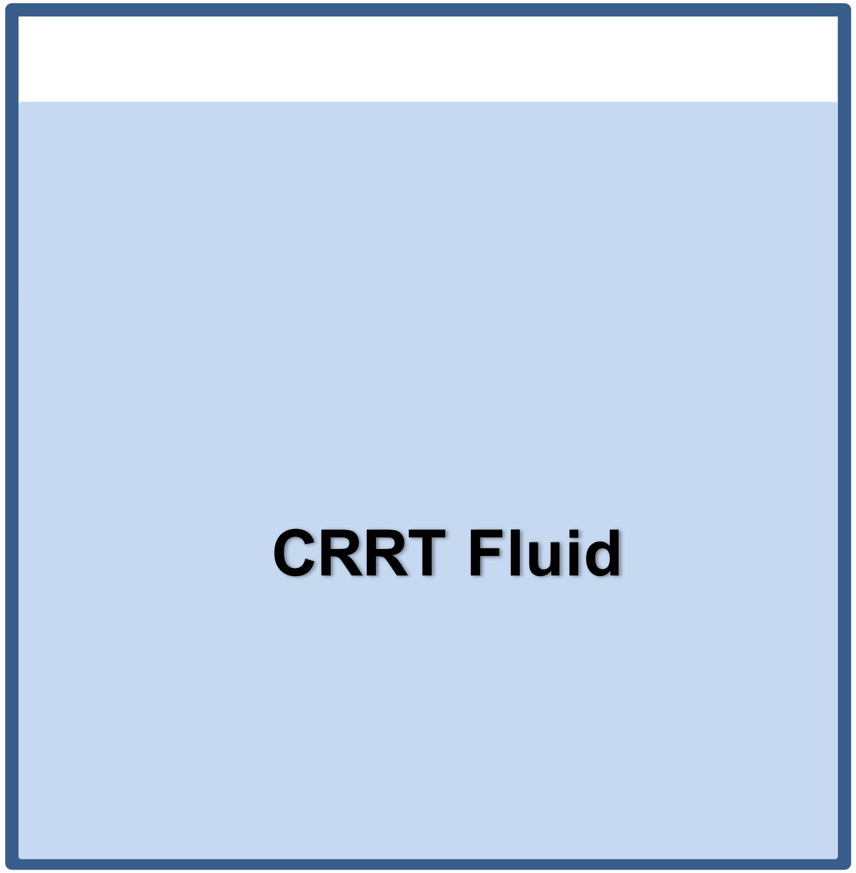
$$V_{add} = \frac{140 \times 5}{100} - 5 \qquad = 2\ \mathrm{L} \qquad 2000\ \mathrm{mL}$$

# If the Volume Doesn't Fit, Must You Quit?

# Exchanging a Certain Volume of CRRT fluid with Sterile Free Water

$$\textit{Volume to exchange} = V_i - \frac{CRRT\ [Na^+]_f}{CRRT\ [Na^+]_i} \times V_i$$




Yessayan L, et al. Am J Kidney Dis. 2014

# Exchanging CRRT Fluid with Free Water

$$\boldsymbol{Volume\ to\ exchange}$$

$$= V_i - \frac{CRRT\ [Na^+]_f}{CRRT\ [Na^+]_i} \times V_i$$

5-L, 140 mEq/L to 100 mEq/L

$$5\ L - \frac{[100] \times 5\ L}{[140]}$$ $=1.428$ L  1428 ml

| Desired [Na+] (mEq/L ) | Free Water to Add (mL) | Free Water Exchange (mL) |
| --- | --- | --- |
| 130 | 385 | 357 |
| 125 | 600 | 536 |
| 120 | 833 | 714 |
| 115 | 1087 | 899 |
| 110 | 1364 | 1071 |
| 105 | 1667 | 1250 |
| 100 | 2000 | 1429 |

**RF bag volume = 5 L for calculations above**

Yessayan L, et al. Am J Kidney Dis. 2014

**Table . Effect of adding different volumes of water to 5 Liter replacement fluid bag (NxStage PureFlow dialysate solutions RFP 401)**

| Volume ml | Sodium mEq/L | Potassium mEq/L | Bicarbonate mEq/L | Calcium mEq/L | Magnesium mEq/L | Chloride mEq/L |
|---|---|---|---|---|---|---|
| 0 | 140 | 4.0 | 34 | 3.0 | 1.00 | 113 |
| 250 | 133 | 3.8 | 32 | 2.9 | 0.95 | 108 |
| 500 | 127 | 3.6 | 31 | 2.7 | 0.91 | 103 |
| 750 | 122 | 3.5 | 30 | 2.6 | 0.87 | 98 |
| 1000 | 117 | 3.3 | 28 | 2.5 | 0.83 | 94 |
| 1250 | 112 | 3.2 | 27 | 2.4 | 0.80 | 90 |

Yessayan L, et al. Am J Kidney Dis. 2014

# Strategies to avoid overly rapid correction of chronic hyponatremia with CRRT:

I. Diluting CRRT solutions based on kinetic principles

**II. Running separate dextrose water infusion**

III. Regulating clearance (i.e. sodium dialysance)

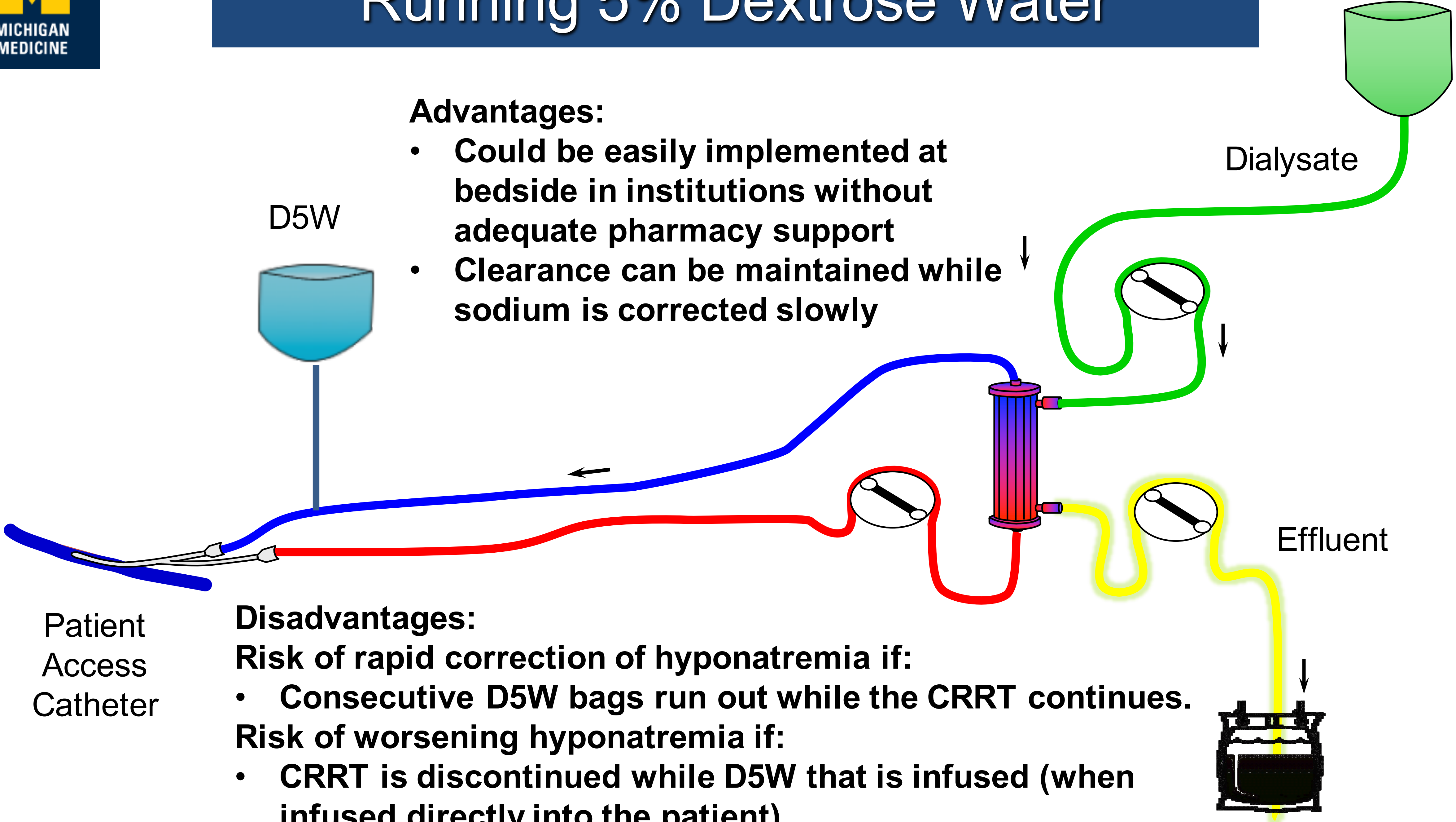
Yessayan et al. Management of dysnatremias with continuous renal replacement therapy. Semin Dial. 2021.

Yessayan et al. Continuous Renal Replacement Therapy for the Management of Acid-Base and Electrolyte Imbalances in Acute Kidney Injury. Adv Chronic Kidney Dis. 2016

# Running 5% Dextrose Water

**Advantages:**

- **Could be easily implemented at bedside in institutions without adequate pharmacy support**
- **Clearance can be maintained while sodium is corrected slowly**




**Disadvantages:**

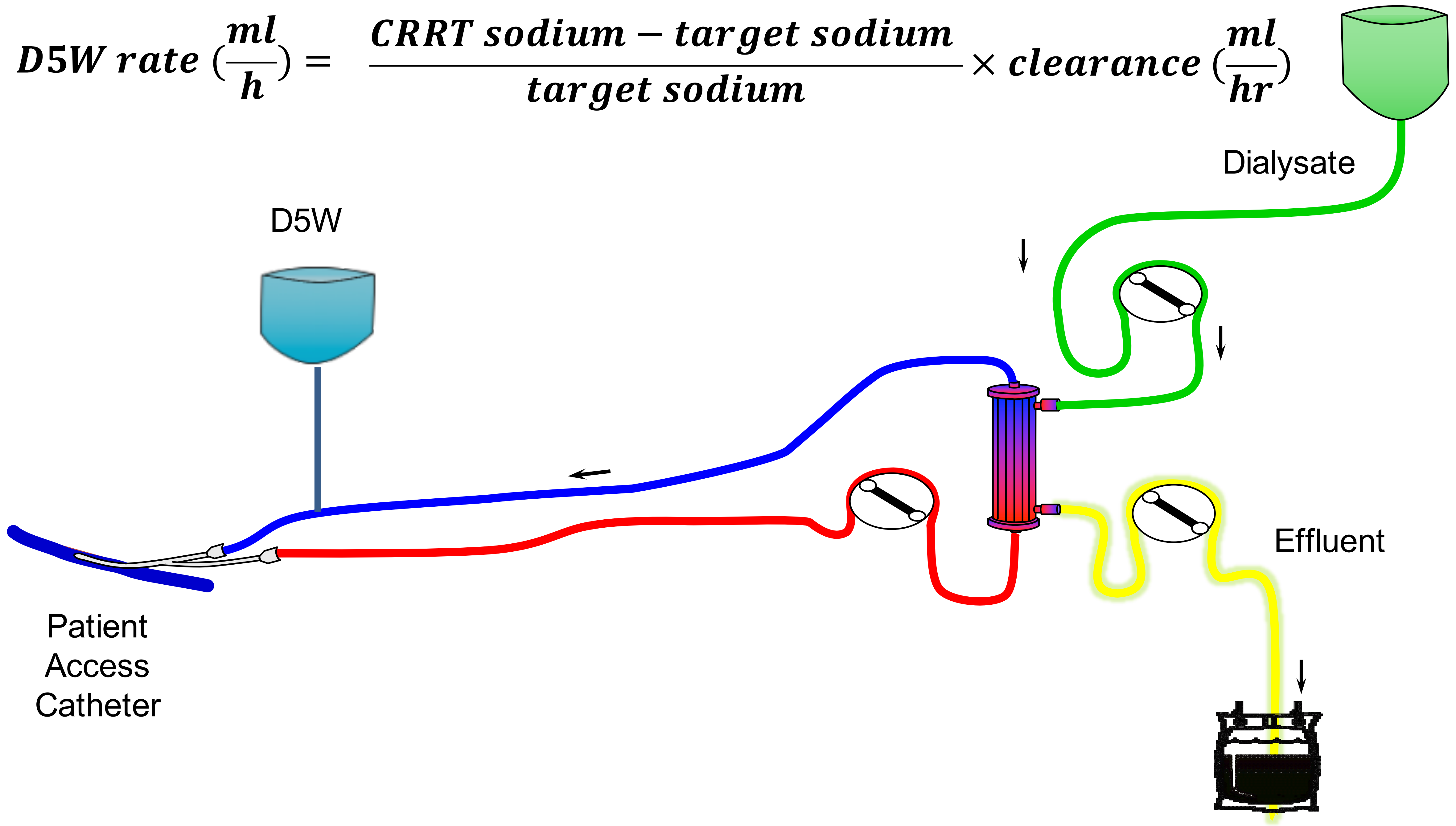
**Risk of rapid correction of hyponatremia if:**

- **Consecutive D5W bags run out while the CRRT continues.**

**Risk of worsening hyponatremia if:**

- **CRRT is discontinued while D5W that is infused (when infused directly into the patient)**

$$D5W\ rate\ \left(\frac{ml}{h}\right) = \frac{CRRT\ sodium - target\ sodium}{target\ sodium} \times clearance\ \left(\frac{ml}{hr}\right)$$



# Running 5% Dextrose Water Infusion

50-year-old woman (weight 70 kg), presenting with initial serum sodium 105 mEq/L. She will be initiated on CRRT (CVVHDF with post-filter RF, DF 1000 ml/hr, RF 1000 ml/hr) and CRRT fluid sodium 140 mEq/L. At what rate should 5% dextrose run to keep target serum sodium at 115 mEq/L?

$$D5W\ rate\ (\frac{ml}{h}) = \frac{CRRT\ sodium - target\ sodium}{target\ sodium} \times clearance\ (\frac{ml}{hr})$$

$$D5W\ rate\ \left(\frac{ml}{hr}\right) = \frac{140 - 115}{115} \times\ 2000\ \frac{ml}{hr} \quad = 435$$

- The initial D5W rate is started at 85-90% of that suggested by equation ( ~ 380 ml/hr) to account for not fully saturated effluent.
- The net ultrafiltration setting should be increased by the rate of the dextrose water.
- D5W adjusted every 6 to 8 hours based on laboratory data to stay within the desired limits of correction.

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# D5W Infusion Rate

Slow down serum sodium correction in patients with hyponatremia on continuous dialysis

**BASELINE INFO**

DIALYSATE SODIUM

140 mmol/L

TARGET SODIUM

115 mmol/L

EFFLUENT RATE

2.00 liters/hour

D5W Infusion Rate

**0.39 liters/hour**



Lenar Yessayan & Sevag Demirjian

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**III. Regulating clearance (i.e. sodium dialysance)**

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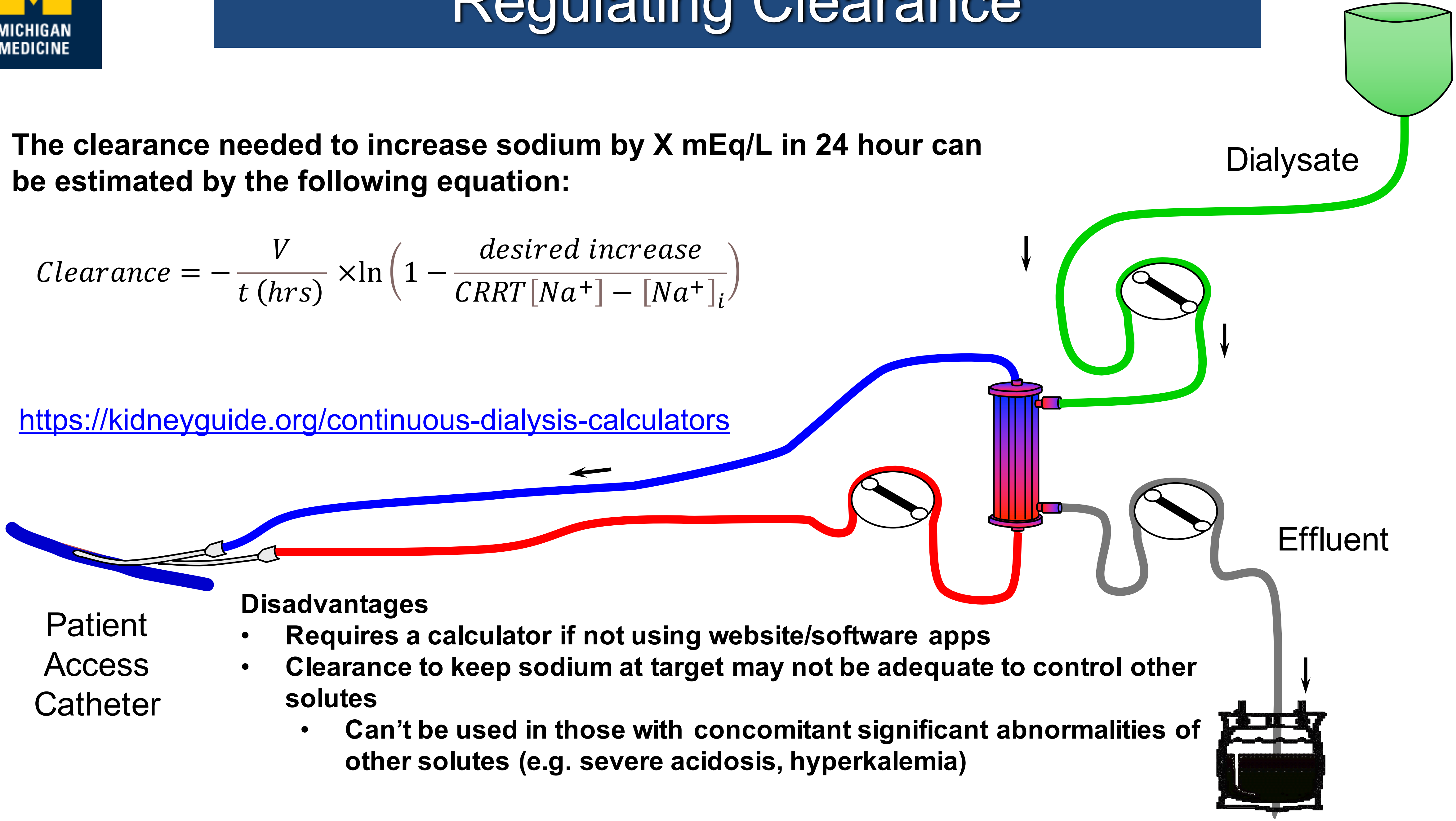
# Regulating Clearance

**The clearance needed to increase sodium by X mEq/L in 24 hour can be estimated by the following equation:**

$$Clearance = -\frac{V}{t\ (hrs)} \times \ln\left(1 - \frac{desired\ increase}{CRRT\,[Na^+] - [Na^+]_i}\right)$$

https://kidneyguide.org/continuous-dialysis-calculators




**Disadvantages**

- **Requires a calculator if not using website/software apps**
- **Clearance to keep sodium at target may not be adequate to control other solutes**
  - **Can't be used in those with concomitant significant abnormalities of other solutes (e.g. severe acidosis, hyperkalemia)**

# Regulating Clearance

- 80-kilogram woman (TBW=36 L) with initial sodium of 105 mEq/L with AKI who needs to be started on CRRT
- Desired increase in serum sodium corrected ~ 8 mEq/L in 24 hours
- CRRT fluid sodium at your disposal is 140 mEq/L. No pharmacy support to dilute your bag. Patient on high doses of insulin precluding dextrose water use.

$$Clearance = -\frac{V}{t\ (hrs)} \times \ln\left(1 - \frac{Desired\ Increase}{CRRT[Na^+] - [Na^+]_i}\right)$$

$$Clearance = -\frac{36}{24} \times \ln\left(1 - \frac{8}{25}\right) = 0.56\ L/hr\ or\ 560\ ml/hr$$

CVVHD= dialysate rate ~ 560 ml/hr

CVVH post-filter RF = ~ 560 ml/hr

CVVHDF with post-filter RF ~ sum of DF and RF ~ 560 ml/hr

# More complicated when using CRRT-RCA
# But not difficult! Extra Slides

**When using ACDA:**

The steady state serum sodium concentration will be few mEq/L higher than the dialysate/RF sodium concentration

- The extent it will be higher will depend on many variables:
  - Blood flow
  - RF/dialysate flow
  - Rate of ACDA
  - Other non isotonic fluid being administered

**Please Refer to paper "Yessayan et al. Management of dysnatremias with continuous renal replacement therapy. Semin Dial. 2021.**

# Summary

- All renal replacement modalities could be potentially harmful when used in a patient with severe hyponatremia.
- Controlled, predictable correction of severe hyponatremia is possible with CRRT.
- Embracing an analytical approach to the understanding of sodium fluxes during CRRT allows for a more regulated correction of serum sodium.

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# THANK YOU
# Questions?

**Email:**
**lenar@med.umich.edu**

For comprehensive review for management of dysnatremias refer to "Yessayan et al. Management of dysnatremias with continuous renal replacement therapy. Semin Dial. 2021"