Renal Replacement Therapy: Choices and Outcomes

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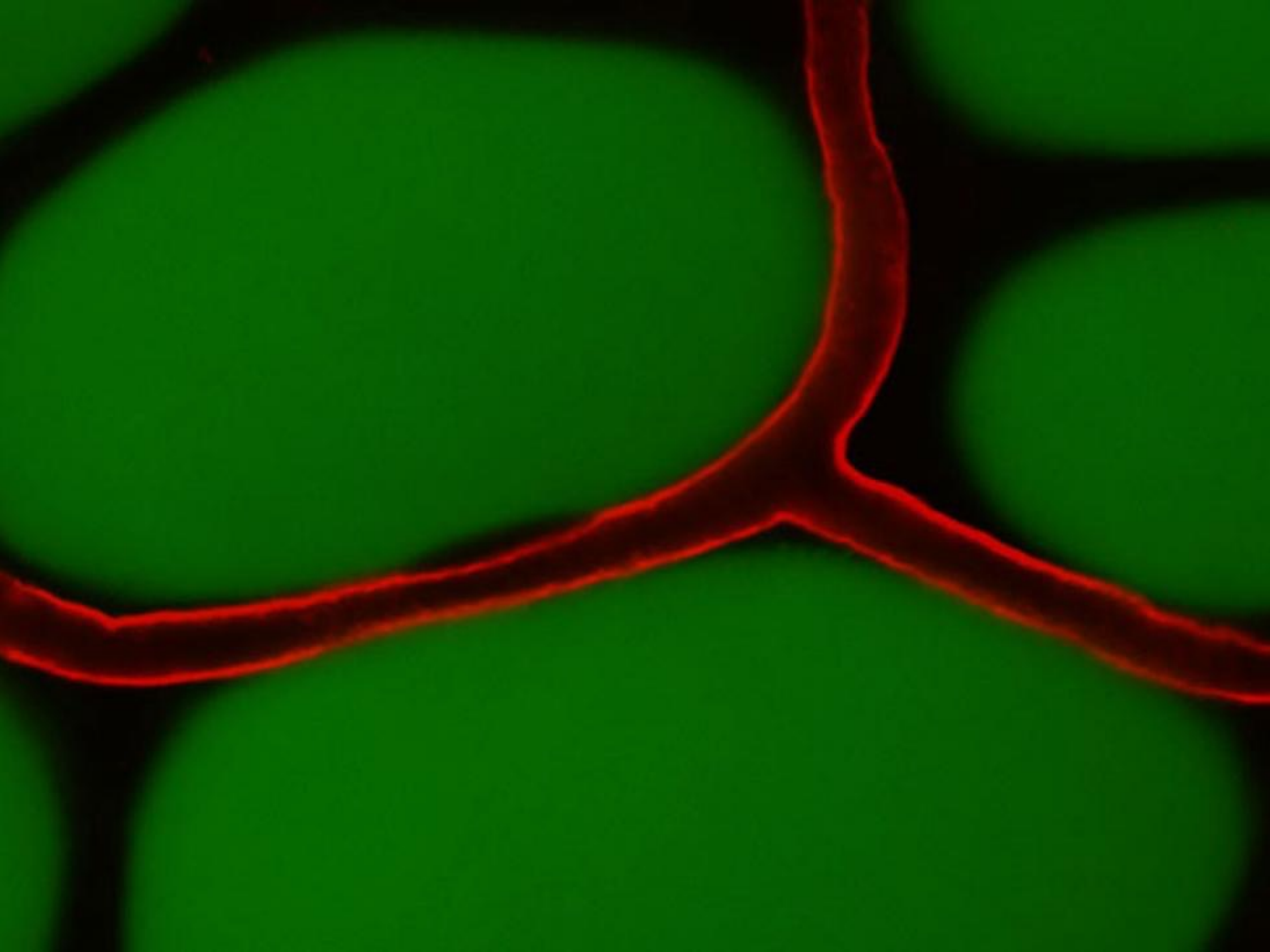


Primary Therapeutic Goals in AKI

Optimize hemodynamic and volume status

Minimize further renal injury

Correct metabolic abnormalities

Removal of Uremic toxins

Permit adequate nutrition

Luyckx VA Semin Dial. 2004;17(1):30-6.

Limitations on RRT Delivery in AKI

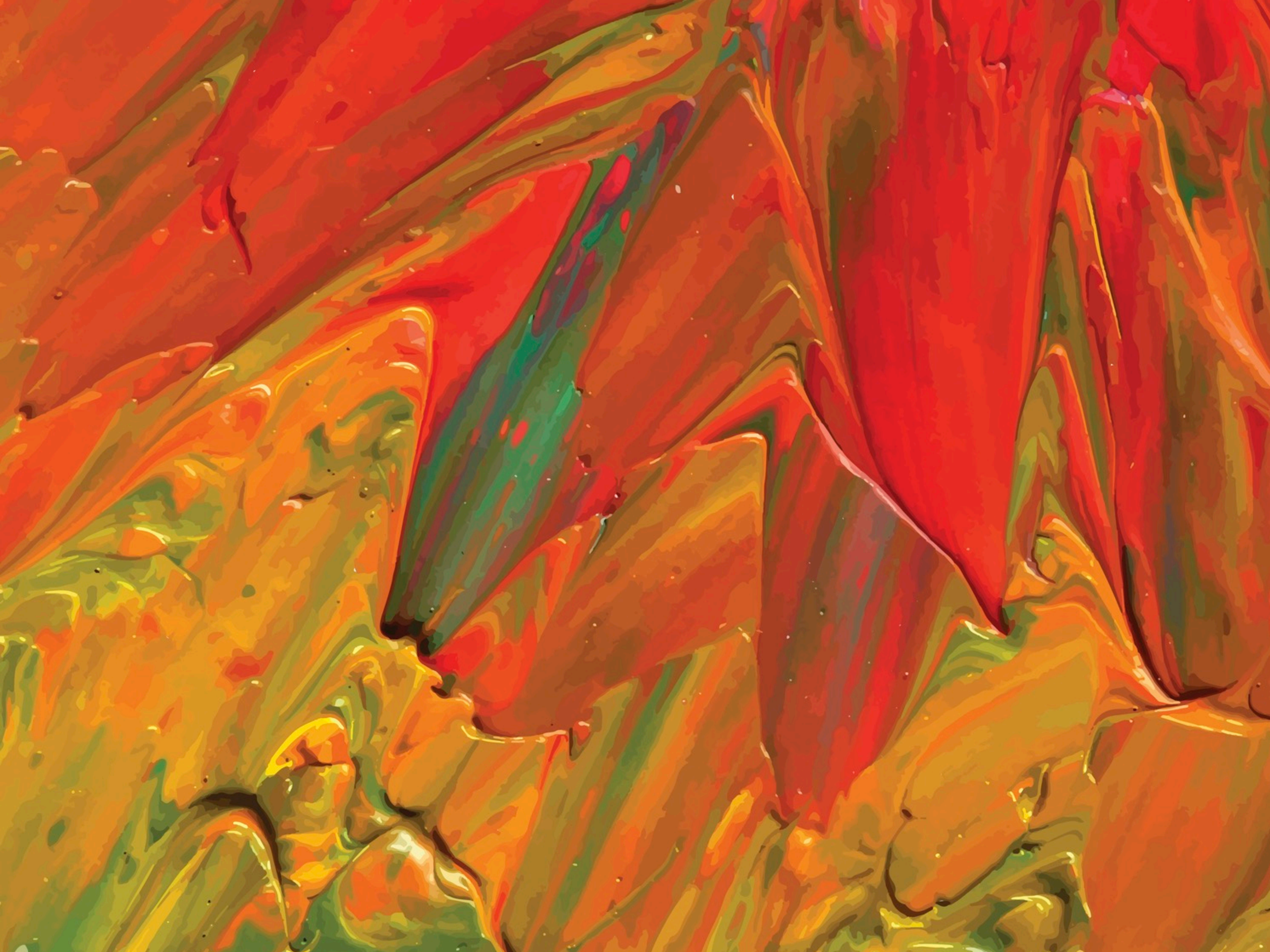
Hypercatabolic state

Hemodynamic instability

Control of Volume status

Primary Therapeutic Goals in CRRT

- Solute Removal
  - Diffusion and Convection
- Solute Addition
  - Replacement Fluid
- Fluid Removal
  - Convection
- Detoxification

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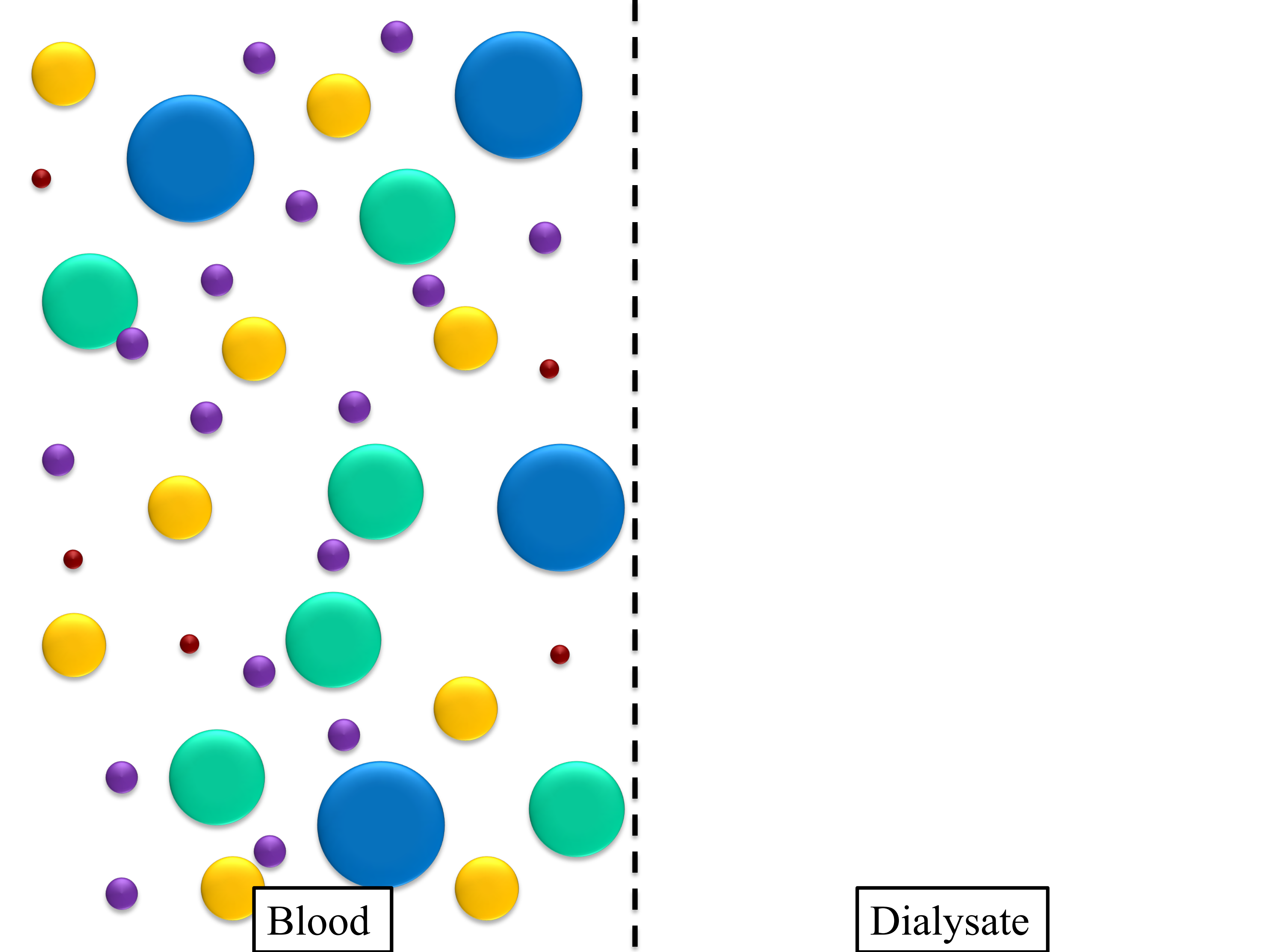
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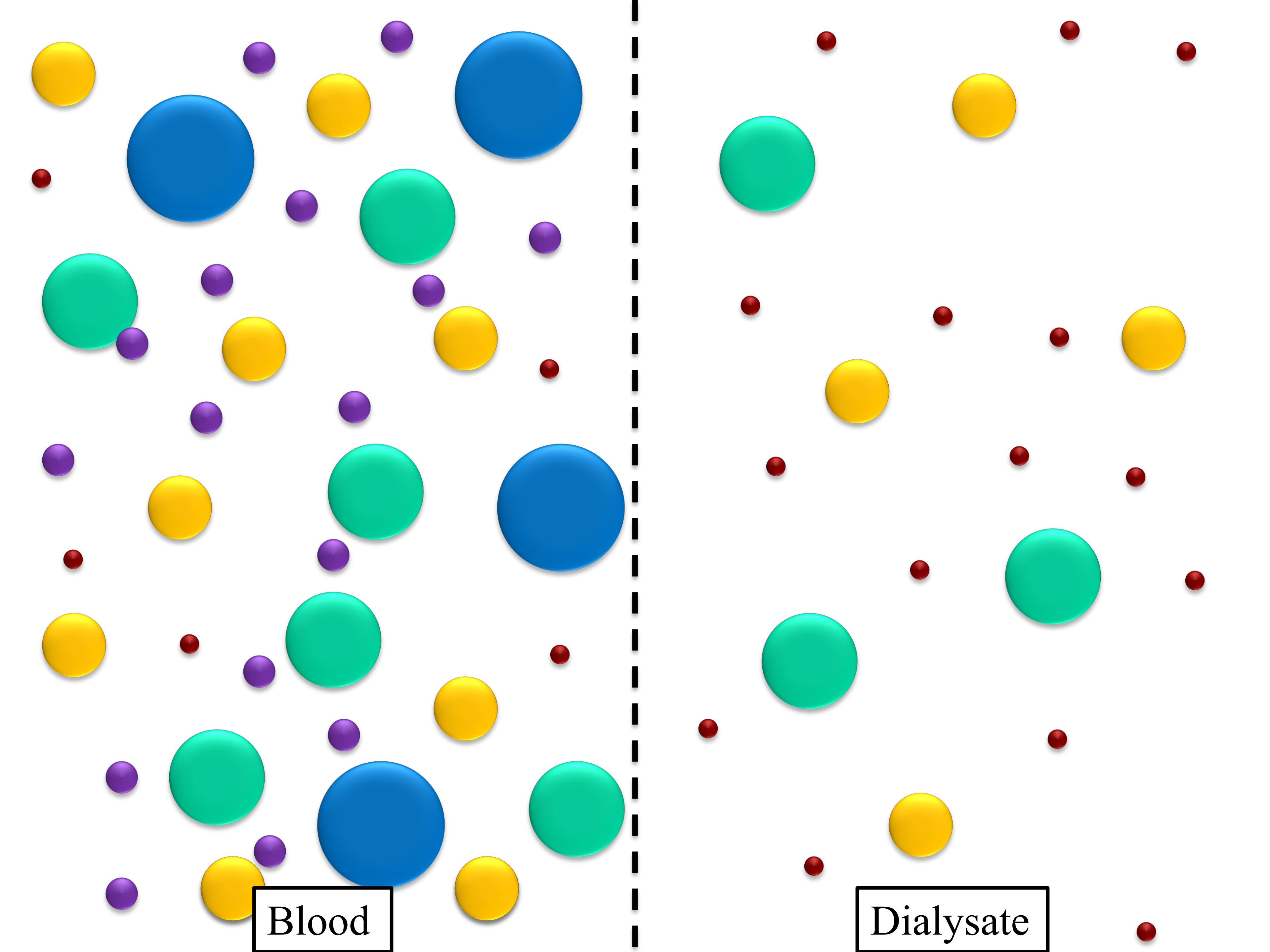
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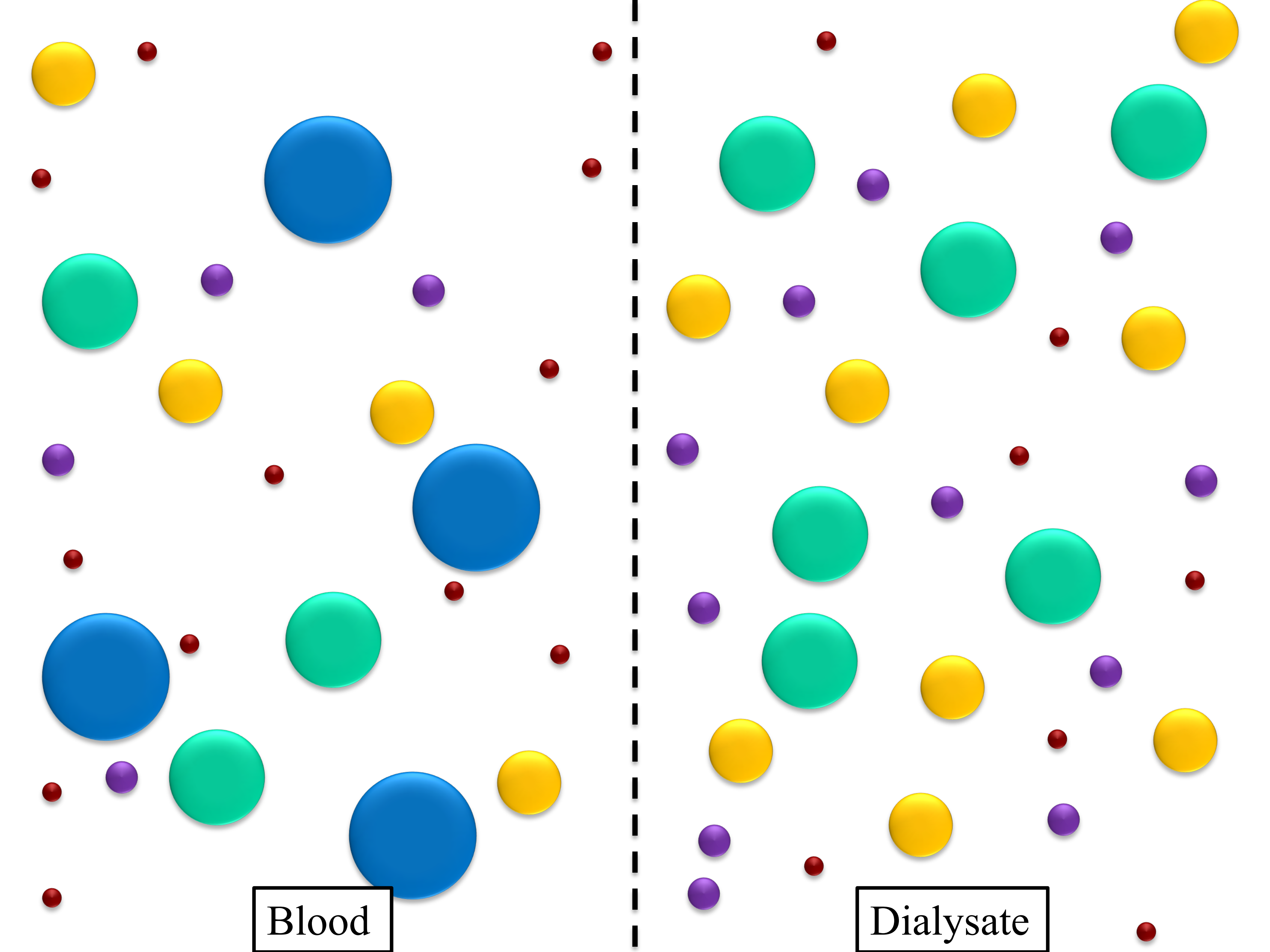
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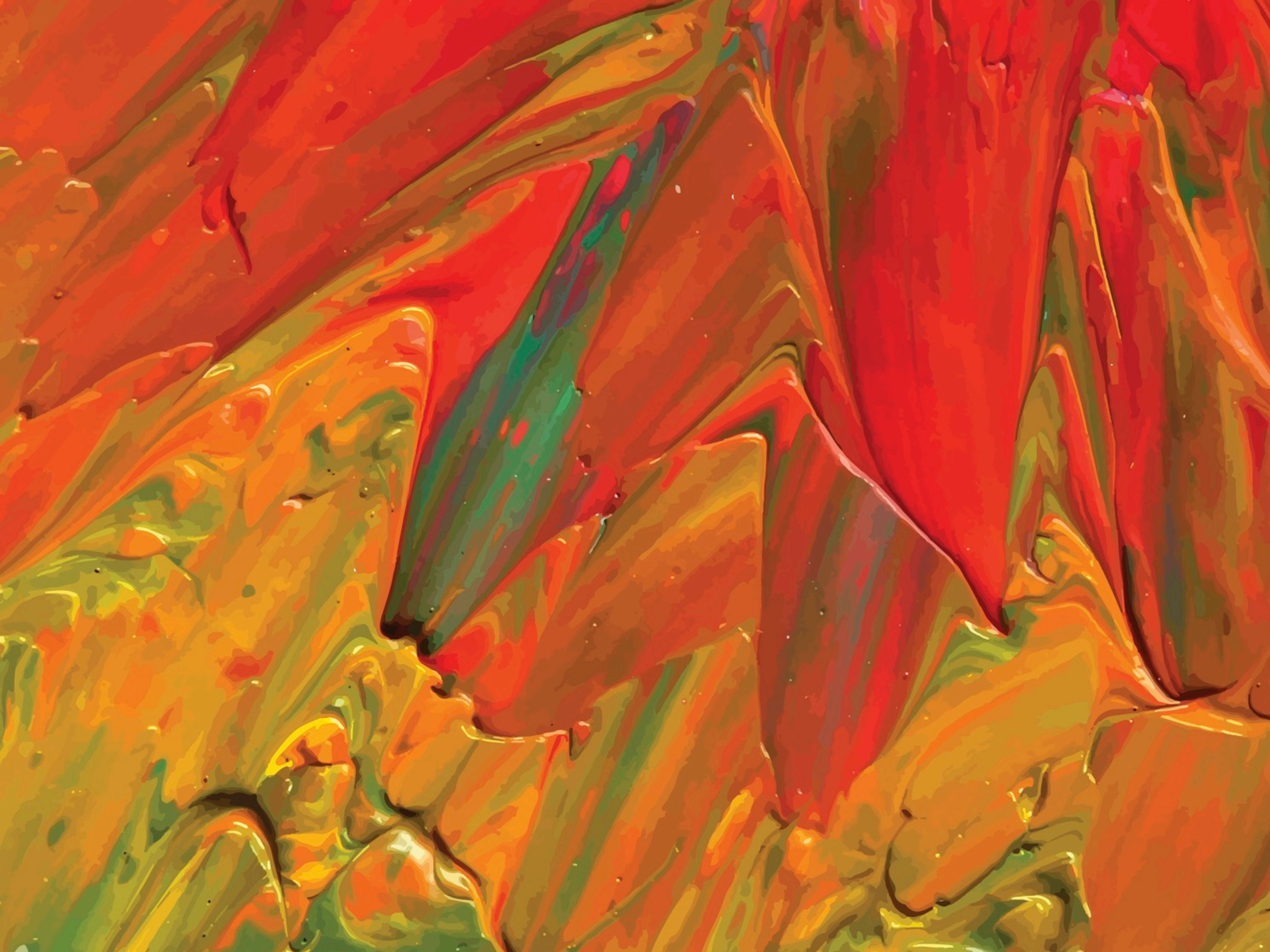


59:55
Hx
Ultrafiltration
50
ml/hr
Pend. Time

Pressures (mmHg)
Access
-100
Venous
200
Effluent
230
Bal Chamber
315
Blood
350
ml/min
Pend. Time
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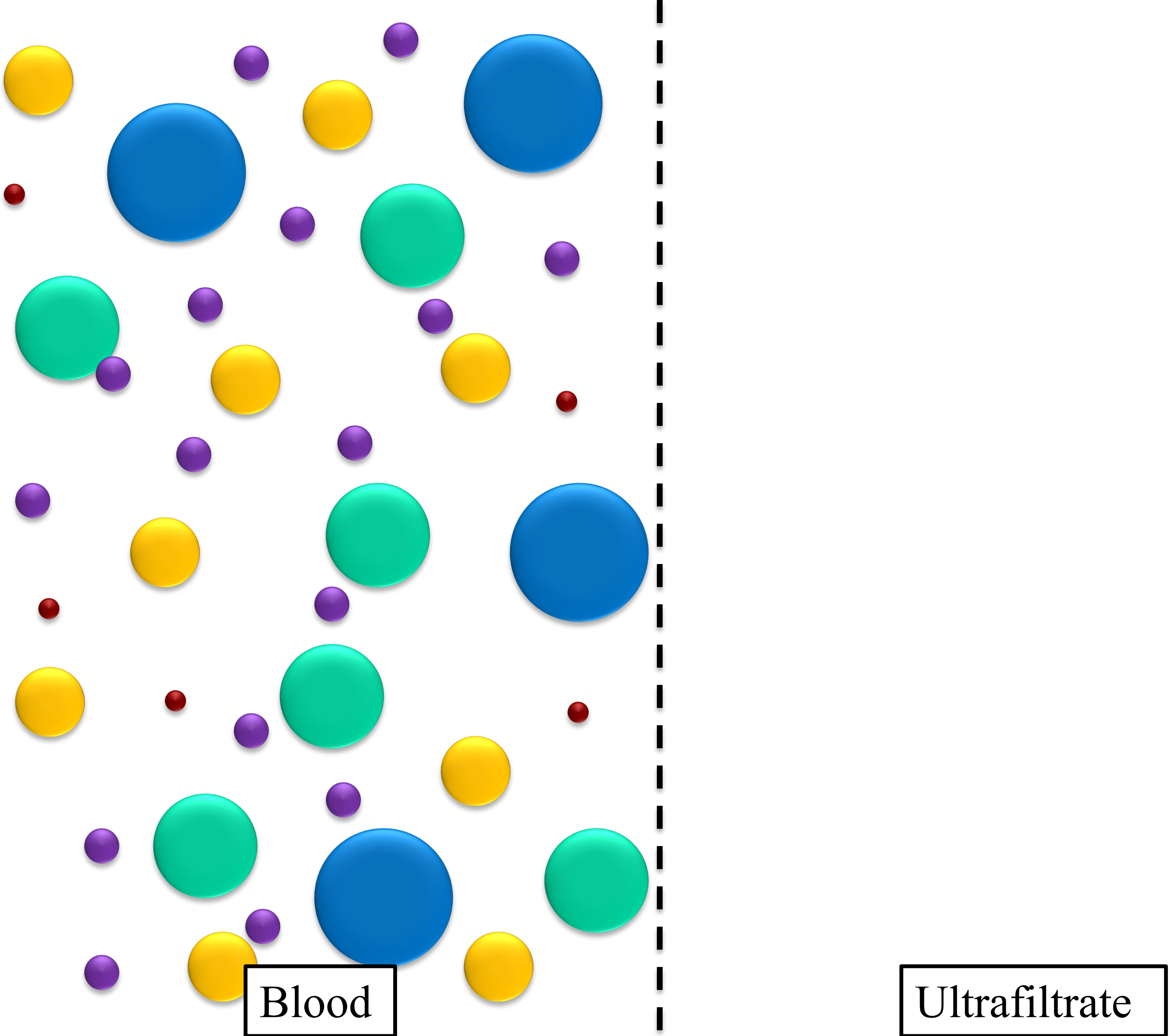
CAR-500
Filtration Fraction
14 %
System One
L/hr
L/hr (0.00) ml/hr (000)
ml/min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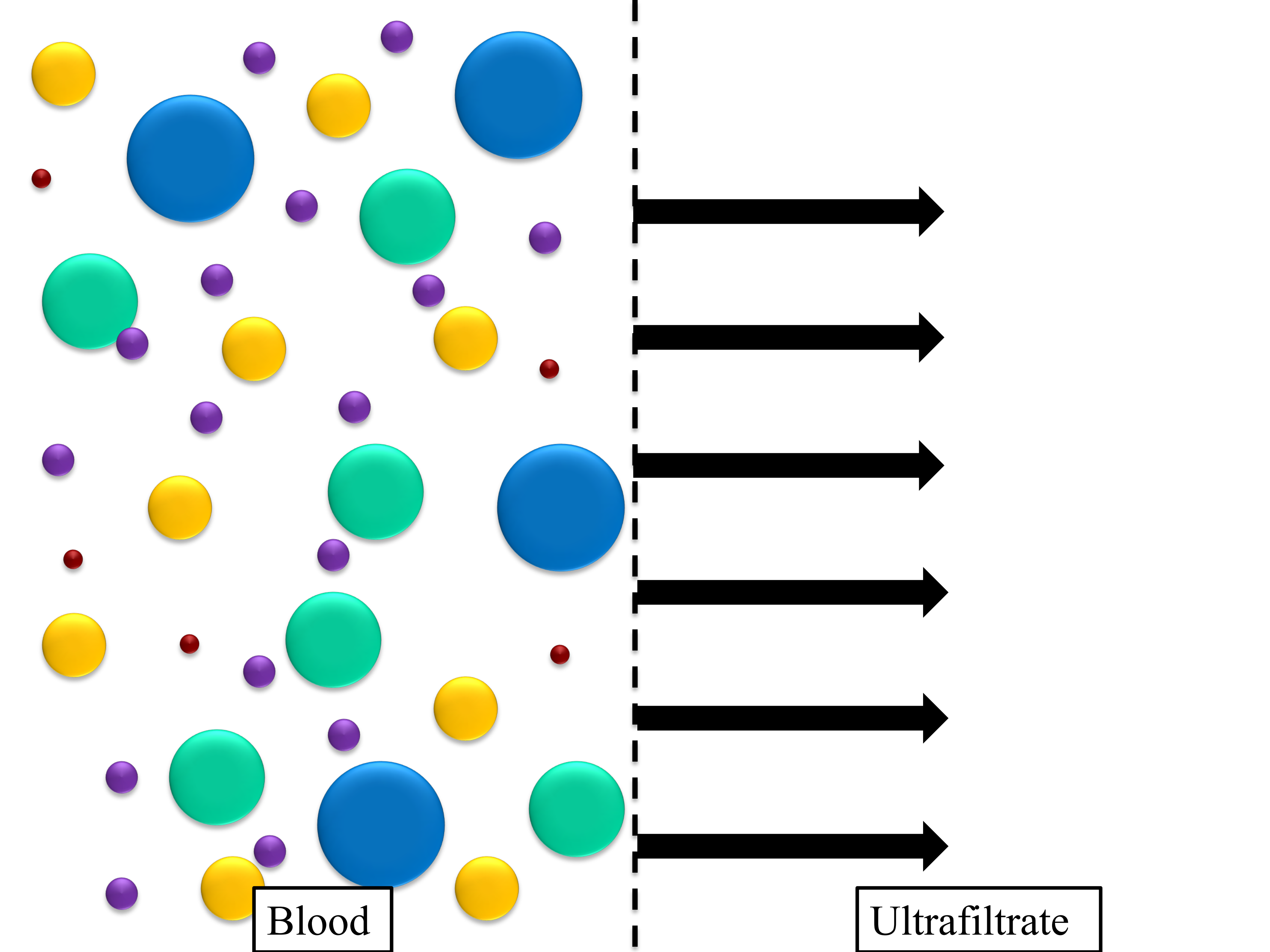
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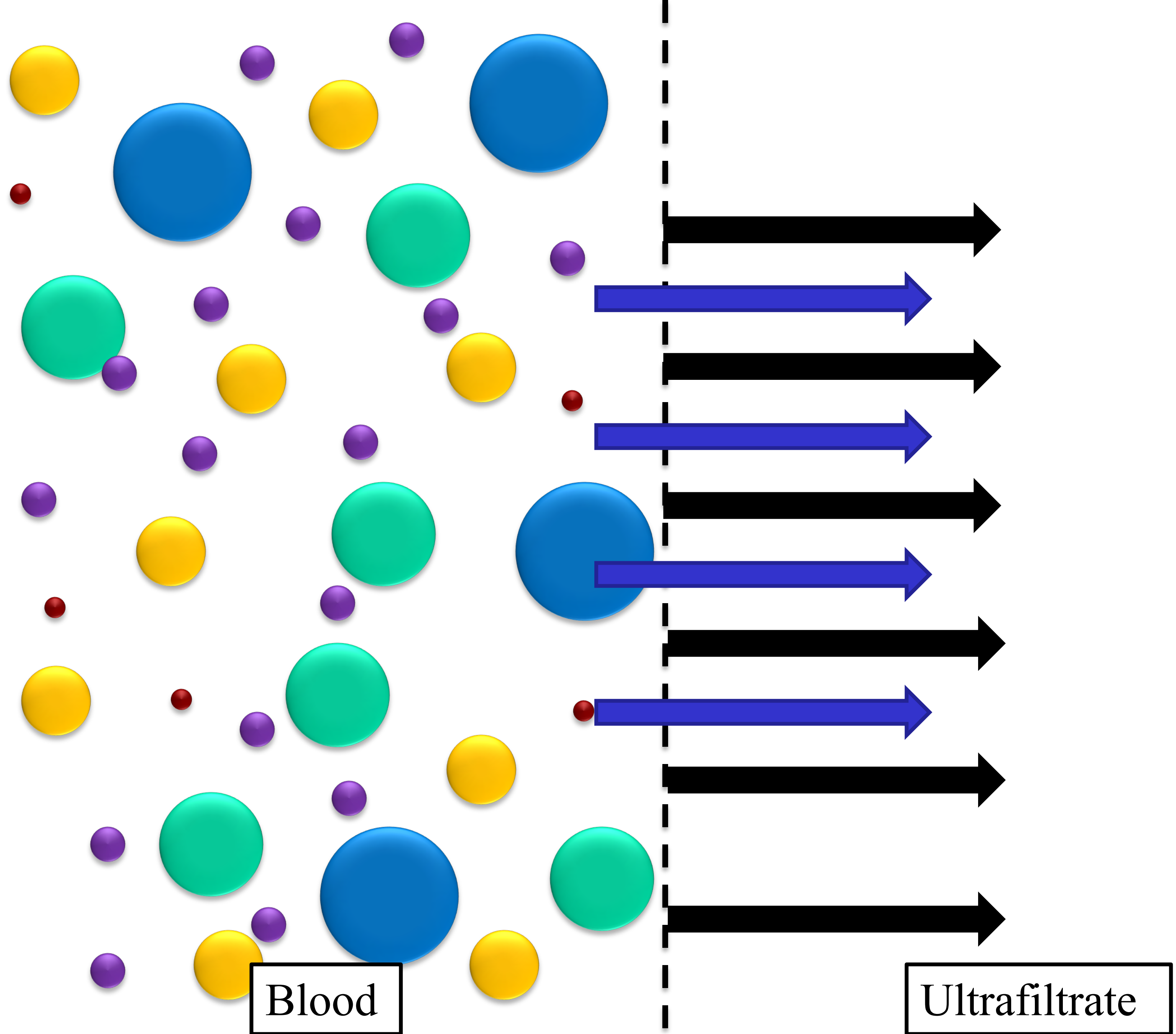
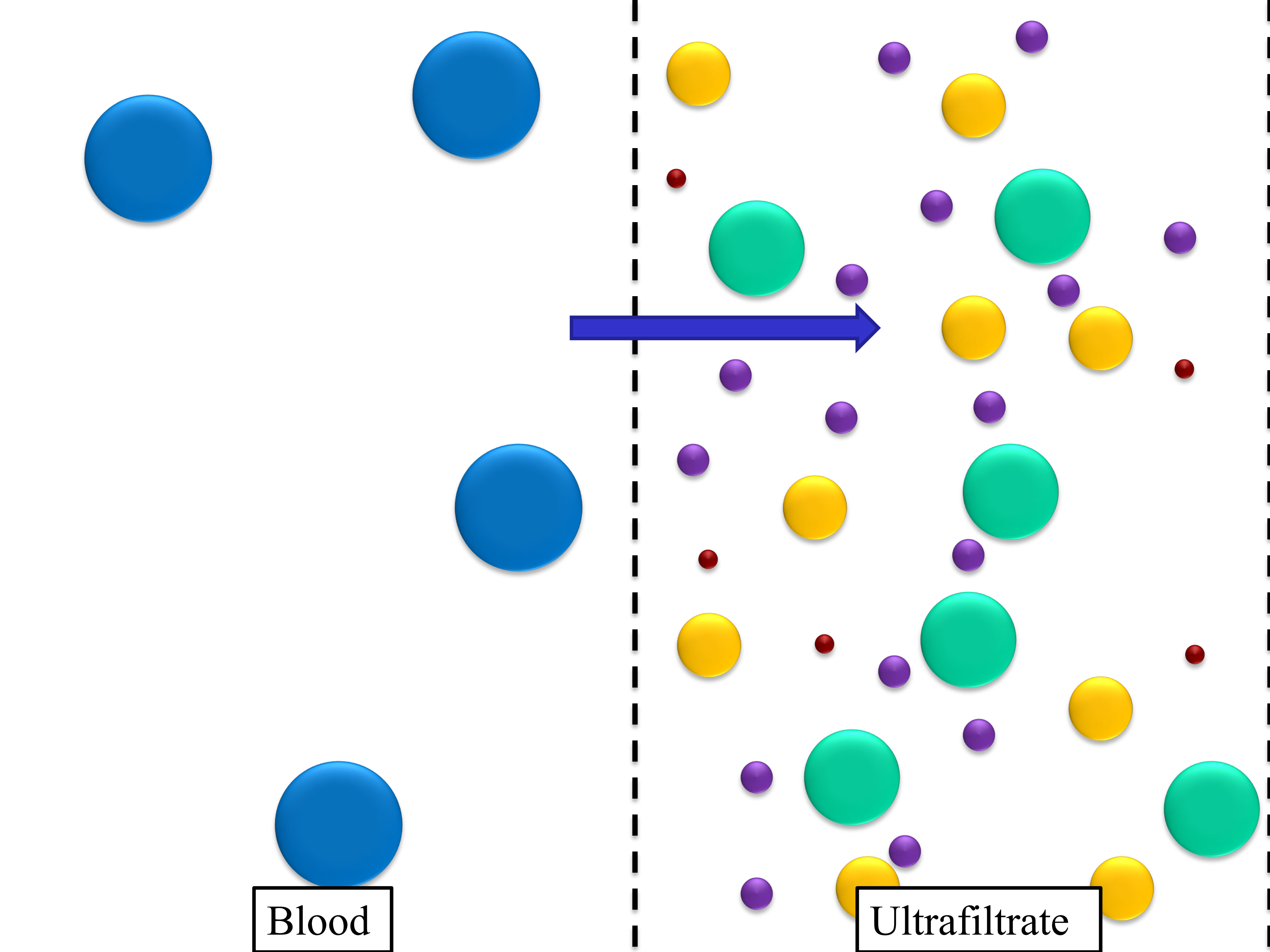


Blood
Ultrafiltrate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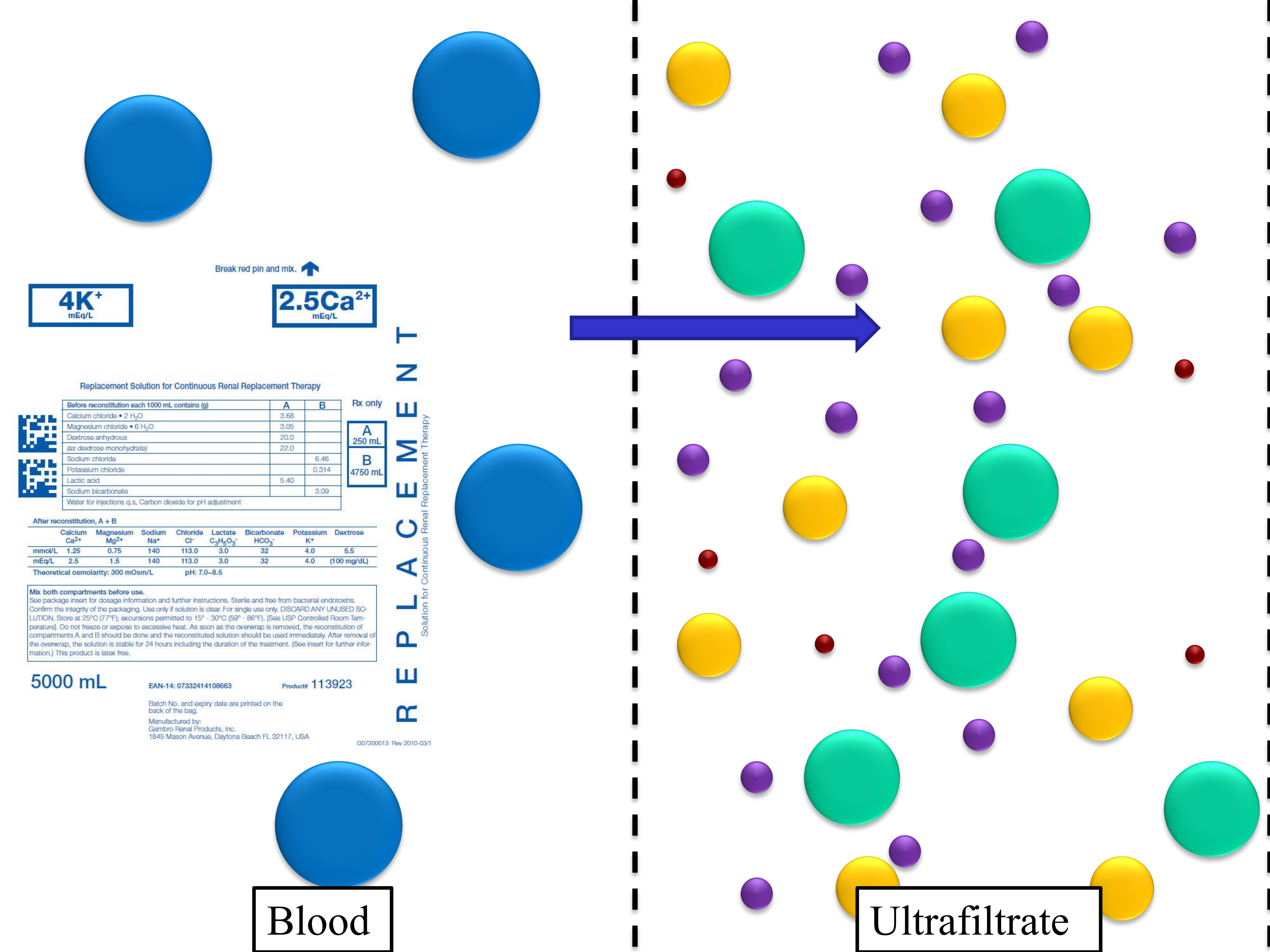
Ultrafiltrate



Break red pin and mix.
4K+ mEq/L
2.5Ca2+ mEq/L
REPLACEMENT
Solution for Continuous Renal Replacement Therapy
Replacement Solution for Continuous Renal Replacement Therapy
Rx only
Before reconstitution each 1000 mL contains (g) A B
Calcium chloride • 2 H2O 3.68
Magnesium chloride • 6 H2O 3.05
Dextrose anhydrous 20.0
(as dextrose monohydrate) 22.0
Sodium chloride 6.46
Potassium chloride 0.314
Lactic acid 5.40
Sodium bicarbonate 3.09
Water for injections q.s, Carbon dioxide for pH adjustment
A 250 mL
B 4750 mL
After reconstitution, A + B
Calcium Ca2+ Magnesium Mg2+ Sodium Na+ Chloride Cl- Lactate C3H5O3- Bicarbonate HCO3- Potassium K+ Dextrose
mmol/L 1.25 0.75 140 113.0 3.0 32 4.0 5.5
mEq/L 2.5 1.5 140 113.0 3.0 32 4.0 (100 mg/dL)
Theoretical osmolarity: 300 mOsm/L pH: 7.0–8.5
Mix both compartments before use.
See package insert for dosage information and further instructions. Sterile and free from bacterial endotoxins. Confirm the integrity of the packaging. Use only if solution is clear. For single use only. DISCARD ANY UNUSED SOLUTION. Store at 25°C (77°F); excursions permitted to 15° - 30°C (59° - 86°F). [See USP Controlled Room Temperature]. Do not freeze or expose to excessive heat. As soon as the overwrap is removed, the reconstitution of compartments A and B should be done and the reconstituted solution should be used immediately. After removal of the overwrap, the solution is stable for 24 hours including the duration of the treatment. (See insert for further information.) This product is latex free.
5000 mL
EAN-14: 07332414108663
Product# 113923
Batch No. and expiry date are printed on the back of the bag.
Manufactured by:
Gambro Renal Products, Inc.
1845 Mason Avenue, Daytona Beach FL 32117, USA
D07200013 Rev 2010-03/1
Blood
Ultrafiltrate

Break red pin and mix. ↑

4K⁺ mEq/L

2.5Ca²⁺ mEq/L

REPLACEMENT

Solution for Continuous Renal Replacement Therapy

Replacement Solution for Continuous Renal Replacement Therapy

Rx only

Before reconstitution each 1000 mL contains (g)	A	B
Calcium chloride • 2 H_2O	3.68	
Magnesium chloride • 6 H_2O	3.05	
Dextrose anhydrous	20.0	
(as dextrose monohydrate)	*22.0*	
Sodium chloride		6.46
Potassium chloride		0.314
Lactic acid	5.40	
Sodium bicarbonate		3.09
Water for injections q.s, Carbon dioxide for pH adjustment		

A 250 mL

B 4750 mL

After reconstitution, A + B

	Calcium Ca^{2+}	Magnesium Mg^{2+}	Sodium Na^+	Chloride Cl^-	Lactate $C_3H_5O_3^-$	Bicarbonate HCO_3^-	Potassium K^+	Dextrose
mmol/L	1.25	0.75	140	113.0	3.0	32	4.0	5.5
mEq/L	2.5	1.5	140	113.0	3.0	32	4.0	(100 mg/dL)

Theoretical osmolarity: 300 mOsm/L **pH: 7.0–8.5**

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After reconstitution, A + B

	Calcium Ca^{2+}	Magnesium Mg^{2+}	Sodium Na^{+}	Chloride Cl^{-}	Lactate $C_3H_5O_3^-$	Bicarbonate HCO_3^-	Potassium K^{+}	Dextrose
mmol/L	1.25	0.75	140	113.0	3.0	32	4.0	5.5
mEq/L	2.5	1.5	140	113.0	3.0	32	4.0	(100 mg/dL)

Theoretical osmolarity: 300 mOsm/L pH: 7.0–8.5

Ca	1.25 mmol/L
Mg	1.5 mEq/L
Na	140 mEq/L
Cl	113 mEq/L
HCO_3	32 mEq/L
K	4 mEq/L

Replacement Solution

Replaces the ultrafiltrate removed by hemofiltration and hemodiafiltration.

Buffers: Lactate, bicarbonate or citrate

Lactate and Citrate metabolized by liver and muscle to bicarbonate.

Bicarbonate is most easily tolerated

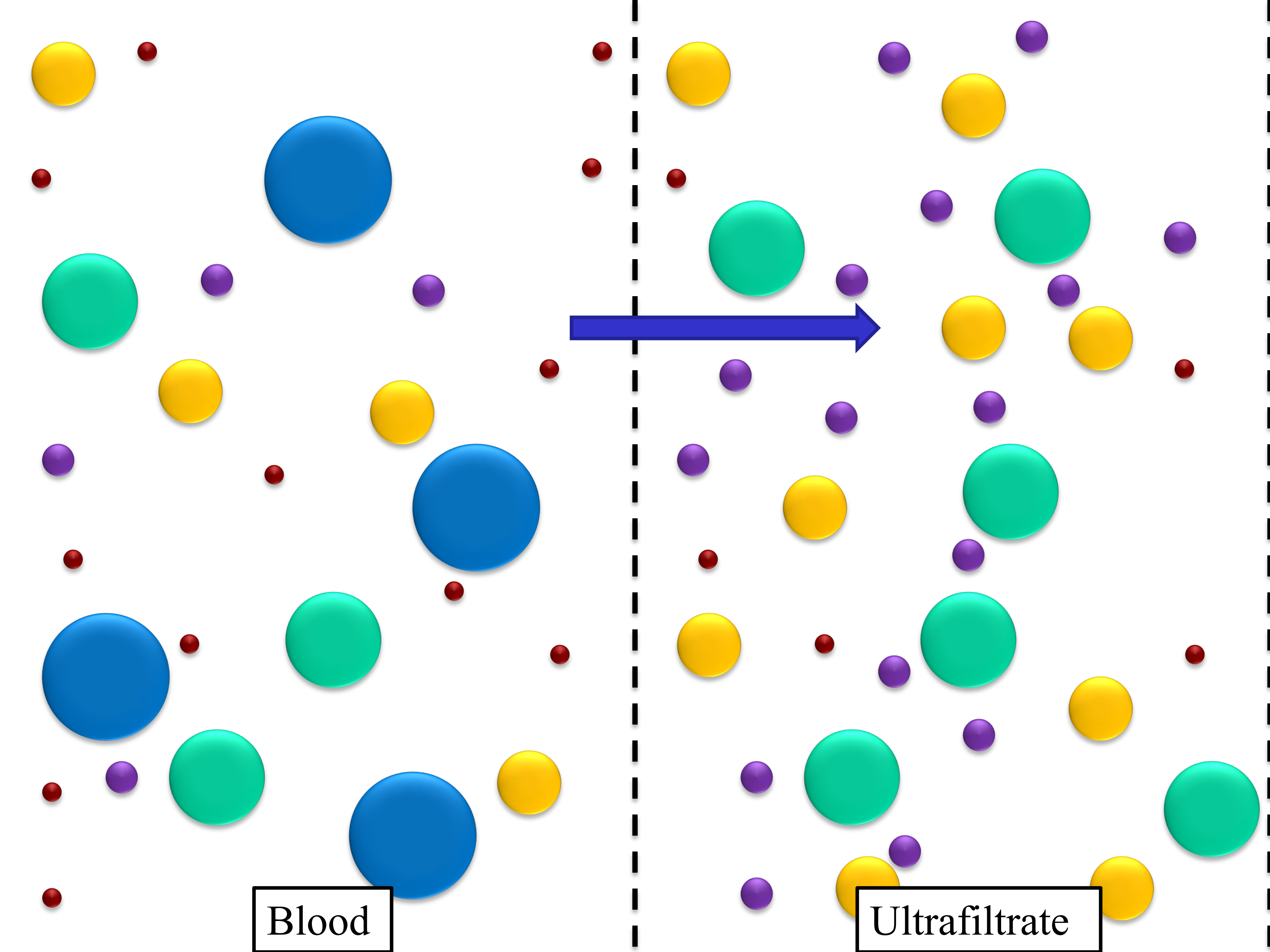
- can be unstable in solution

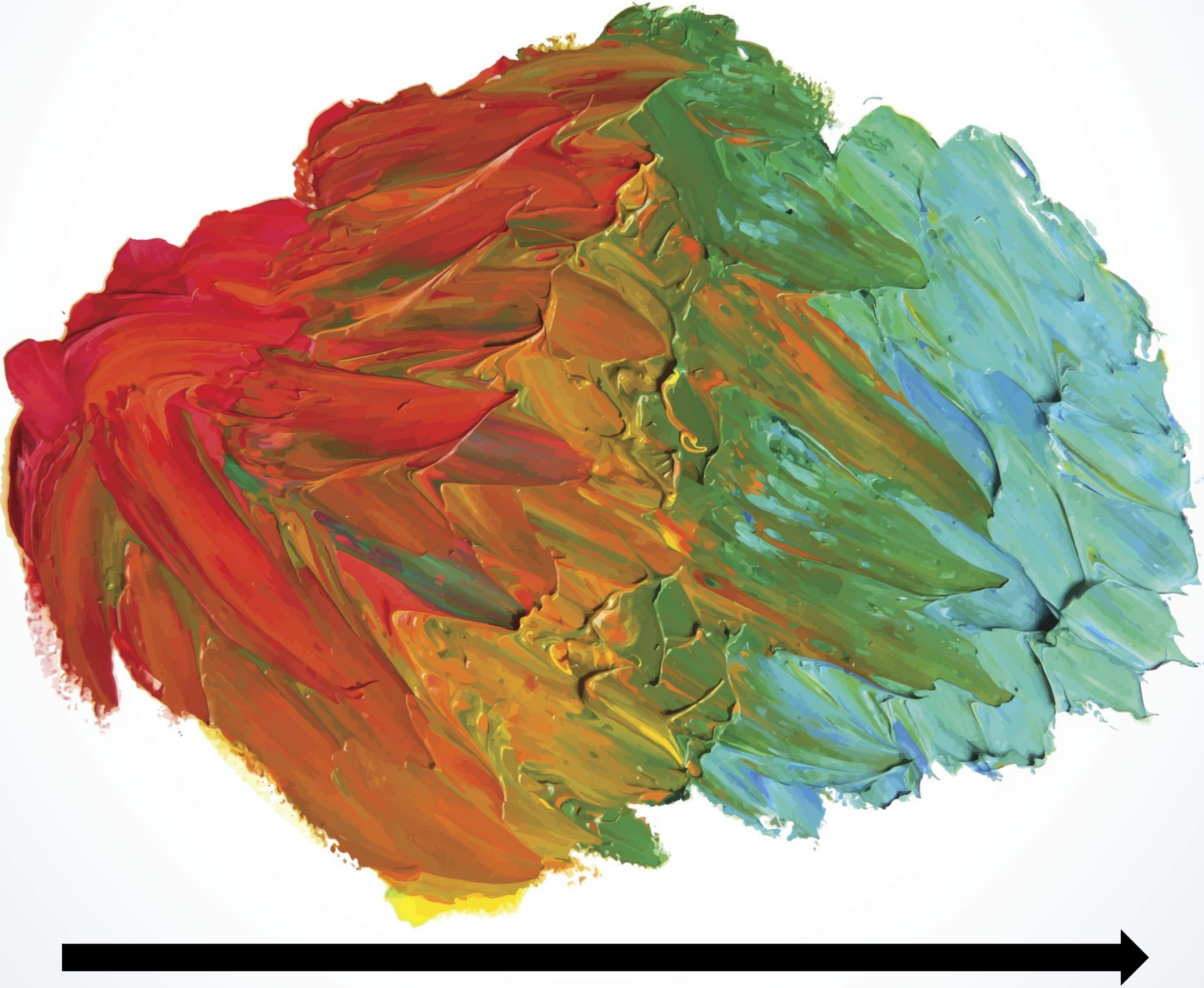
Citrate

- Regional anticoagulation

P Heering Intensive Care Med 1999, 25:1244-1251

Tan HK Int J Artif Organs. 2003 Jun;26(6):477-83.


Blood
Ultrafiltrate



Continuous Renal Replacement Therapy (CRRT)

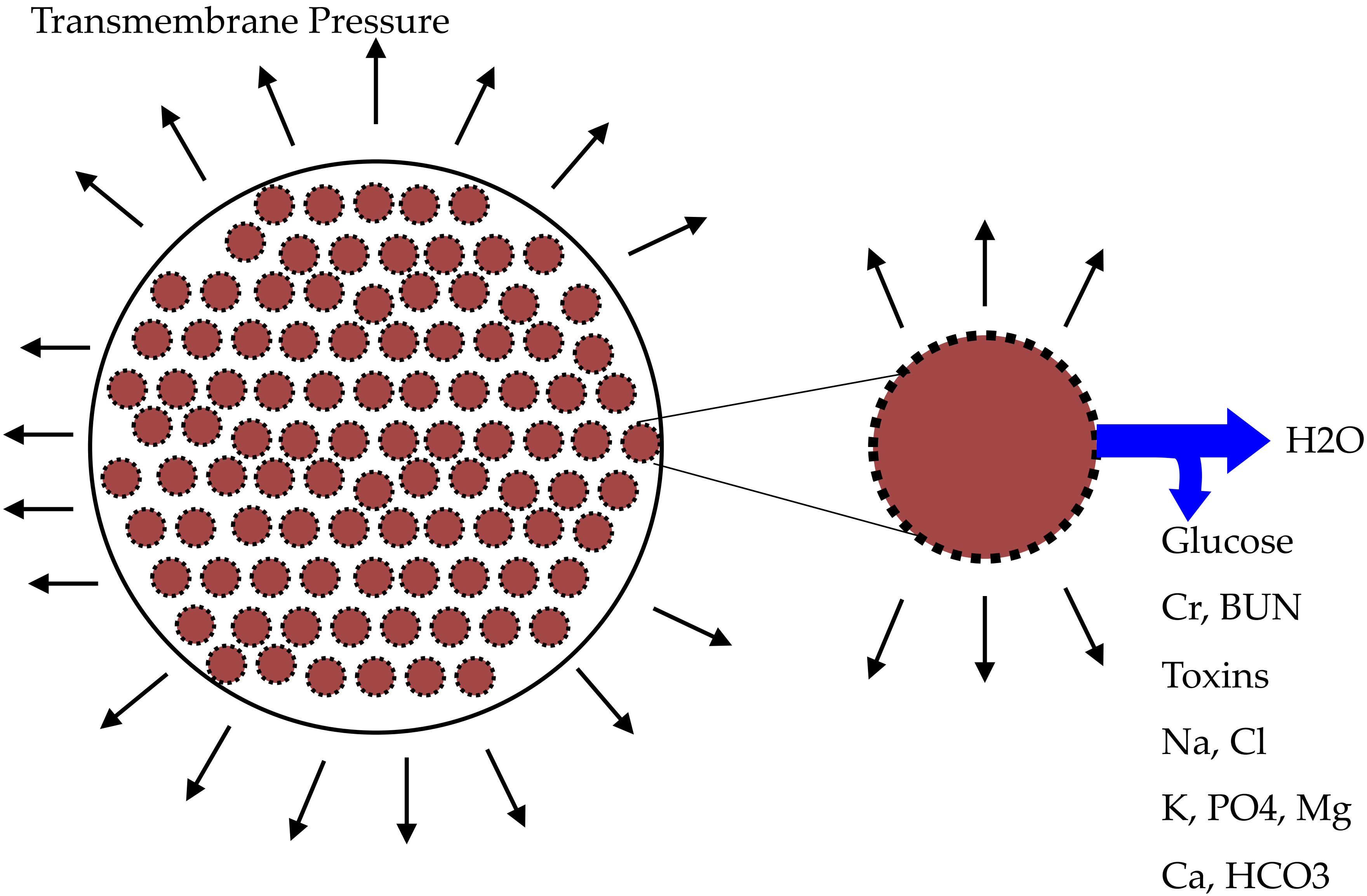
CVVH	**Continuous Veno-Venous Hemofiltration**
CVVHD	**Continuous Veno-Venous Hemodialysis**
CVVHDF	**Continuous Veno-Venous Hemodiafiltration**
SCUF	**Slow Continuous Ultra-Filtration**
SLED	**Slow Low Efficiency Dialysis**

Convection

- Fluid Removal and Solute Removal
- Movement of fluid across the membrane via transmembrane pressure
- Water moves across the membrane and carries dissolved solutes with it via solvent drag
  - Ultrafiltration is fluid removal
  - Hemofiltration involves partial or total replacement of fluid removed

Luciano A. Pedrini J Nephrol 2003; 16 (suppl 7): S57-S63

Convection


Transmembrane Pressure
H2O
Glucose
Cr, BUN
Toxins
Na, Cl
K, PO4, Mg
Ca, HCO3

Diffusion

Movement of solutes down a concentration gradient across a semipermeable membrane.

Solutes cross the membrane from the blood to the dialysis fluid compartment.

Fluid in the dialysis compartment moves in a counter-current direction, thereby maintaining a concentration gradient.

Luciano A. Pedrini J Nephrol 2003; 16 (suppl 7): S57-S63

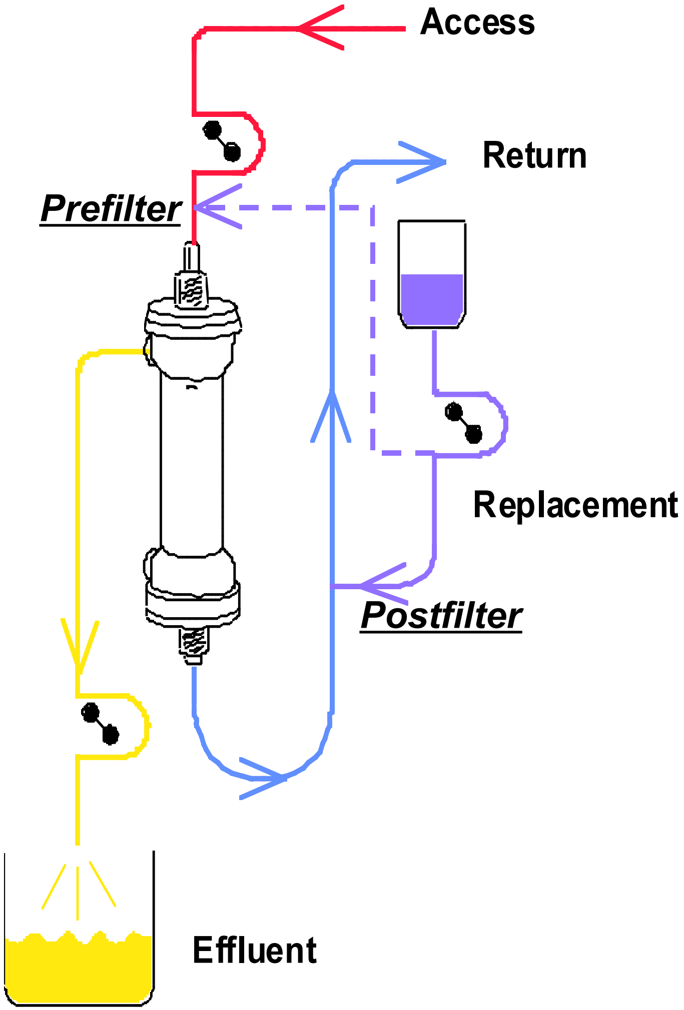
Diffusion

Diffusive clearance is determined by

- Molecular weight of the solute
- Concentration gradient across the membrane
- Membrane surface area
- Thickness and pore size

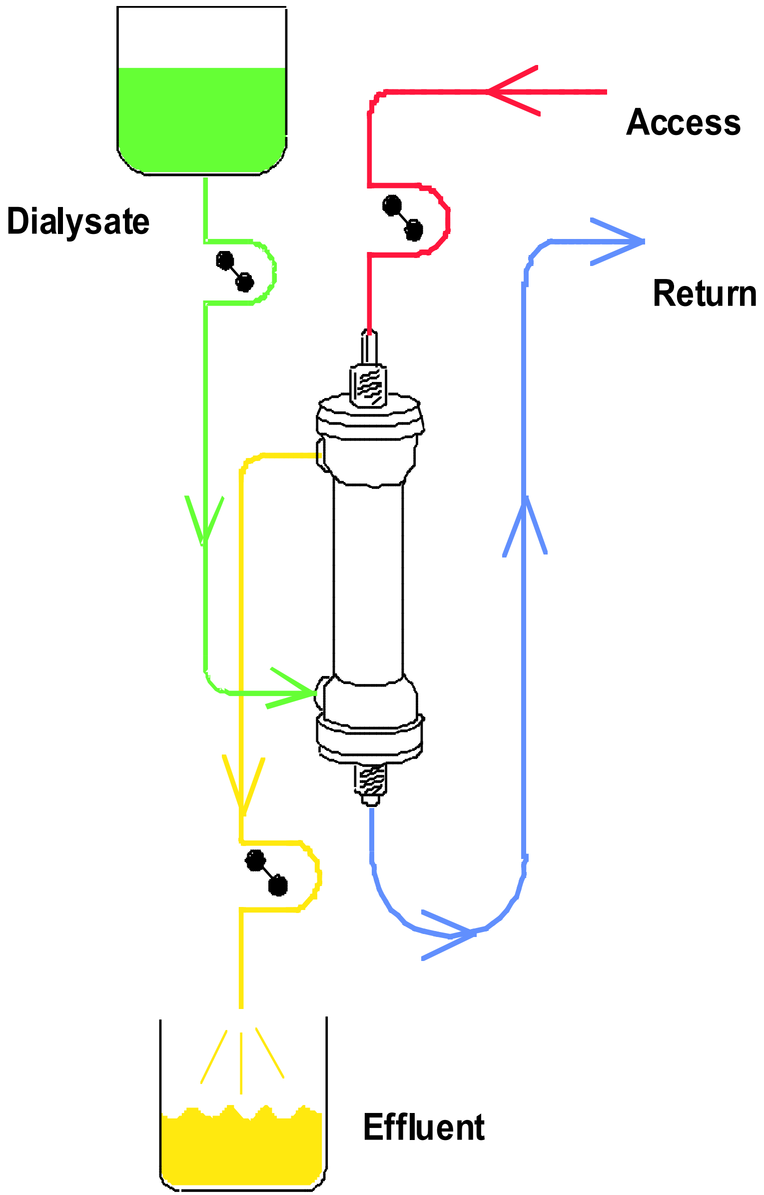
CVVH

Continuous
Veno-Venous
Hemofiltration



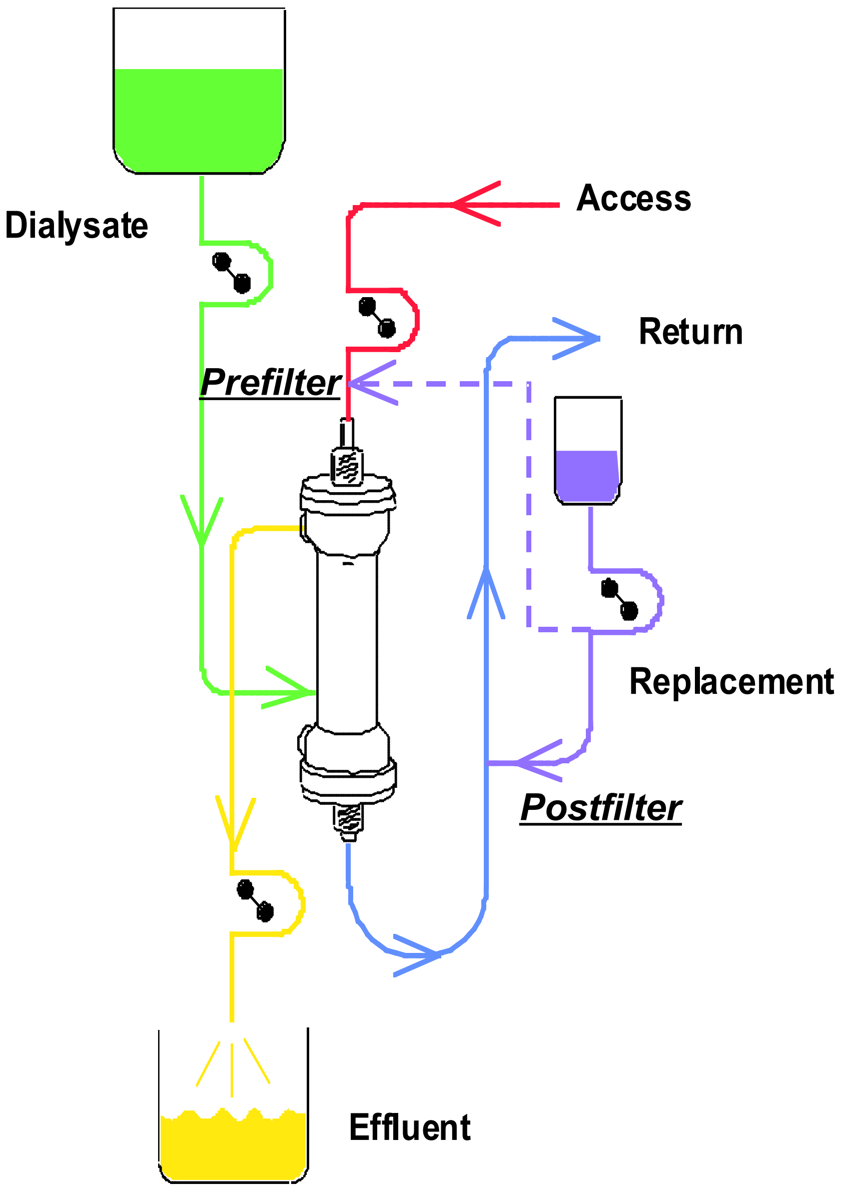
CVVHD

Continuous
Veno-**V**enous
Hemo**D**ialysis



CVVHDF

Continuous
Veno-Venous
HemoDiaFiltration



Effluent

Represents the end product of the filtration process

CVVH:	Ultrafiltrate
CVVHD:	Dialysate plus variable ultrafiltrate
CVVHDF:	Dialysate plus ultrafiltrate

Case 1

64 year old diabetic female on Lisinopril
Witnessed PEA arrest
Resuscitated

Progressive volume overload (+15L)
Oliguric, diuretic resistant

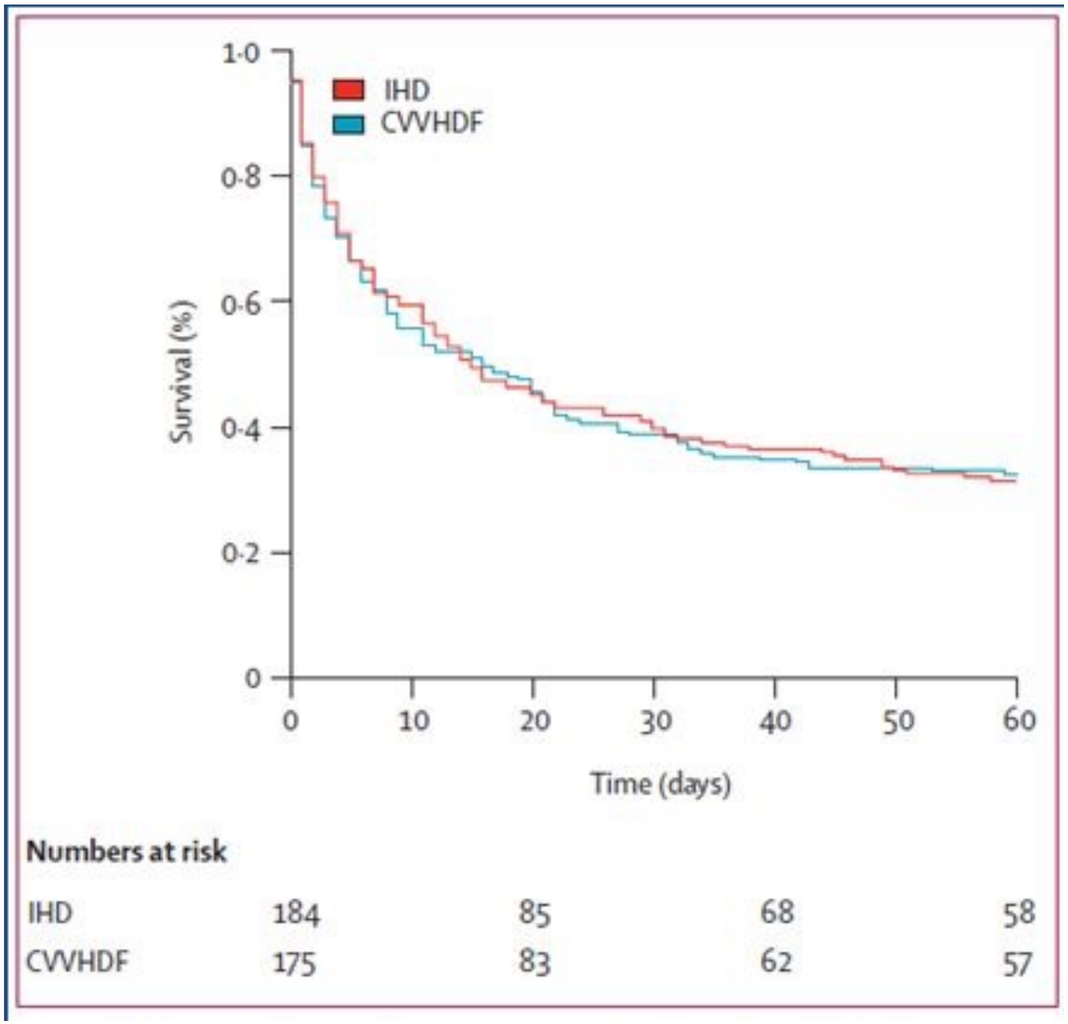
BP 100/60 on moderate dose norepinephrine
Mechanically ventilated and sedated
Na 129, K 5.7, CO_2 14, BUN 69, Cr 4.7
Best Renal Replacement modality?

Case 1

Best Renal Replacement modality?

CRRT vs Hemodialysis

No difference in survival in RCTs



Vinsonneau et al. Lancet 2006; 368: 379-85

CRRT vs Hemodialysis

Both methods are complementary

IHD

- Faster Potassium elimination
- Faster Drug/ Toxin elimination
- Better for overdose

CRRT

- Regulation of higher calories requirements
- Hemodynamically unstable patients
- Precise adaptable volume control

1 minute

Case 2

53 year old male with cryptogenic cirrhosis with septic shock and AKI, on CVVH

136	104	32	106
4.3	14	2.9	

Total Ca 9.6 mg/dl

Ionized Ca 0.8 mmol/L

Case 2

53 year old male with cryptogenic **cirrhosis** with septic shock and AKI, on CVVH

136	104	32	106
4.3	14	2.9	

Total Ca 9.6 mg/dl

Ionized Ca 0.8 mmol/L

Anion Gap 18

Citrate Toxicity

Low ionized Calcium despite repletion
Elevated total serum Calcium in response to repletion
Exacerbation of serum acidosis
Elevation of anion gap

Decrease Citrate replacement solution rate
Switch replacement solutions

Citrate Regional Anticoagulation

- Citrate causes anticoagulation by chelation of calcium in the extracorporeal system
- Systemic anticoagulation does not occur
  - as ionized calcium level is restored when blood returning from the extracorporeal system is mixed with venous blood
- Rapid metabolism of citrate restores bicarbonate level and releases calcium
- Patients with severe liver failure and lactic acidosis may have difficulty metabolizing citrate and develop citrate toxicity

Citrate Replacement solution

Sodium Citrate = 40 mEq/Liter,
Dextrose = 2 gm/Liter,
Sodium Chloride = 105 mEq/Liter,
Magnesium Sulfate = 1.5 mEq/Liter.

CVVH with maximum replacement of 2000 cc citrate/hour.

CVVHDF add dialysate to improve clearance.

Calcium replacement scales adjusted depending on clearance

Clearance

Clearance is the rate at which solutes are cleared

excretion rate of solute / blood concentration of solute

Solute clearance in CVVH depends on UF Rate

Strategies to Increase Solute Clearance

Increase Transmembrane pressure

Johnson RJ, Feehally J, Comprehensive Clinical Nephrology 2nd Edition

Strategies to Increase Solute Clearance

Increase Transmembrane pressure

Increase blood flow

CVVHDF

- Add dialysis to convection

Johnson RJ, Feehally J, Comprehensive Clinical Nephrology 2nd Edition

Indications for CRRT

Patients with/ at risk for hypotension:

- severe hemodynamic instability
- hepatic failure
- CHF
- sepsis or multiple organ failure

Patients at risk of cerebral complications:

- hepatic failure, stroke or head trauma
- high risk for cerebral edema

Indications for CRRT

- Increased metabolic needs
  - massive burns
  - sepsis
  - multiple organ failure
- Volume overload
  - massive volume overload
  - Patients receiving large amounts of fluids or blood products
  - When volume management is critical

Non-renal Indications for CRRT

- Lactic acidosis
  - Ongoing production – removes a little
- Crush injury
  - Myoglobin Removal – a little
- Tumor lysis syndrome
- Temperature control
  - Relative hyper or relative hypothermia*
- Massive volume overload without AKI
- High NH_3

Kopcke J. Anaesthesiol Reanim. 1996;21(6):159-62

Potential Advantages of CRRT

Increased total solute clearance

Gradual clearance may be better tolerated

- Decreases frequency of hypotension
- Decreases risk of cerebral edema

Continuous clearance may help in removal of toxins with high intracellular concentrations

Increased clearance of middle molecules

<u>**Precise adaptable volume control**</u>

Potential disadvantages of CRRT

Anticoagulation requirement

Lack of rapid fluid and solute removal

Limited role in overdose setting

Relative Hypothermia

Electrolyte Depletion

- K, PO_4, Ca

Contraindications of CRRT

Life-threatening hyperkalemia

group

Case 3

35 year old female with aggressive lymphoma (Burkitt subtype) to undergo cytotoxic chemotherapy

136	104	12	106
4.3	24	1.0	

Total Ca and PO_4 normal

Case 3

Oncology asks for CRRT prior to cytotoxic chemotherapy to prevent Tumor Lysis Syndrome

Oncology asks how the CRRT will alter the chemotherapy clearance

Drug Dosage in CRRT

Minimal removal of protein bound drugs
Some may be removed via membrane adsorption

Drug clearances increased with CVVHDF
Higher doses may be needed with higher UF rates

GFR = 10 ml/min Low UF rate
GFR = 30 ml/min Medium UF rate
GFR = 50 ml/min High UF rate

Mehta R, Atlas of Diseases of the Kidney 1999
Bugge JF.Acta Anaesthesiol Scand. 2001;45(8):929-34.

Timing of CRRT

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Early vs Delayed Initiation of Renal Replacement Therapy on Mortality in Critically Ill Patients With Acute Kidney Injury

The ELAIN Randomized Clinical Trial

JAMA. 2016;315(20):2190-2199.

- Single-center RCT
- 231 patients
- Early RRT was initiated within 8 hours of diagnosis of stage 2 AKI using the KDIGO classification
- Delayed RRT was initiated within 12 hours of stage 3 AKI using the KDIGO classification

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Early vs Delayed Initiation of Renal Replacement Therapy on Mortality in Critically Ill Patients With Acute Kidney Injury

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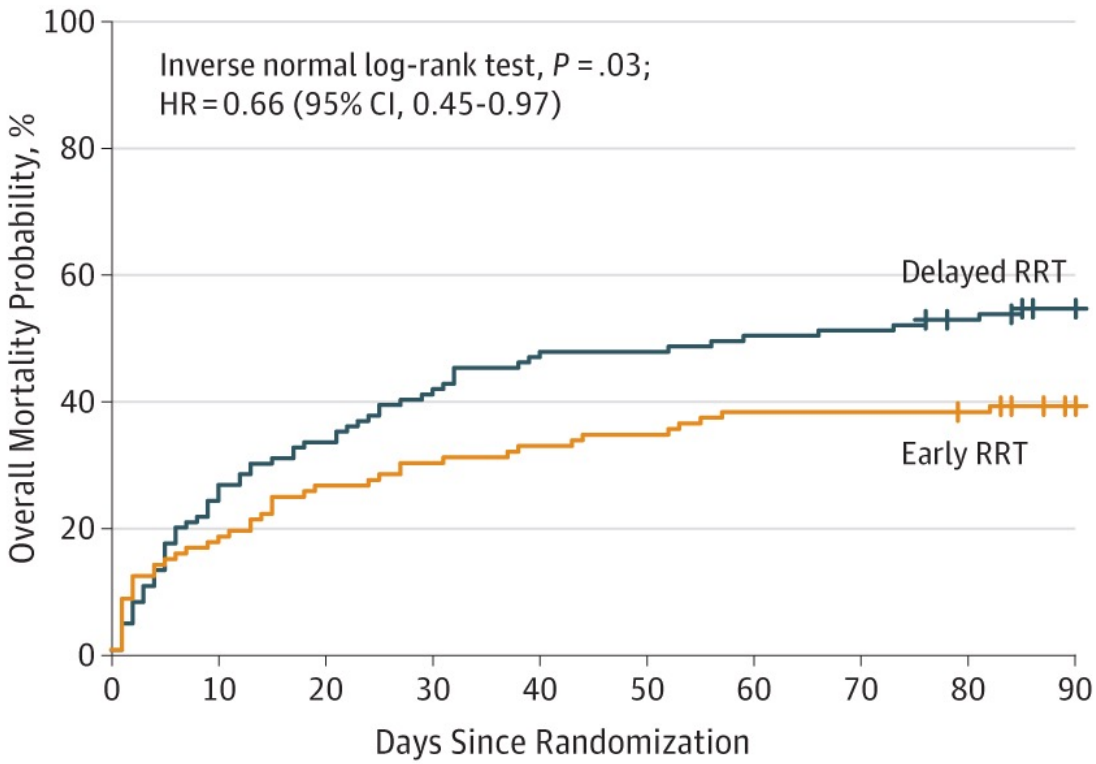


No. at risk										
Early RRT	112	92	82	78	75	73	69	69	66	55
Delayed RRT	119	90	79	70	63	62	59	58	54	48

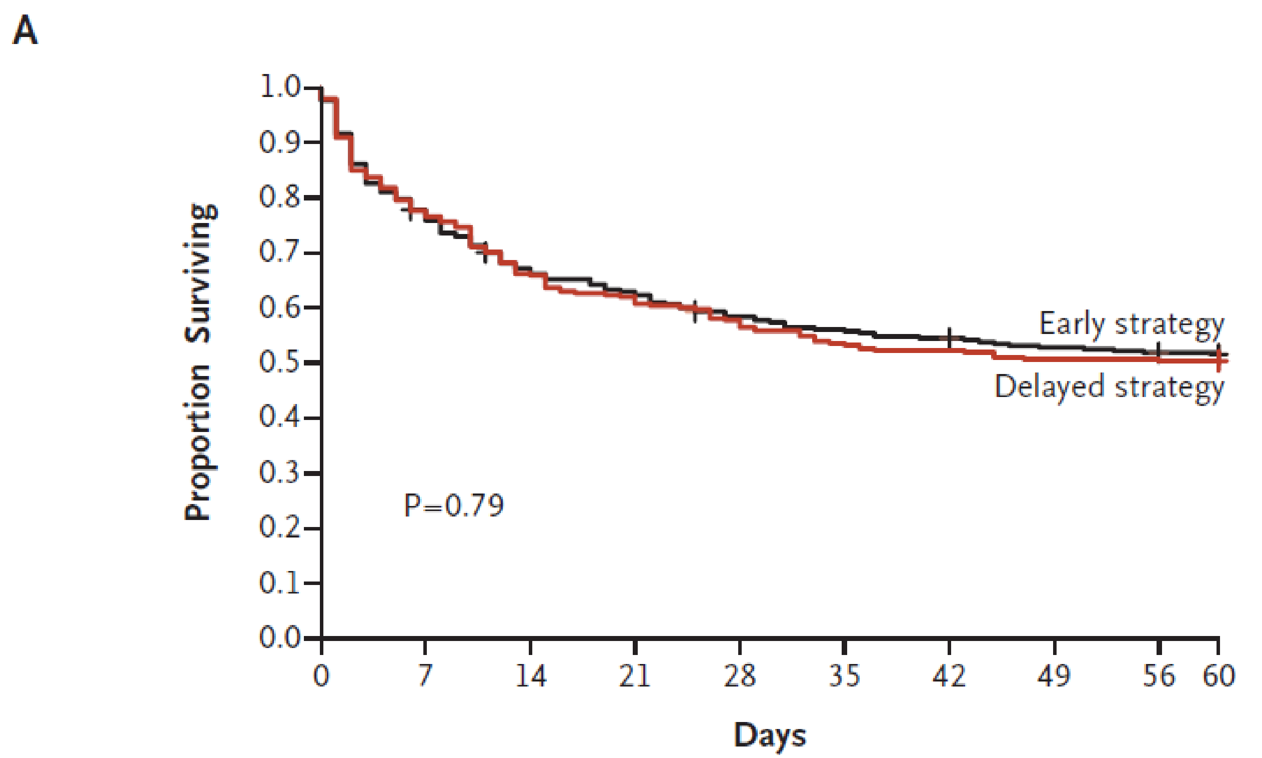
Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit

N Engl J Med 2016;375:122-33.

- Multicenter RCT
- Severe AKI (KDIGO stage 3) on Mechanical Ventilation and/or catecholemines
- 620 patients
- Early strategy - Immediately after randomization
- Delayed Strategy – Severe hyperkalemia, metabolic acidosis, pulmonary edema, BUN>112 mg/dl or oliguria > 72 hours after randomization

Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit

N Engl J Med 2016;375:122-33.



No. at Risk

Early strategy	311	241	207	194	179	172	167	161	158	157
Delayed strategy	308	239	204	191	178	165	161	156	156	155

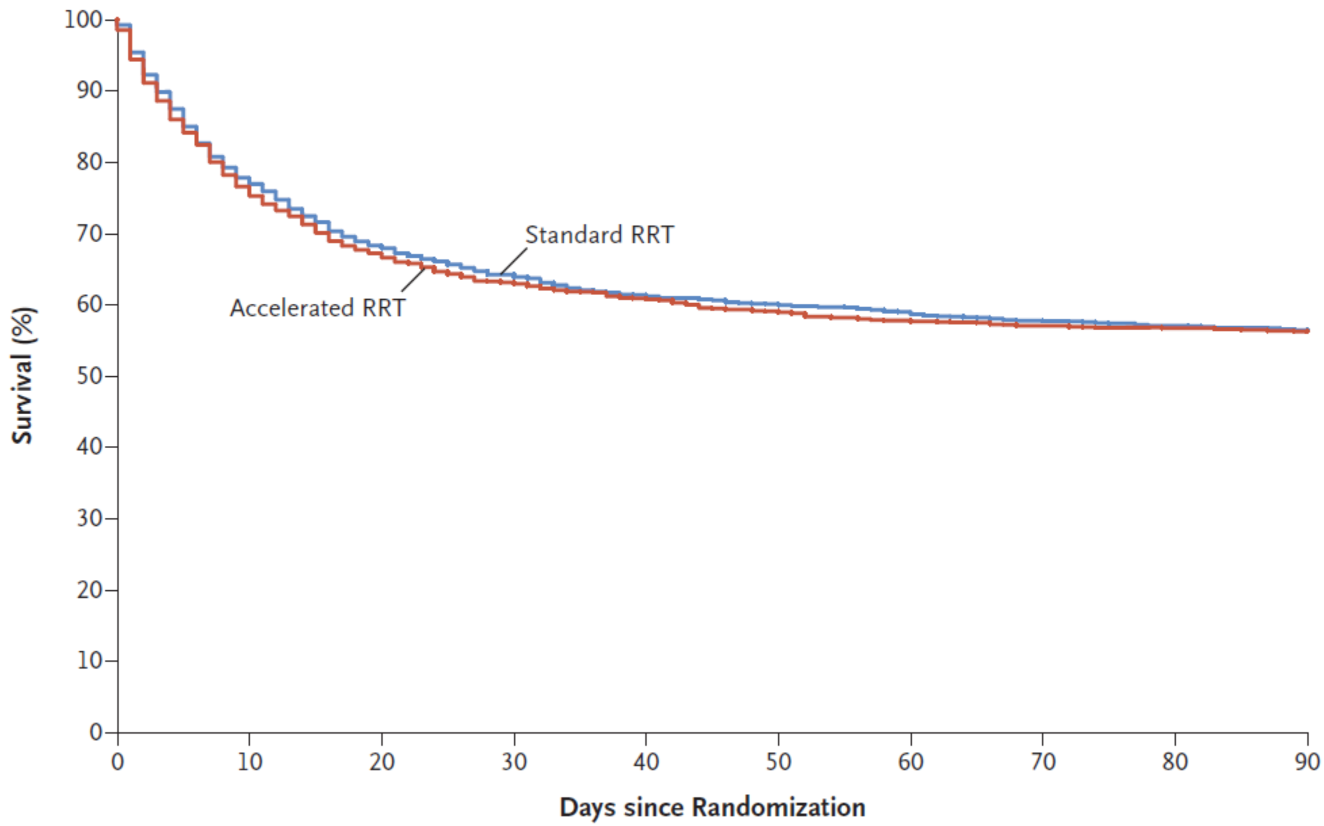
Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury

N Engl J Med 2020;383:240-51.

- Multicenter RCT
- Severe AKI
- 2927 patients
- Accelerated strategy – Within 12 hours
- Standard Strategy – RRT discouraged unless conventional indications developed or AKI persisted > 72 hours

Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury

N Engl J Med 2020;383:240-51.



No. at Risk

Standard RRT	1462	1138	999	939	897	878	862	844	833	823
Accelerated RRT	1465	1122	985	925	892	865	846	835	830	823

Intensity of Renal Replacement

No consistent statistically significant difference in survival regarding intensity

1. The VA/NIH Acute Renal Failure Trial Network. N Engl J Med 2008; 359:7-20
2. Tolwani AJ. J Am Soc Nephrol. 2008;19(6):1233-8.
3. RENAL Replacement Therapy Study Investigators. N Engl J Med. 2009;361:1627–1638

More is **not** better

CRRT and Sepsis

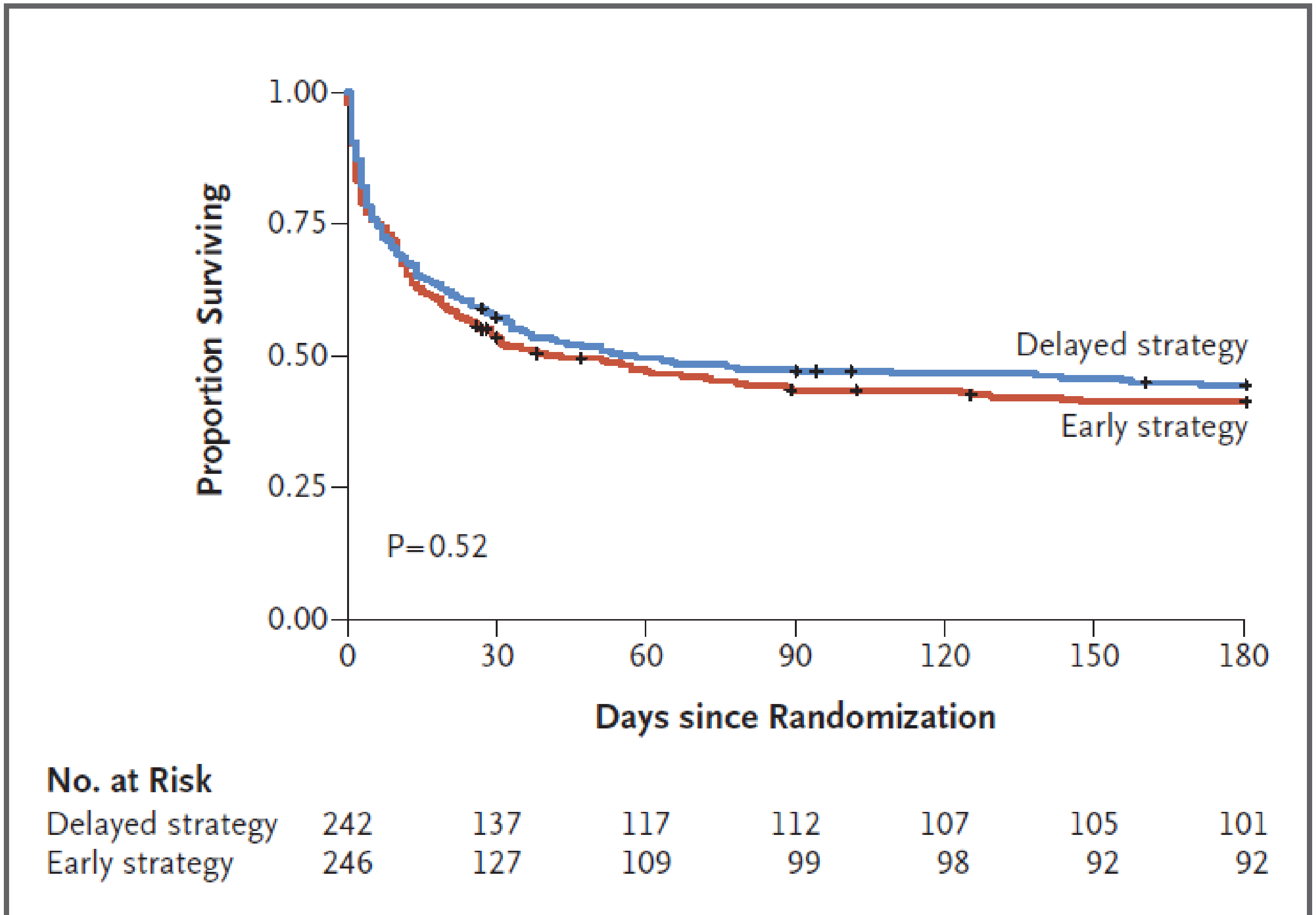
Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis

N Engl J Med 2018;379:1431-42.

- Multicenter RCT
- Early stage Sepsis with RIFLE stage Failure
- 488 patients
- Early strategy – RRT within 12 hours of RIFLE Failure stage
- Delayed Strategy – RRT within 48 hours of RIFLE Failure stage if no recovery had occurred

Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis

N Engl J Med 2018;379:1431-42.



Cessation of CRRT

All criteria for initiating CRRT are absent
Fluid balance can be kept approximately neutral with current **urine output**
There is a complication related to CRRT

When criteria are fulfilled begin a 12-24 hour period without CRRT
Reevaluate for indications for CRRT

CRRT should be initiated early and ceased late

Key Take-Home Points

Dialysis utilizes **D**iffusion for clearance

Continuous Renal Replacement utilizes **C**onvection for clearance

No difference in survival between HD and CRRT

HD has much higher clearance per unit time

CRRT not suitable for toxin removal

Life threatening Hyperkalemia is a contraindication for CRRT – CRRT works slowly

CRRT is not effective in improving sepsis

CRRT is more effective in getting patients to euvolemia

Board Question

Which One Renal Replacement method has the highest probability of in hospital survival?

A. Intermittent hemodialysis

B. CVVHDF

C. Sustained Low-Efficiency Dialysis

D. CVVH

E. All are equal