CONTINUOUS RENAL REPLACEMENT THERAPY

CRRT

The Critically Ill Patient with Acute Kidney Injury

- **Etiology of AKI**
  Clinical features may suggest the cause of AKI and dictate further investigation.

- AKI is common in the critically ill, especially in patients with sepsis and other forms of systemic inflammation (e.g., major surgery, trauma, burns), but other causes must be considered.

- **Volume-Responsive AKI**

  It is estimated that as many as 50% of cases of AKI are “fluid responsive,” and the first step in managing any case of AKI is to ensure appropriate fluid resuscitation.

- However, volume overload is a key factor contributing to the mortality attributable to AKI, so ongoing fluid administration to nonfluid-responsive patients is discouraged.

- **Sepsis-Induced AKI**
  Sepsis is a primary cause or contributing factor in more than 50% of cases of AKI, which includes cases severe enough to require RRT.

- Patients with sepsis,
  including those outside the ICU, develop AKI at rates as high as 40%. Incidence increases with the severity of sepsis.

- Sepsis-induced AKI can develop in patients with normal, decreased, as well as increased renal blood flow.

- In sepsis, the kidney often has a normal histological appearance.

- **Hypotension**

  Hypotension is an important risk factor for AKI, and many patients with AKI have sustained at least one episode of hypotension.

- **Treating fluid-responsive**

  AKI with fluid resuscitation is clearly an important step, but many patients also require vasoactive therapy (e.g., norepinephrine) to maintain arterial blood pressure

- **Postoperative AKI**
- Risk factors of postoperative AKI include

- hypovolemia, hypotension, major abdominal surgery, and sepsis.
- Surgical procedures (particularly gynecological) may be complicated by damage to the lower urinary tract with an obstructive nephropathy.
- Abdominal aortic aneurysm surgery may be associated with renal arterial disruption.
- Cardiac surgery may be associated with atheroembolism, hemolysis, and sustained periods of reduced arterial pressure as well as systemic inflammation.

Other Causes

- *Rhabdomyolysis*: Suggested by myoglobinuria and increased creatine kinase levels in patients who have experienced a crush injury, coma, or seizures.
- Often, elevated liver transaminases—aspartate aminotransferase > alanine aminotransferase—are also noted as a result of muscular injury.

- ***Nephrotoxins*:**
- **May cause renal failure via direct tubular injury, interstitial nephritis, or renal tubular obstruction.**
- **In patients with AKI, all potential nephrotoxins should be withdrawn.**

- *Glomerular disease*:
- Red cell casts, hematuria, proteinuria, and systemic features (e.g., hypertension, purpura, arthralgia, vasculitis) are all suggestive of glomerular disease.
-
- Renal biopsy or specific blood tests (e.g., Goodpasture's syndrome, vasculitis) are required to confirm diagnosis and guide appropriate treatment

- *Hemolytic uremic syndrome*:
- Suggested by hemolysis, uremia, thrombocytopenia, and neurological abnormalities

  and……..

Medical Demand/Necessity for Continuous Renal Replacement Therapy

- **Clinical Picture of Acute Renal Failure Changed during the 1980s**
- **Underlying diseases leading to acute renal failure (ARF) were severe sepsis and occurred frequently after abortions before, whereas its epidemiological pattern and the involvement of other organs became more and more common after the 1990s.**

Pathogenesis of ARF Changed

The main factors recently responsible for ARF include the following:

- • Shock
- • Perfusion disturbances
- • Hypoxia

- **1960** The idea for continuous renal replacement therapy (CRRT) was born,
- but supplies and technology were not available. Most of ARF was treated with Peritoneal dialysis (PD), because hemodialysis (HD) was difficult to perform and it was not tolerated by ICU patients
- **1970s** Henderson played an important role in the technical groundwork for hemofiltration.
- Isolated ultrafiltration (UF) and use of convection for solute removal was established experimentally.

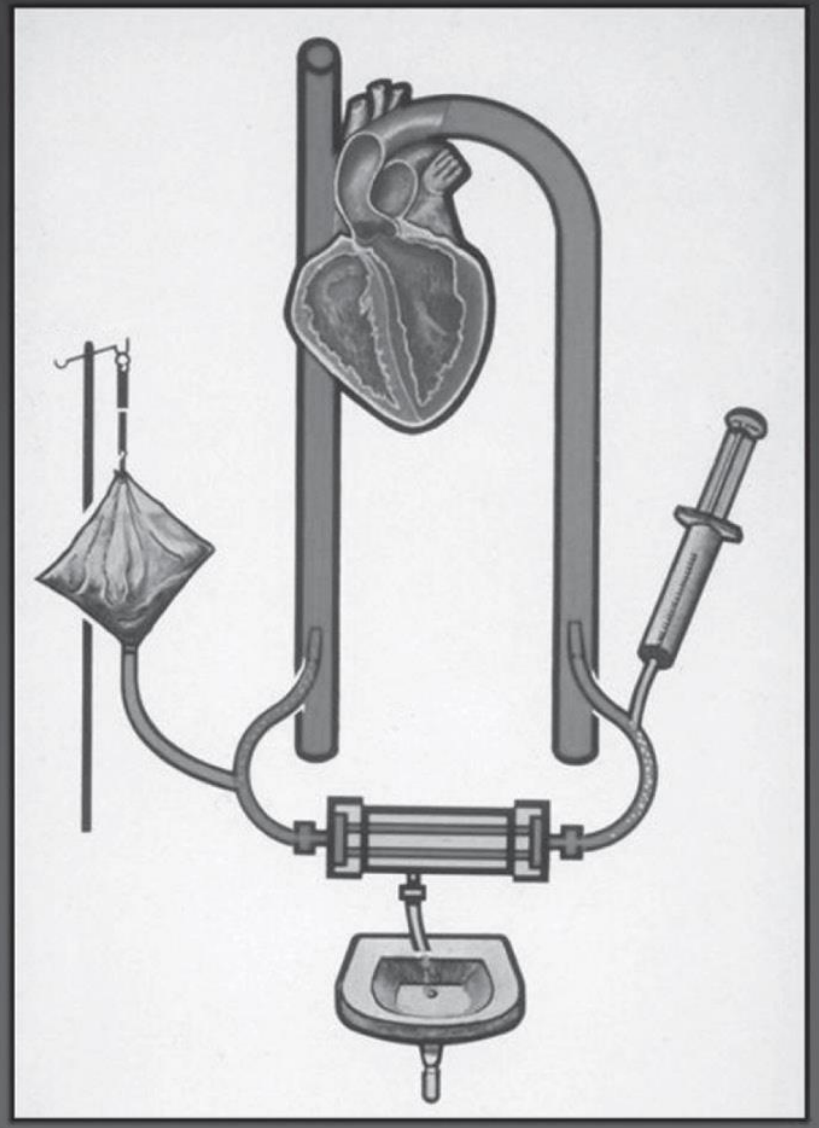
- **1977** First description of an arteriovenous hemofiltration technique by Kramer and colleagues in Göttingen, Germany

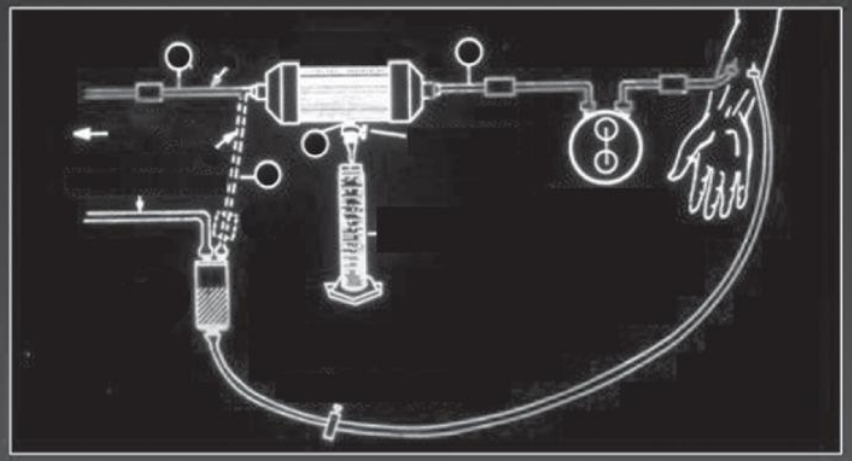
- **After a vascular catheter was placed accidentally into the femoral artery raised the idea to use the systemic arteriovenous pressure difference in an extracorporeal circuit to generate the ultrafiltrate providing an effective**

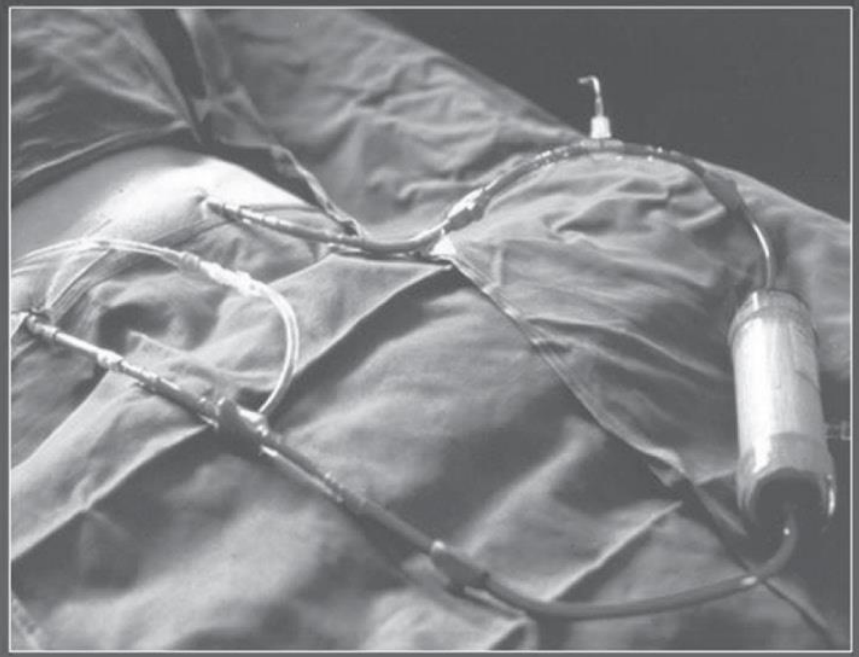
- **method for elimination of both fluid and solutes. Heparin could be added before and fluid could be reinfused after the filter. Continuous arteriovenous hemofiltration (CAVH) was soon accepted worldwide in ICUs**

- **Advantages of CAVH**
- • Hemodynamic stability over conventional HD at that time
- Simple
-
  - No necessity for blood pump
  - Continuous physiological fluid removal

- **Limitations of CAVH**
  - Low efficiency compared with HD
-
  - Reduced clearance capacity in the presence of high catabolic states
-
  - Additional intermittent HD or hemofiltration (HF) often necessary
- • Complications associated with arterial access (indwelling catheters,thrombosis)
-
  - Reliance on arterial pressure to pump blood through the circuit Danger of balancing errors
- • Necessity for continuous supervision by the staff

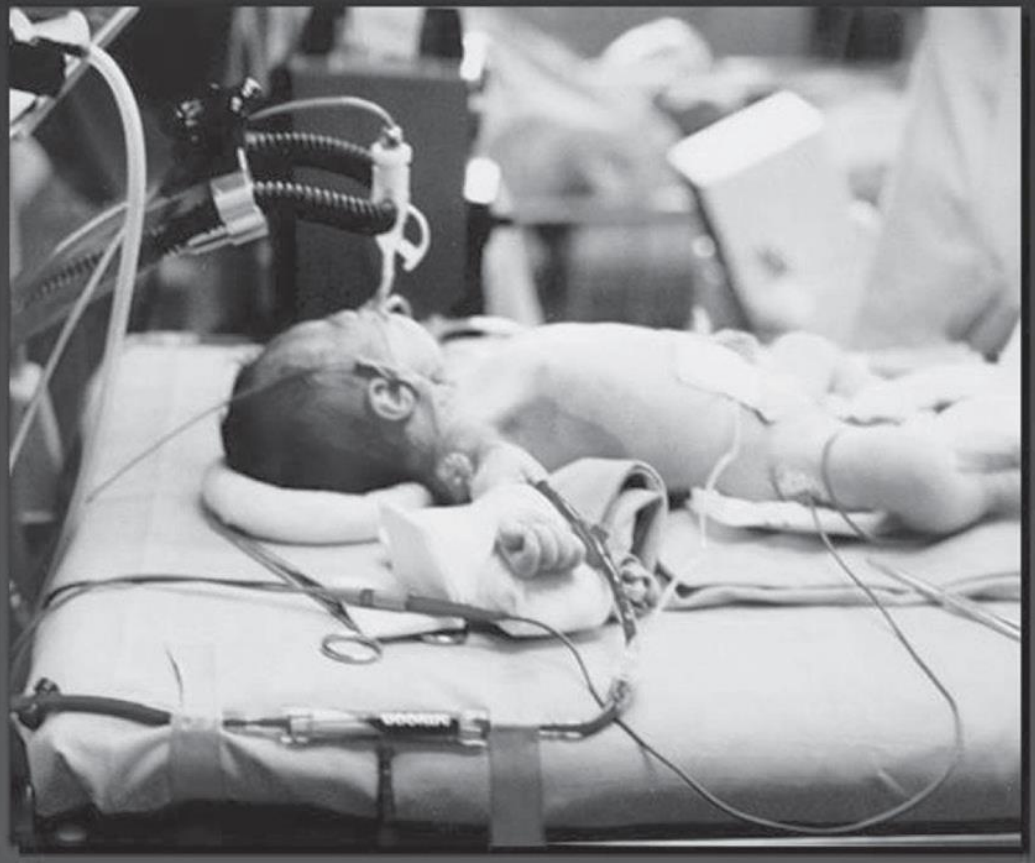


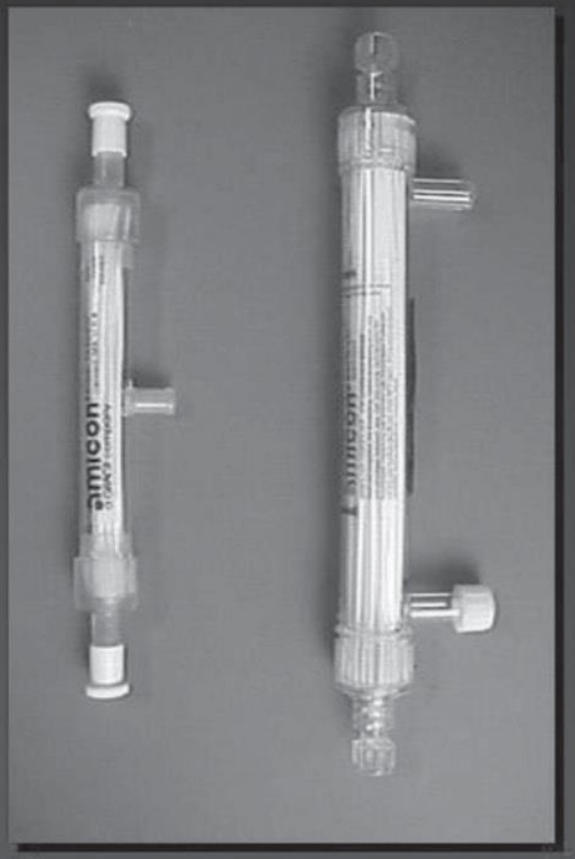




- **1979** Continuous venous–venous hemofiltration (CVVH) was first used in
  ARF after cardiac surgery in Cologne, Germany. Any desired filtrate volume could be arranged, and uremia was controlled.
- A pump, control, and balancing system became necessary
- **1980s** Numerous technical and methodical
  improvements in CRRT have contributed

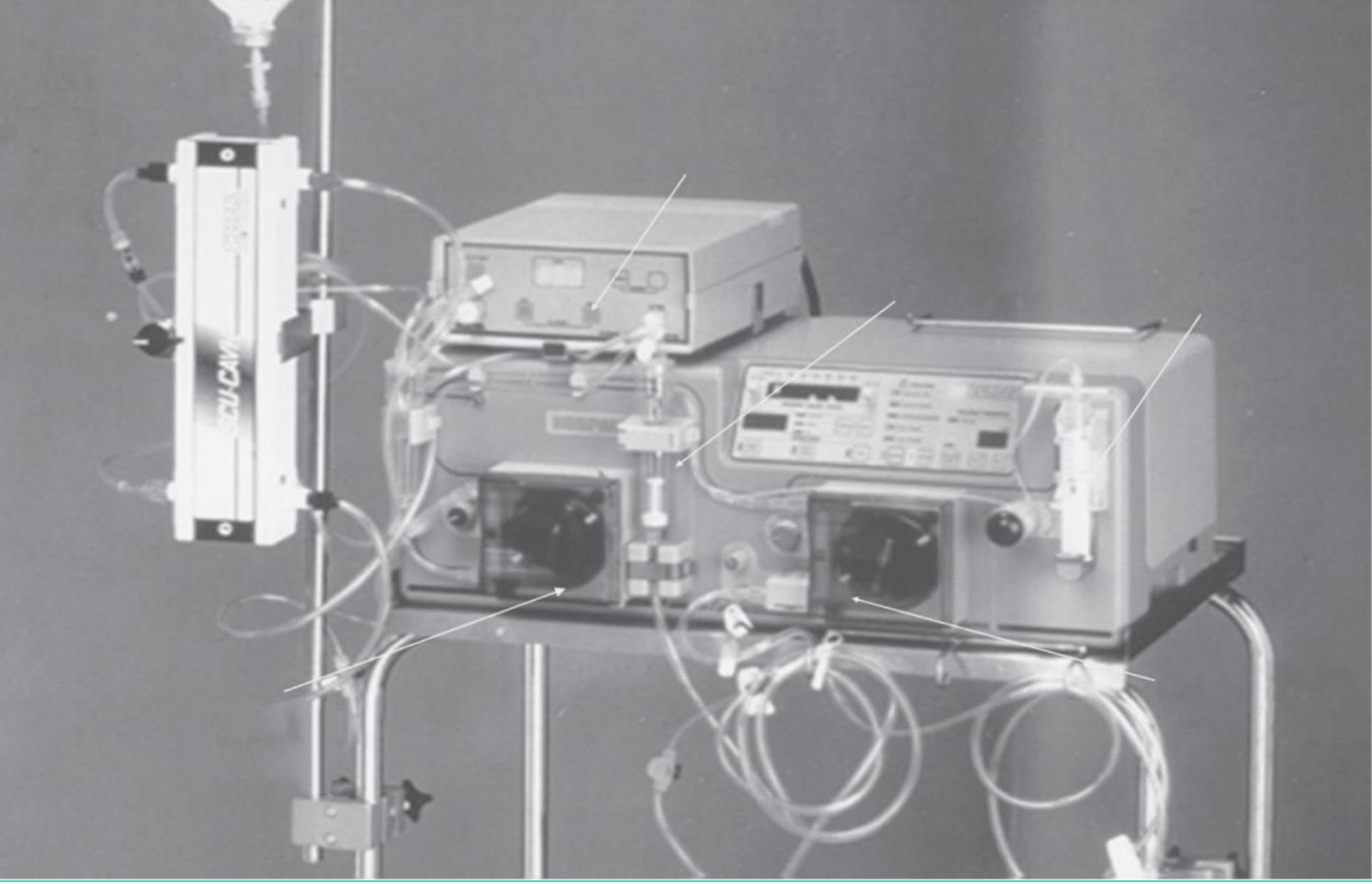
- **Changes in Arteriovenous Technique**
  - Different types of catheters to obtain adequate blood flow
-
  - Shorter blood line with no gadgets to reduce resistance
-
  - Positioning the collecting bag to apply a negative pressure
-
  - Optimization of treatment parameters, concept of filtration fraction
-
  - Changes in filter geometry and in the structure of fiber (An entire family of hemofilters was created to fulfill hemodynamic requirements.)
-
  - An increase in efficiency as a result of dialysis fluid being filtered through the external port of the filter; Continuous arterio-venous hemodialysis (CAVHD) implemented
-
  - Combination of hemofiltration and hemodialysis; Continuous arteriovenous hemodiafiltration (CAVHDF) was performed




amicon

- **Pump-Driven Venous–Venous Techniques Replaced Arteriovenous Techniques**
- • Blood pump to increase efficiency further; CVVH introduced
  • Double-lumen catheters used in jugular vein
- • Highly permeable polysulfone, polyacrylonitrile, and polyamide membranes
  developed with a cutoff between 15,000 Da and 50,000 Da.
- • Bicarbonate–buffer solutions became available
- • New anticoagulation methods established, even for patients at high risk of bleeding

- **1982** Use of CAVH in ICU patients approved by the Food and Drug Administration in the United States.
- **1984** The first neonate was treated with CAVH in the world occurred in Vicenza, Italy
- **1990–2000** establishment of new technologies, modalities, and adequate dose of CRRT:
- • Adoptive technology
- • Machines created specifically for CRRT
- • Different therapies chosen based on the needs of the patient
  • Progression of dose delivery and prescription
  CRRT is achievable in most ICUs worldwide.
- **2000** Multiorgan support therapy (MOST)



The first neonate treated in the world with continuous arteriovenous hemofiltration and a special minifilter in Vicenza, Italy, in 1984

- **kidney and the severity of physiological disorders.**
- The proper goal of extracorporeal blood purification in the ICU should be MOST.
- Treatment should not directed at various organs as separate entities it should be integrated and patient directed.
- Therefore, a wide range of supportive therapies in sepsis and liver failure were established, such as high-volume hemofiltration (HVHF), coupled plasma filtration and adsorption (CPFA), bio-artificial livers, and endotoxin removal strategies.

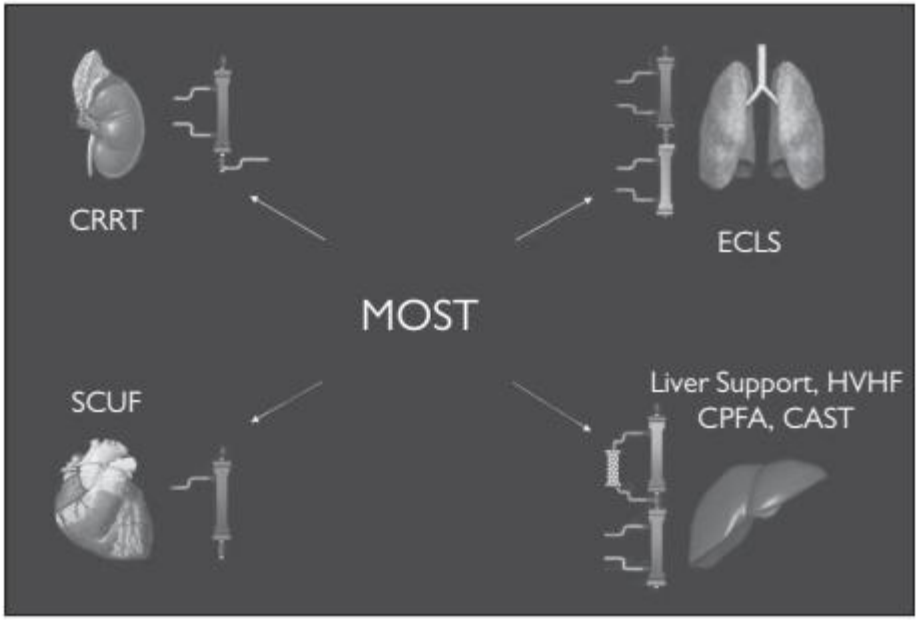


Figure 2.5 The concept of multiorgan support therapy (MOST). Blood can be circulated by a platform through different filtration/adsorption systems, leading to removal of specific compounds and support to different failing organs. CAST, XXXXX; CPFA, coupled plasma filtration adsorption; CRRT, continuous renal replacement therapy; ECLS, extracorporeal lung support system; HVHF, high-volume hemofiltration; SCUF, slow continuous ultrafiltration.

- **2000** Founding of the Acute Dialysis Quality Initiative (ADQI)
- The ADQI is an ongoing process that seeks to produce evidence-based recommendations for the prevention and management of acute kidney injury (AKI) and on different issues concerning acute renal replacement therapy (RRT). The following goals have been achieved:
- • Definition and classification of ARF (RIFLe criteria, acute kidney injury network (AKIN))
- • Practice guidelines adopted in clinical practice (cardiac surgeryassociated AKI)
- ***Recent interest focuses on the timing of treatment initiation on patient survival, dose of RRT, fluid management, and the effect of RRT modality on recovery of renal function in ARF.***

All patients are treated with:

- ✓Intermittent hemodialysis

or

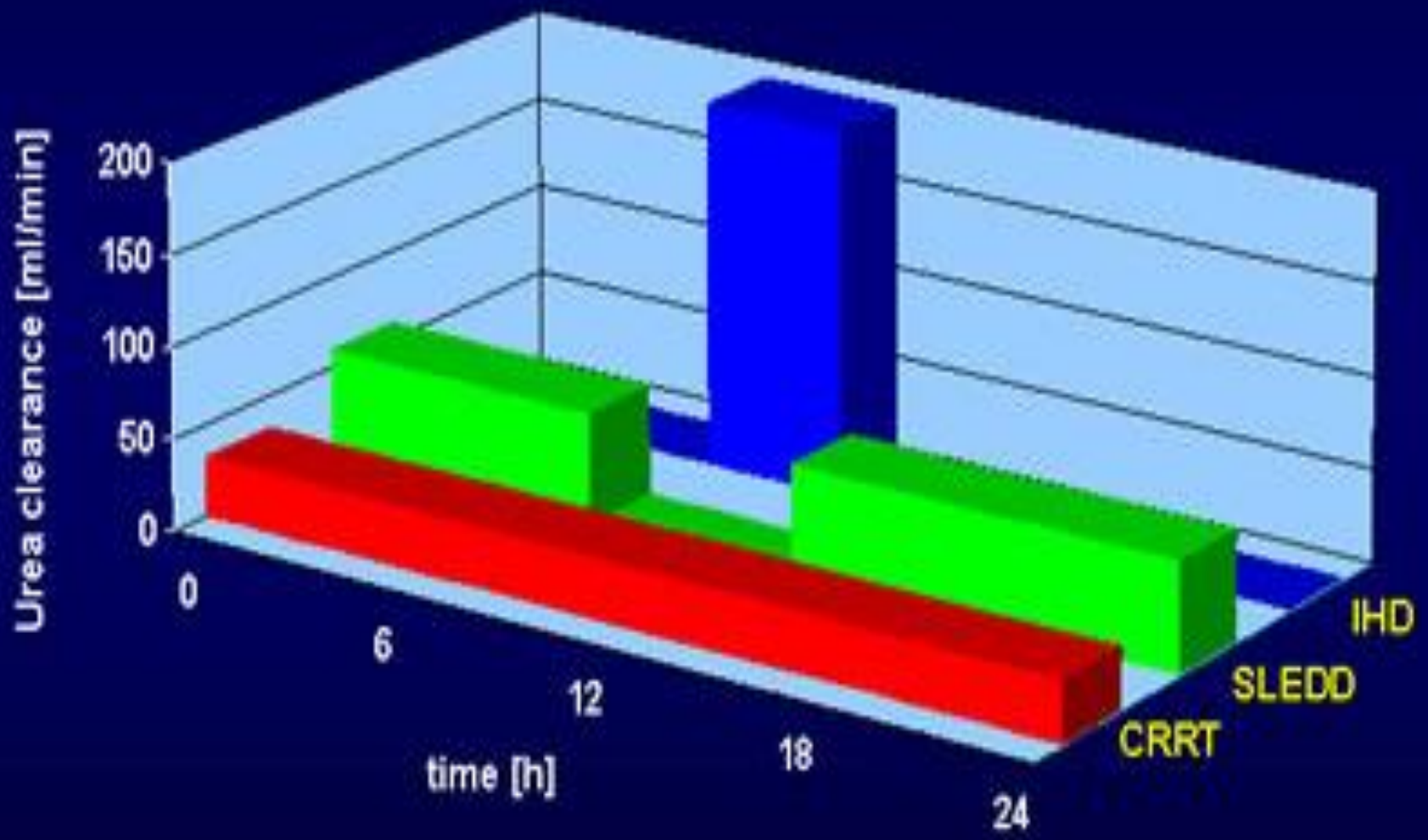
- ✓Continuous renal replacement therapy (CRRT)

or

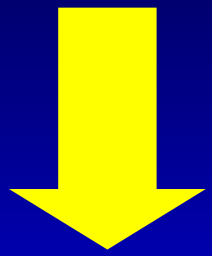
- ✓Slow Low Efficiency Dialysis (SLED) based on hemodynamic status.

or

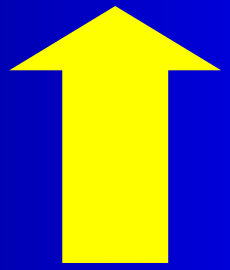
- ✓Peritoneal dialysis


Urea clearance [ml/min]
200
150
100
50
0
0
6
12
18
24
time [h]
IHD
SLEDD
CRRT

- “Classic IHD” 4 hours 3 times/week



- “SLEDD”



- “Classic CRRT”

Indications of CRRT

Bellomo & Ronco. Critical Care. 2000; 4:339 - 345

- **Acute renal failure, which often is a part of multi-organ failure with complications such as shock, cardial and non-cardial pulmonary edema, hemodynamic instability, bleeding, hypercatabolism**
- **Non obstructive oliguria (u/o <200 ml/12 hr) or Anuria.**
- **Severe Acidemia (pH <7.1) d/t metabolic acidosis**
- **sepsis**
- **Hyperkalemia (K >6.5 mmol/L)**
- **Progressive severe dysnatremia (Na >180 or 115 mmol/L)**
- **Suspected uremic organ involvement (pericarditis)**
- **Drug overdose for dialyzable toxins**
- **Hyperthermia (core temp. >39.5oC)**

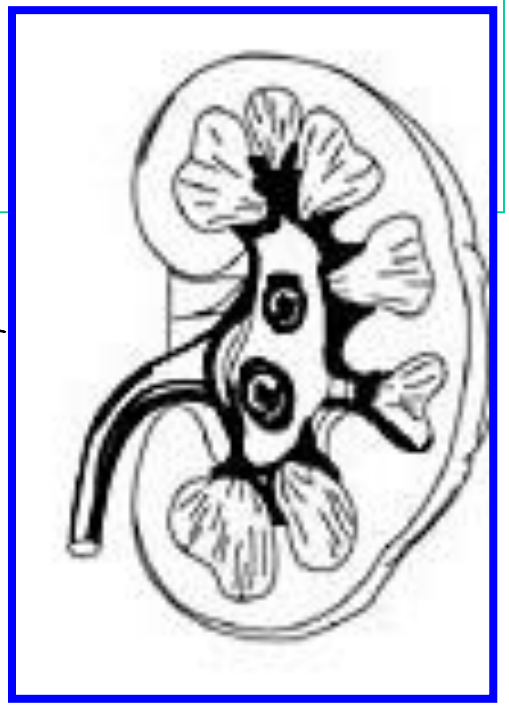
Clinical Conditions to Consider

- ARF and need for fluid management related to:
  - SIRS
  - Unstable on IHD
  - Organ transplants
  - CHF /volume overload
  - Post CV surgery
  - Post trauma patients
  - Severe Burns

Removal of immunomodulatory substances in sepsis

- **Middle to large molecules**
  - with cardiodepressant, vasodilatory, or immunomodulatory properties in septic or highly catabolic patients.
- **Examples of such toxins are**

- **endotoxin,**
- **interleukin-1,**
- **complement anaphylatoxins,**
- **platelet activating factor,**
- **tumor necrosis factor**



The most important complication of intermittent hemodialysis

1 - Hypotension % 25 – 50

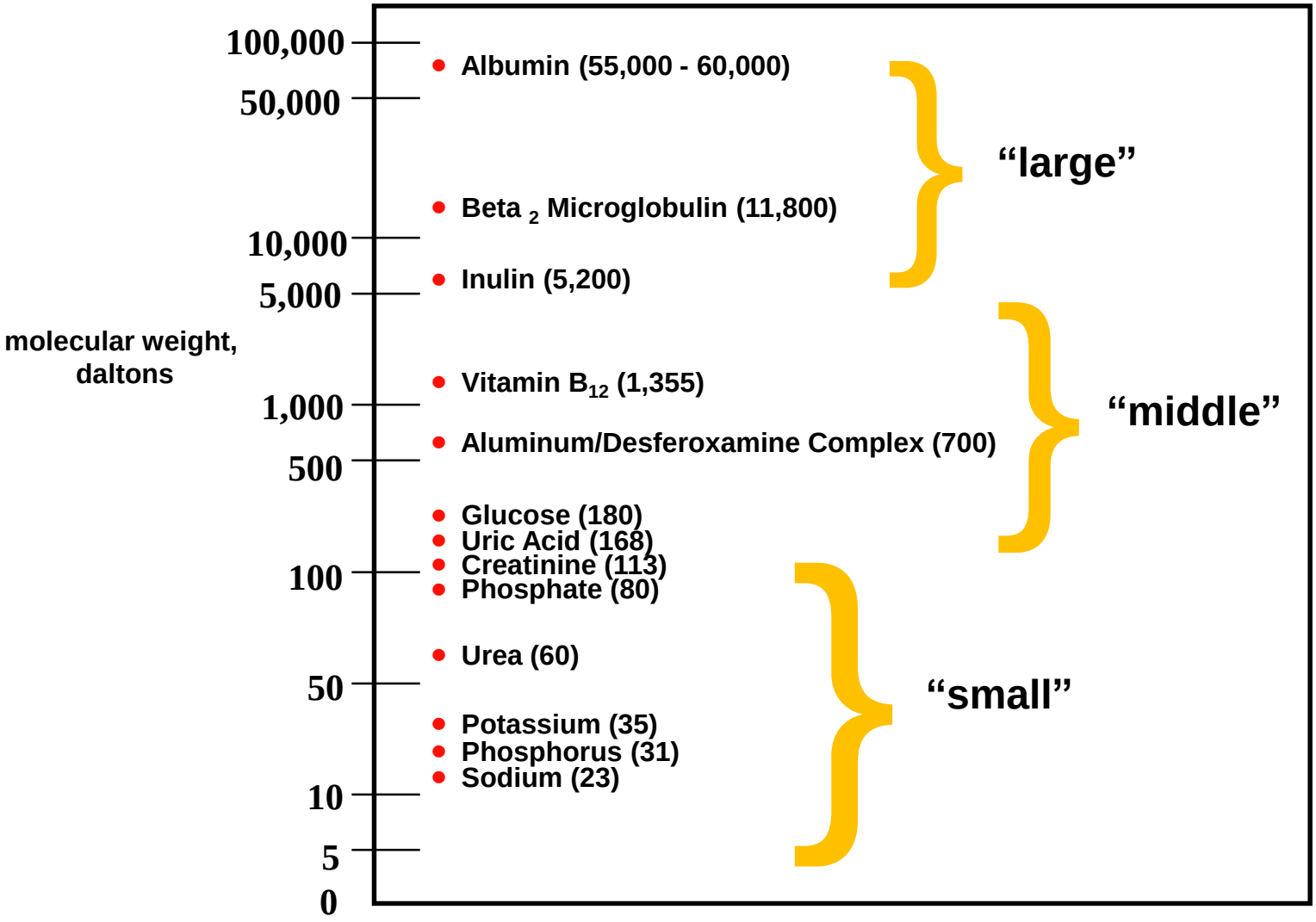
2 – Muscle cramp % 5 - 20

3 – Arrythmia

Suitable Dialysis

1 – Better clinical tolerance
2 – Better solute clearance
3 – Improvement acid , base & electrolytes
4 – Biocompatibility
5 – Minimum complications
6 – Suitable monitoring during the treatment

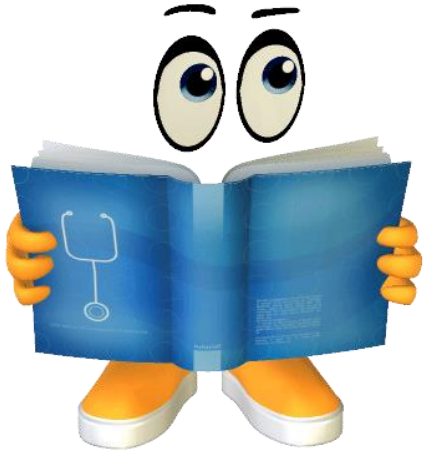
Molecular Weights



Terminology

- **Hemodialysis**
  - transport process by which a solute passively diffuses down its concentration gradient from one fluid compartment (either blood or dialysate) into the other
- **Hemofiltration**
  - use of a hydrostatic pressure gradient to induce the filtration (or convection) of plasma water across the membrane of the hemofilter.
- **Hemodiafiltration**
  - dialysis + filtration.
  - Solute loss primarily occurs by diffusion dialysis but 25 percent or more may occur by hemofiltration

Overview of CRRT:



- Slow Continuous Therapy
- Low Blood Flow Rate
- Low Dialysate Flow Rate
- Low Replacement Flow Rate
- Low Ultrafiltration Rate

THERAPIES

Renal therapies

Continue	*Intermittent*
•SCUF	•IHF-HVHF
•CVVH	•IHD-SLED
•CVVHD	•IHDF
•CVVHDF	

•**CPFA**

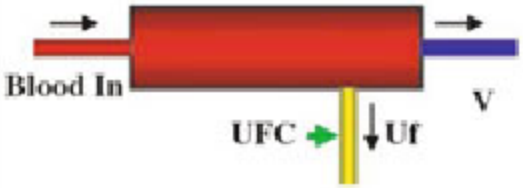
Extra Renal Therapies

Standard

- •PEX
- •HEMOPERFUSION

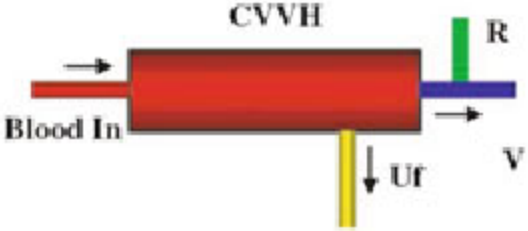
MODALITIES OF CRRT

SCUF



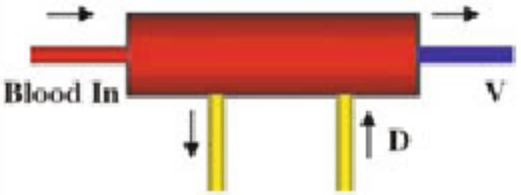
Qb = 100 ml/min Qf = 2-8 ml/min

CVVH



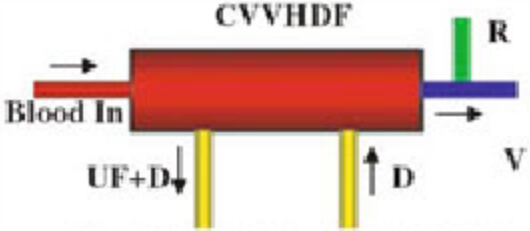
Qb = 100-200 ml/min Qf = 10-30 ml/min
K = 15-45 L/24 h

CVVHD



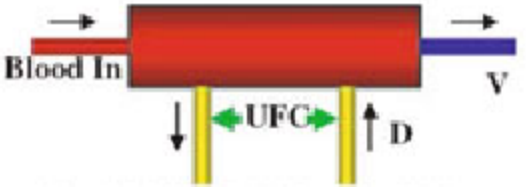
Qb = 100-200 ml/min Qf = 2-4 ml/min
Qf = 10-30 ml/min K = 15-45 L/24 h

CVVHDF



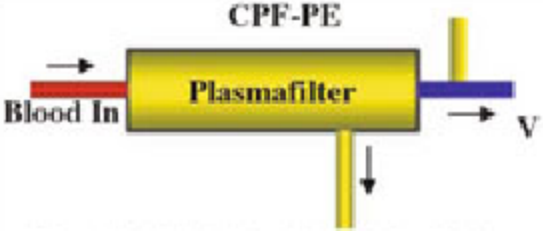
Qb = 100-200 ml/min Qf = 10-30 ml/min
Qd = 10-30 ml/min K = 20-50 L/24 h

CVVHDF-SLED



Qb = 100-200 ml/min Qf = 2-8 ml/min
Qd = 50-200 ml/min K = 40-60 L/24 h
Diffusion+Convection (Back Filtration)

CPF-PE

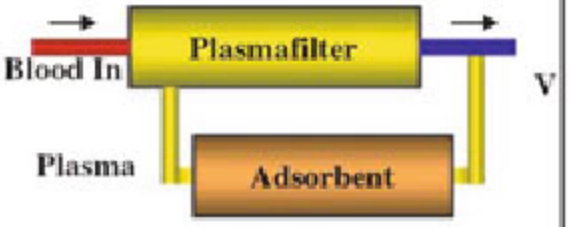


Qb = 100-200 ml/min Pf = 20-30 ml/min
Can be coupled with CVVH or CVVHDF

CHP

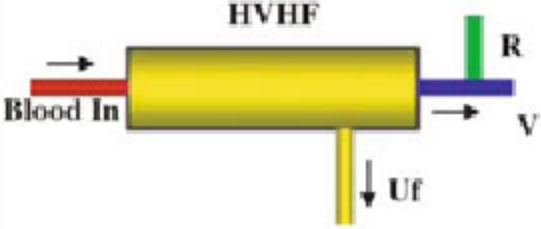
Qb = 100-200 ml/min
Can be coupled with CVVH or CVVHDF

CPFA



Qb = 100-200 ml/min Pf = 20-30 ml/min
Can be coupled with CVVH or CVVHD/F

HVHF



Qb = 200-300 ml/min Qf = 50-100 ml/min
K = 60-120 L/24 h

Treatment Modalities

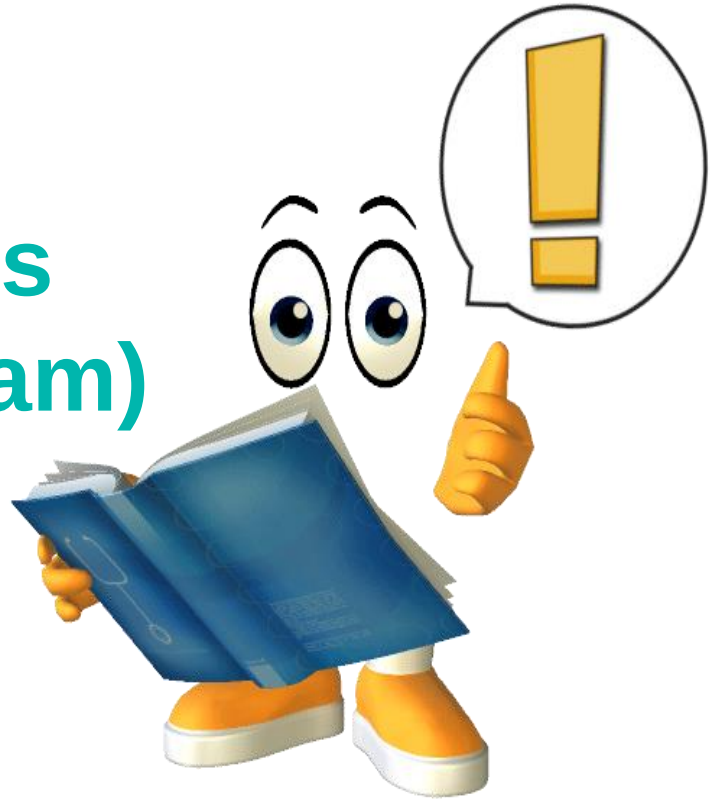
- **SCUF – Slow Continuous Ultrafiltration (Ultrafiltration)**
- **CVVH – Continuous VenoVenous Hemofiltration (Convection)**

- **CVVHD – Continuous VenoVenous Hemodialysis (Diffusion)**
- **CVVHDF – Continuous Venovenous Hemodiafiltration**
- (Diffusion and Convection)
- **TPE or PEX – Therapeutic Plasma Exchange**
- **HP – Hemoperfusion**
- **CPFA – coupled plasma filtration adsorbtion**

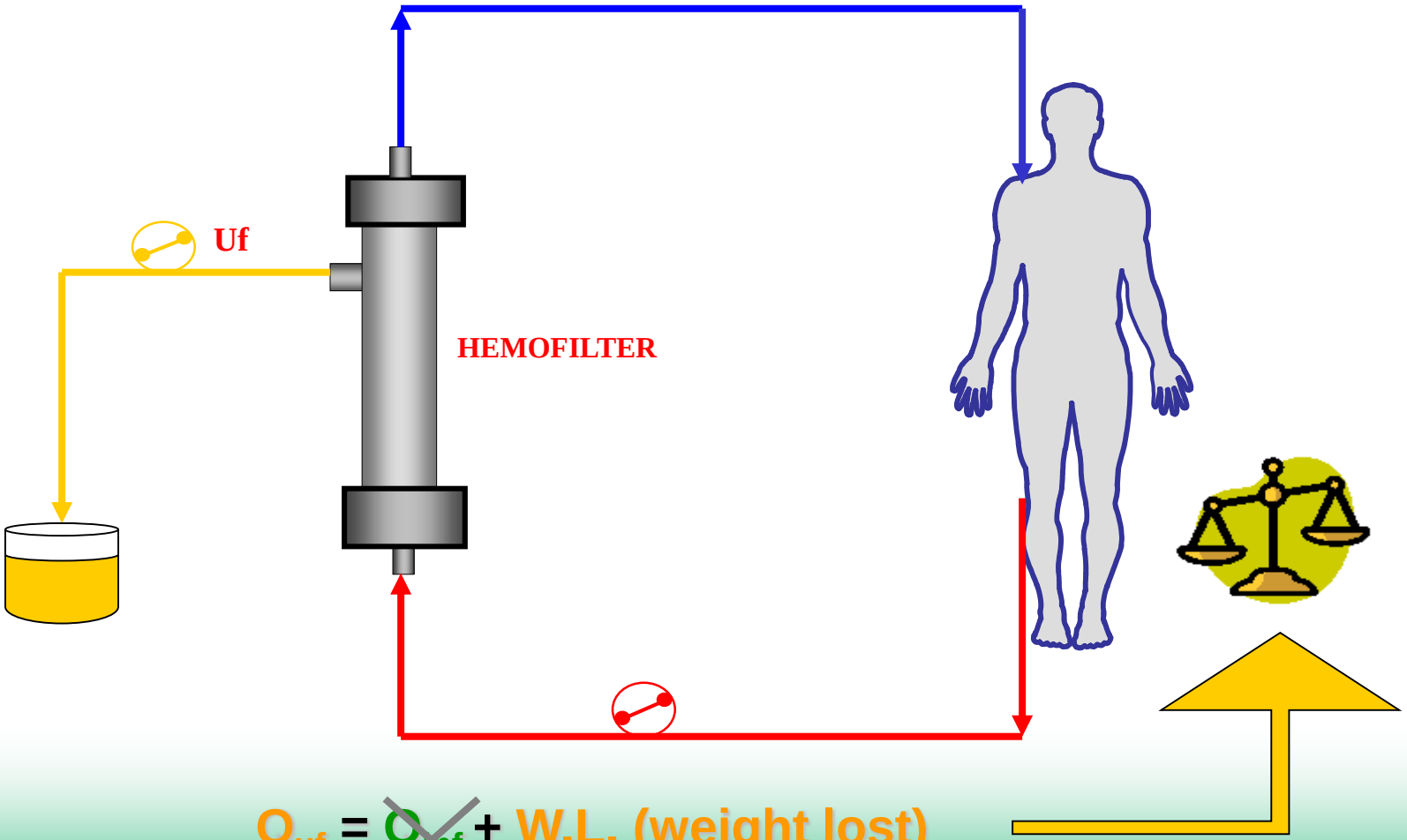
Differential Indication

SCUF	Fluid Overload
CVVH	Hemodinamic Unstibility, Middel Molecules toxins , Sepsis
CVVHD	Hemodinamic Unstibility, Small Molecules toxins (Hyperkalemia)
CVVHDF	Hemodinamic Unstibility, Middel / Small Molecules toxins , Sepsis
HF	Rapid Elimination Middel Molecules , Sepsis , High Bleeding Risk
HD	Rapid Elimination Small Molecules , High Bleeding Risk
HDF	Rapid Elimination Middel / Small Molecules , Sepsis , High Bleeding Risk
HP	Drug Intoxication , poisoning
PEX	Liver Failure , Sepsis , Autoimmuno Dissease
CPFA	middle molecules toxins . Sepsis

CRRT Modalities (Schematic Diagram)



SCUF
(SLOW CONTINUOUS ULTRAFILTRATION)



$Q_{uf} = \cancel{Q_{inf}} + W.L.\ (weight\ lost)$

SCUF
Slow Continuous Ultrafiltration

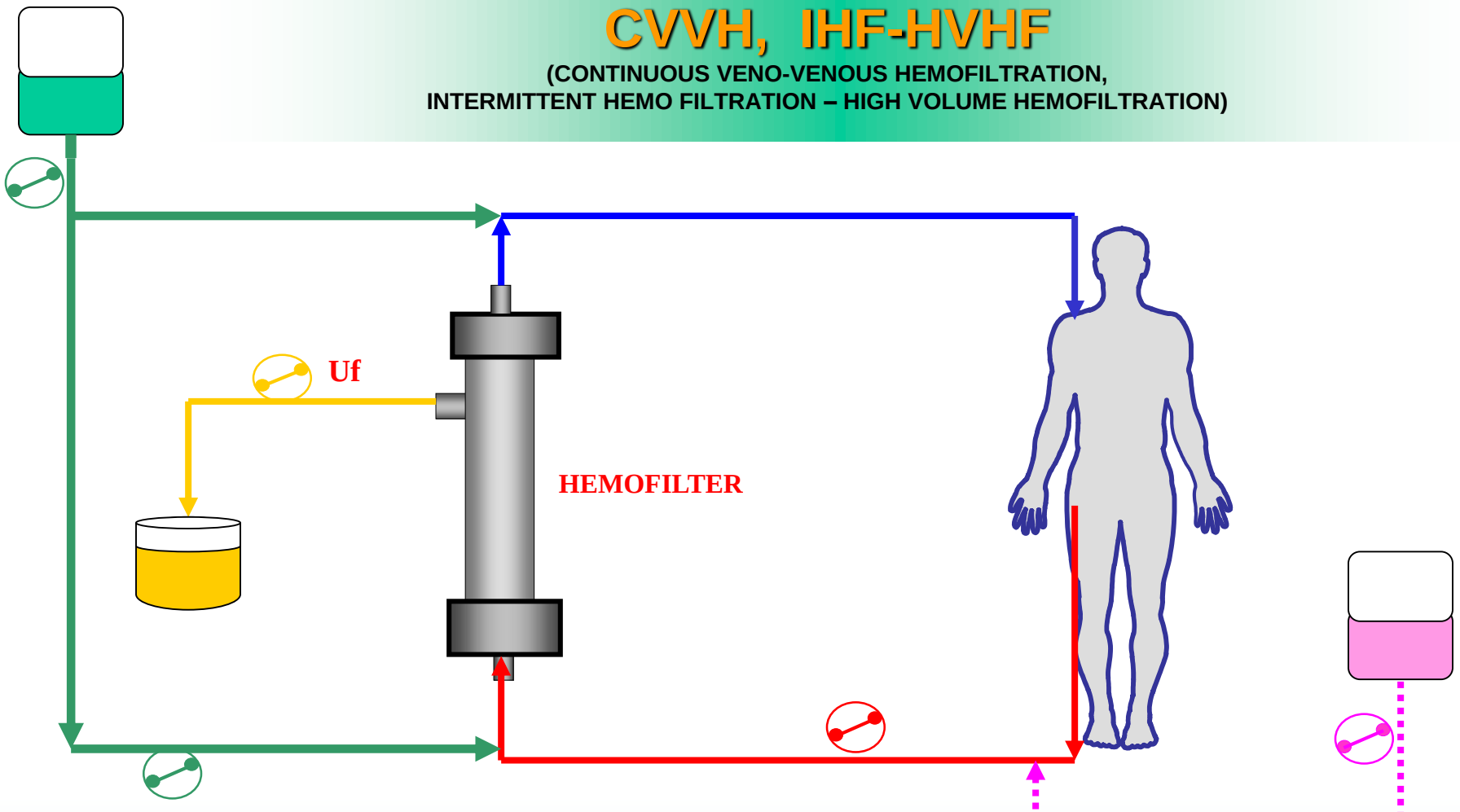
- **Primary therapeutic goal:**
  - Safe management of fluid removal
- **UF rate ranges up to 2 L/Hr**
- **No** dialysate
- **No** replacement **fluids**
- **Large fluid removal by ultrafiltration**
- **Blood Flow rates = 10 - 450 ml/min**

Goals of Fluid Management

- **Normovolemia**
- **Remove fluid to create a space for fluid therapy.**
- **Optimize hemodynamic parameters.**
- **Avoid hypotension - drop down of systemic BP will cause marked fall in renal blood flow and will lead to further damage, insult or injury to kidneys.**

CVVH, IHF-HVHF

**(CONTINUOUS VENO-VENOUS HEMOFILTRATION,
INTERMITTENT HEMO FILTRATION – HIGH VOLUME HEMOFILTRATION)**



(0:80%)

$Q_{uf} = Q_{inf} + W.L.\ (weight\ lost)$

$Q_{uf} = (Q_{inf\ PRE} + Q_{inf\ POST}) + W.L.\ (weight\ lost)$

CVVH
Continuous VV Hemofiltration

- Primary therapeutic goal:
  - convective solute removal and safe mgmt. of fluid volume
- UF rate ranges 12-20 L/24 hours (>500 ml/hr)
- Requires replacement solution to drive convection or solvent drag.
- Solute (urea, creatinine) clearance depends on the rate of Replacement solution.
- (the higher the volume of Replacement used, the faster / greater the solute removal).
- No dialysate fluid required.

CVVH:

- **Pre – dilution:**

  Advantages:

  > Less chances of filter clotting
  > Less heparinization

  Disadvantages:

  > Less solute removal

- **Post – dilution:**

  Advantages:

  > Higher solute removal

  Disadvantages:

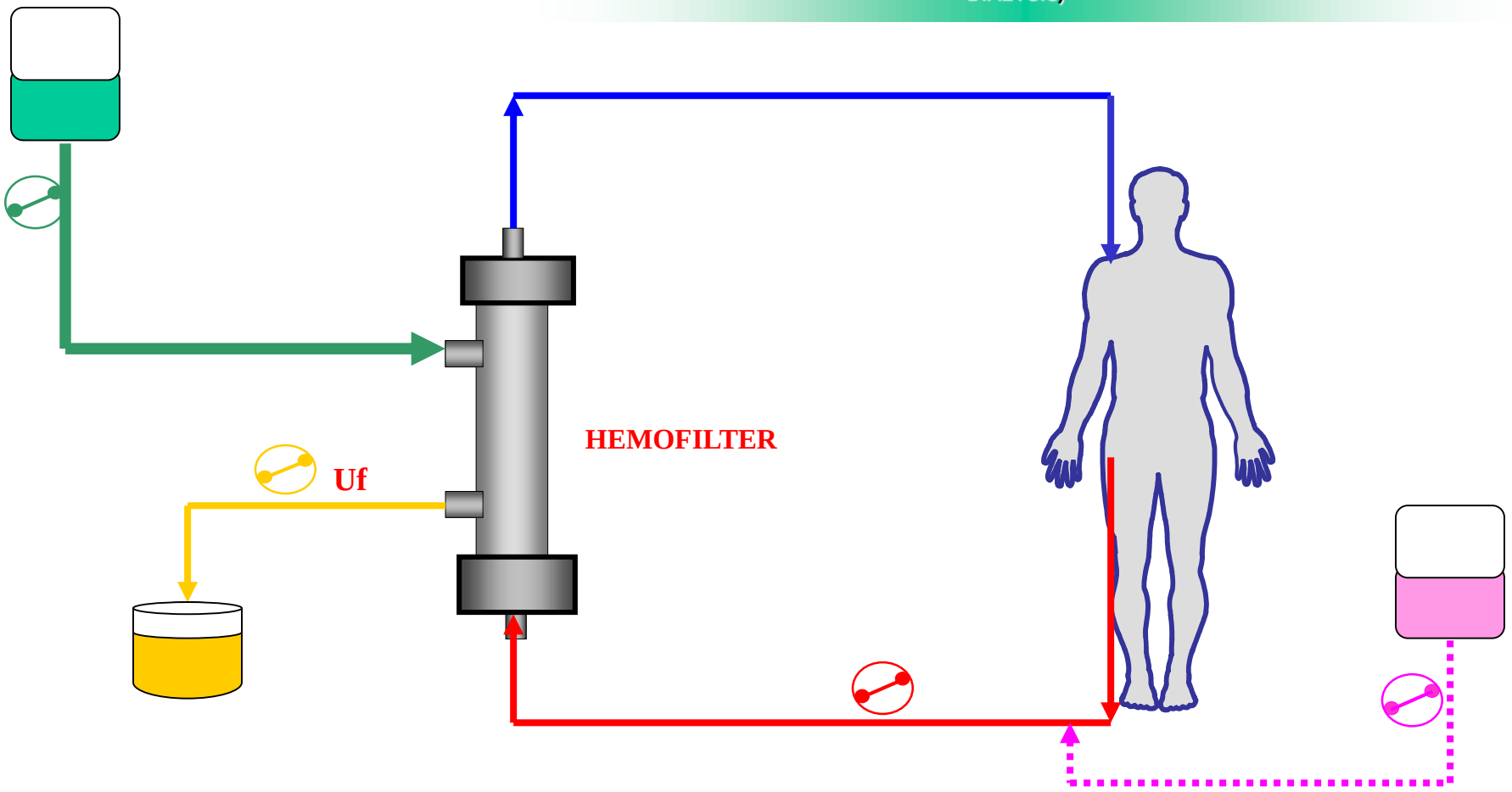
  > Higher chances of filter clotting.

Replacement Fluids

- **Drives convective transport.**
- **Physician Rx and adjusted based on patient's clinical need.**
- **Administered pre or post filter.**
- **Physiological sterile replacement solutions may be:**
  - Bicarbonate – based buffered solutions
  - Lactate – based buffered solution

CVVHD/ IHD-SLED

(CONTINUOUS VENO-VENOUS HEMODIALYSIS / INTERMITTENT HEMODIALYSIS SLOW EXTENDED DIALYSIS)



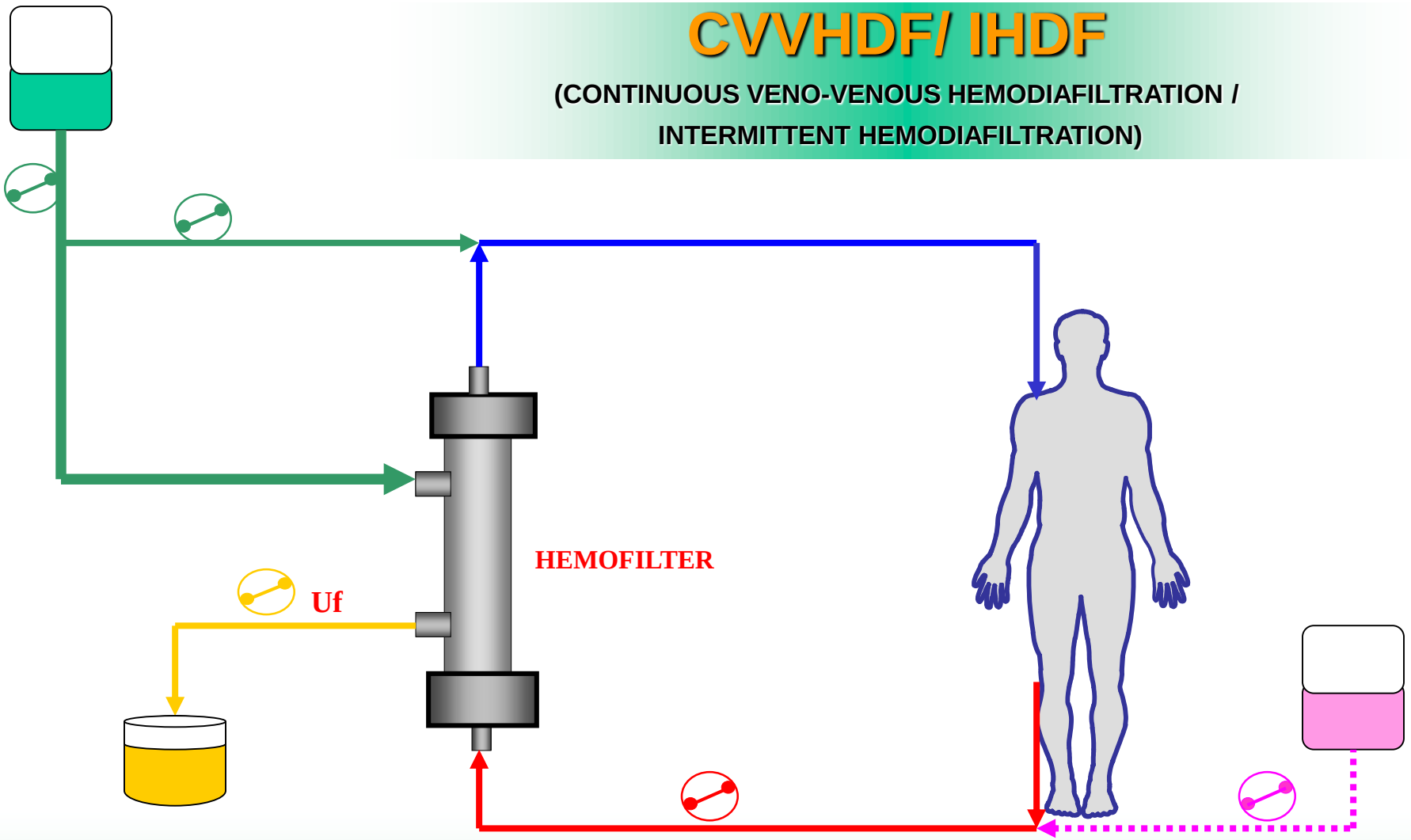
$$Q_{uf} = \cancel{Q_{inf}} + \text{W.L. (weight lost)}$$

CVVHD
Continuous VV Hemodialysis

- **Primary therapeutic goal:**
  - Solute removal by diffusion
  - Safe fluid volume management
- **Requires dialysate solution**
- Dialysate Flow rate = up to 133 ml/min (8 L/hr)
- **Blood Flow rate = 10 - 450 ml/min**
- **No** replacement **solution**
- **Solute removal determined by Dialysate Flow rate.**

CVVHDF/ IHDF

(CONTINUOUS VENO-VENOUS HEMODIAFILTRATION / INTERMITTENT HEMODIAFILTRATION)



$Q_{uf} = Q_{inf} + W.L.\ (weight\ lost)$

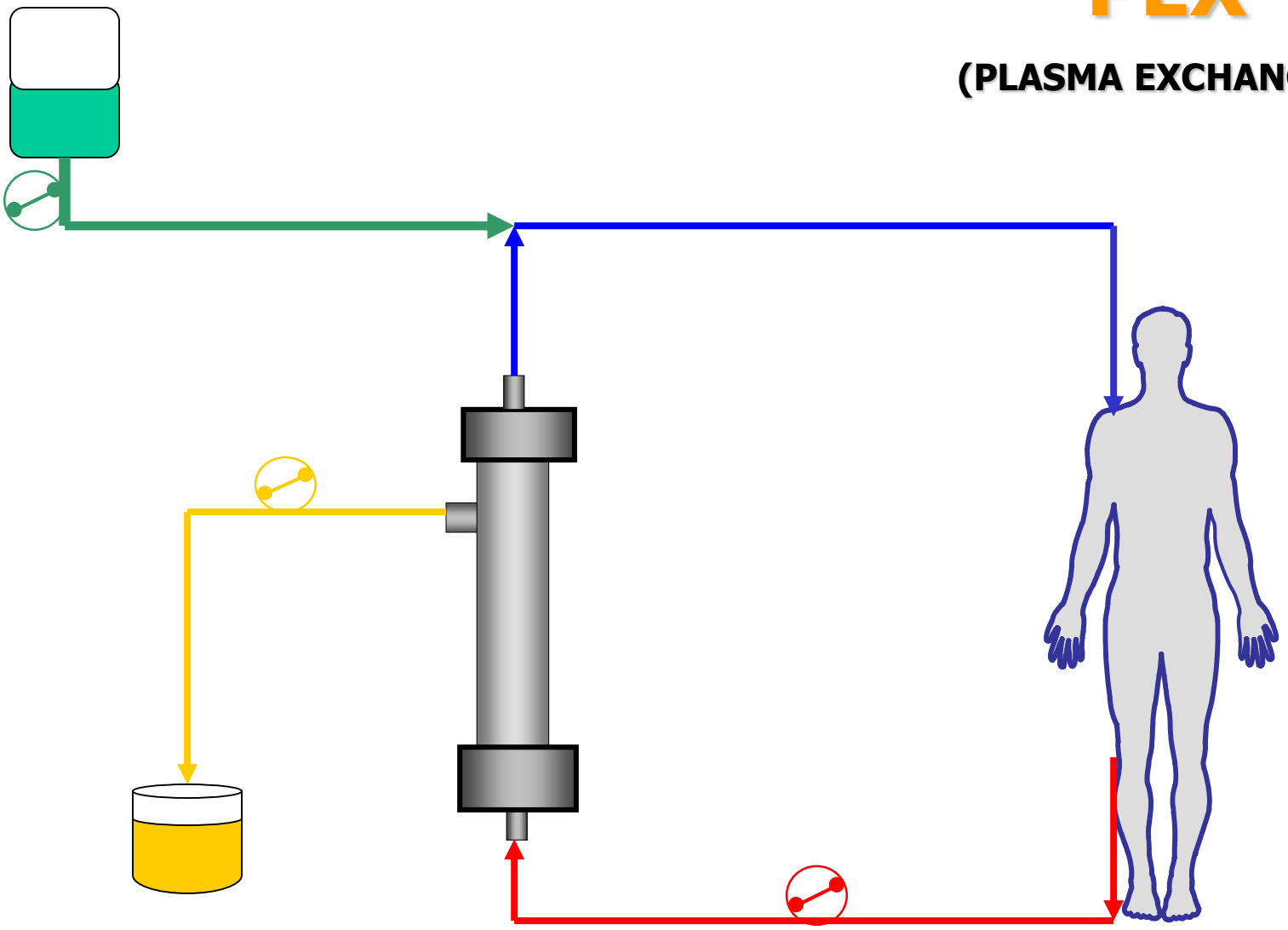
$Q_{uf} = (Q_{inf\ PRE} + Q_{inf\ POST}) + W.L.\ (weight\ lost)$

CVVHDF
Continuous VV Hemodiafiltration

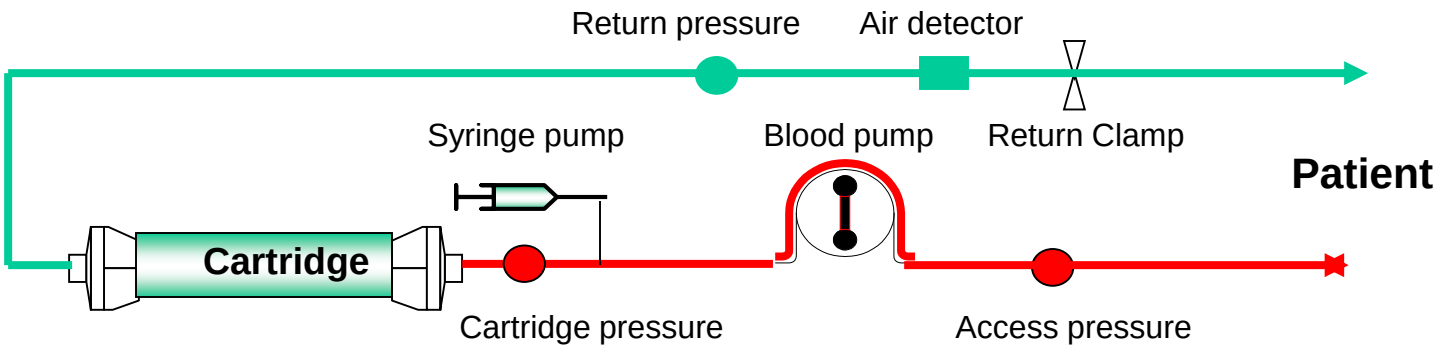
- **Primary therapeutic goal:**
  - Solute removal by diffusion and convection
  - Safe fluid volume mgmt.
- **Combines CVVH and CVVHD therapies**
- **UF rate ranges 12 - 20L/24hr**
- **Uses** dialysate **solution**
- **Uses** replacement **solution**
- **Blood Flow rate = 10 - 450ml/min**
- Dialysate Flow rate = up to 133 ml/min

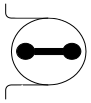
PEX

(PLASMA EXCHANGE)



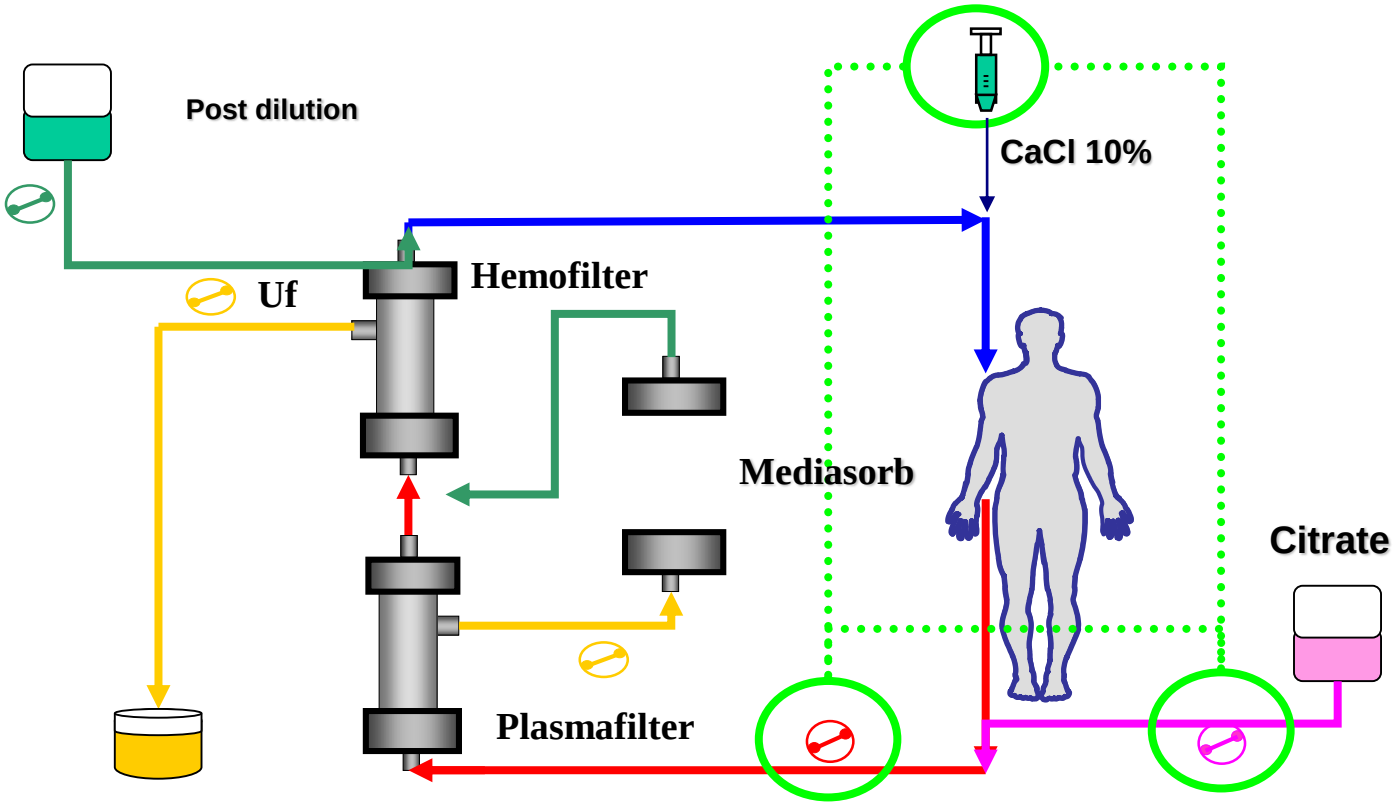
Hemoperfusion





COMPLETENESS

CPFA with Citrate



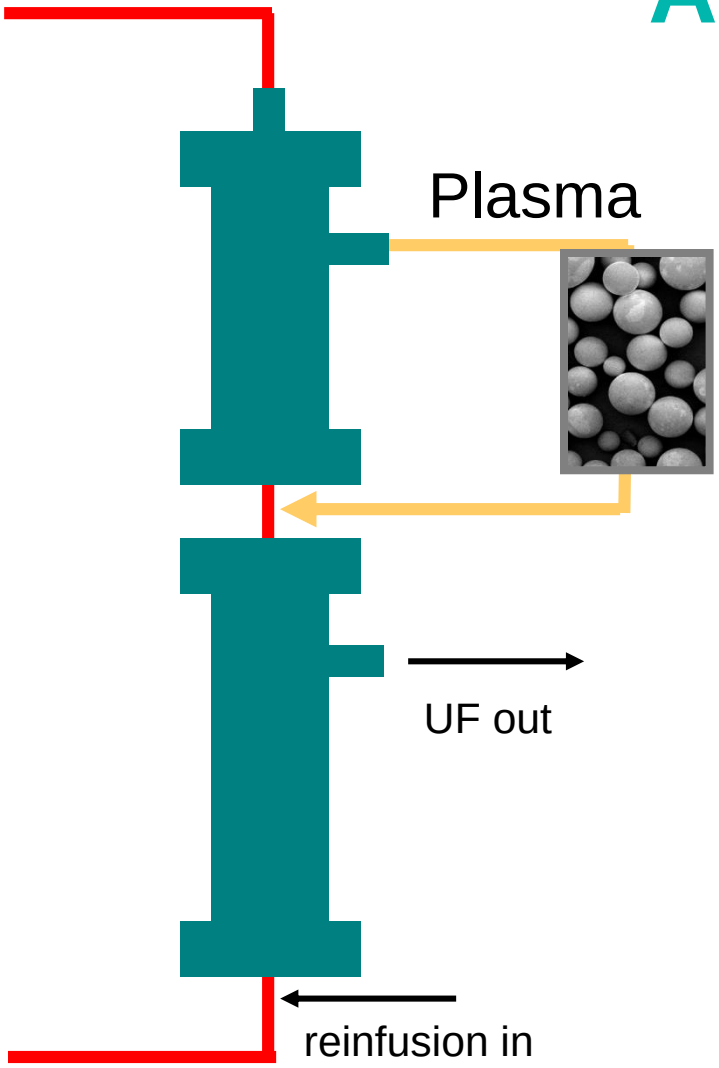
What is Sepsis ?
ACCP/SCCM Consensus Definitions

- **Infection**
  - Inflammatory response to microorganisms, or
  - Invasion of normally sterile tissues
- **Systemic Inflammatory Response Syndrome (SIRS)**
  - Systemic response to a variety of processes
- **Sepsis**
  - Infection plus
  - ≥2 SIRS criteria

- **Severe Sepsis**
  - Sepsis
  - Organ dysfunction
- **Septic shock**
  - Sepsis
  - Hypotension despite fluid resuscitation
- **Multiple Organ Dysfunction Syndrome (MODS)**
  - Altered organ function in an acutely ill patient
  - Homeostasis cannot be maintained without intervention

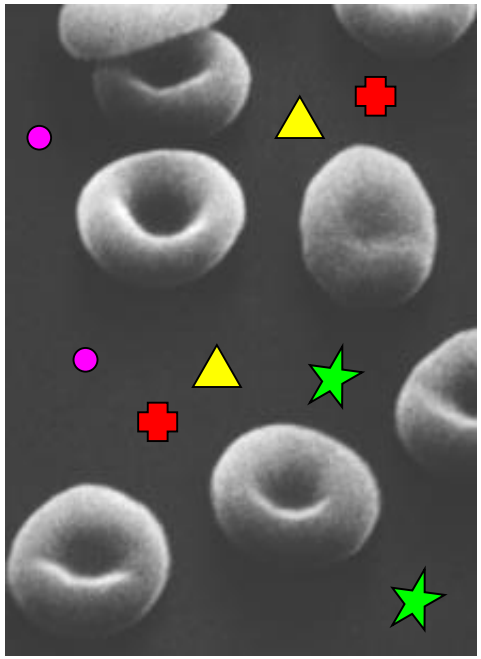
.

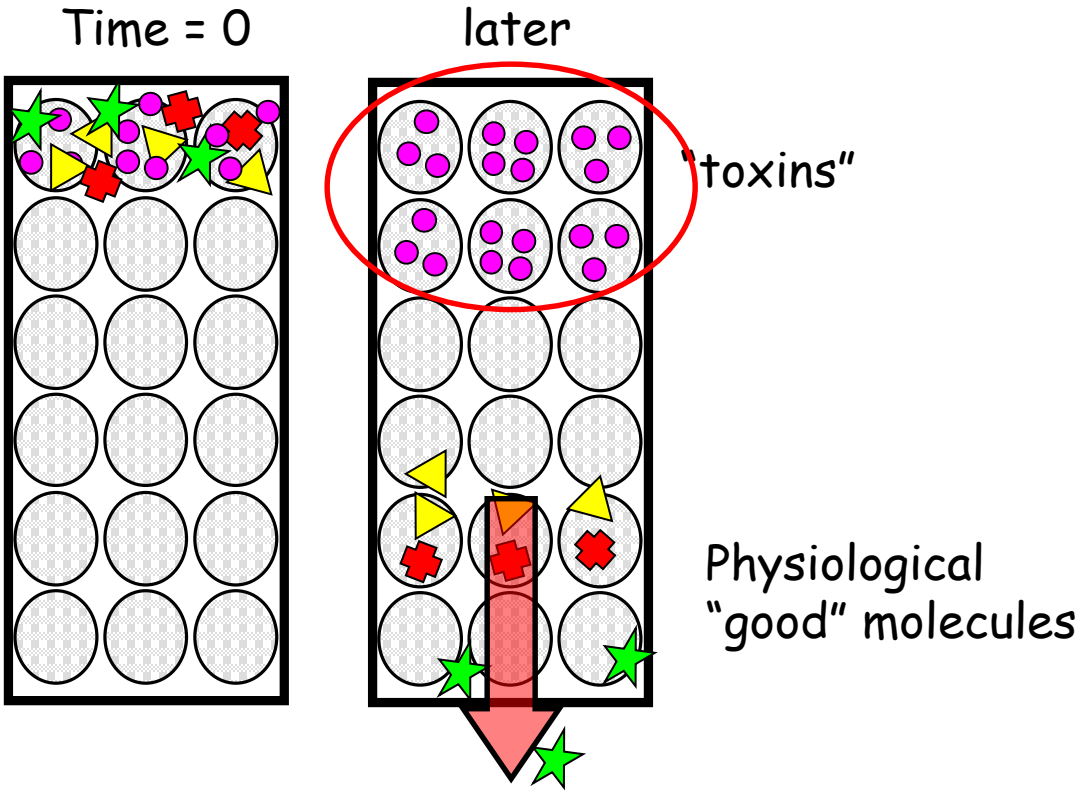
Coupled Plasma Filtration Adsorption



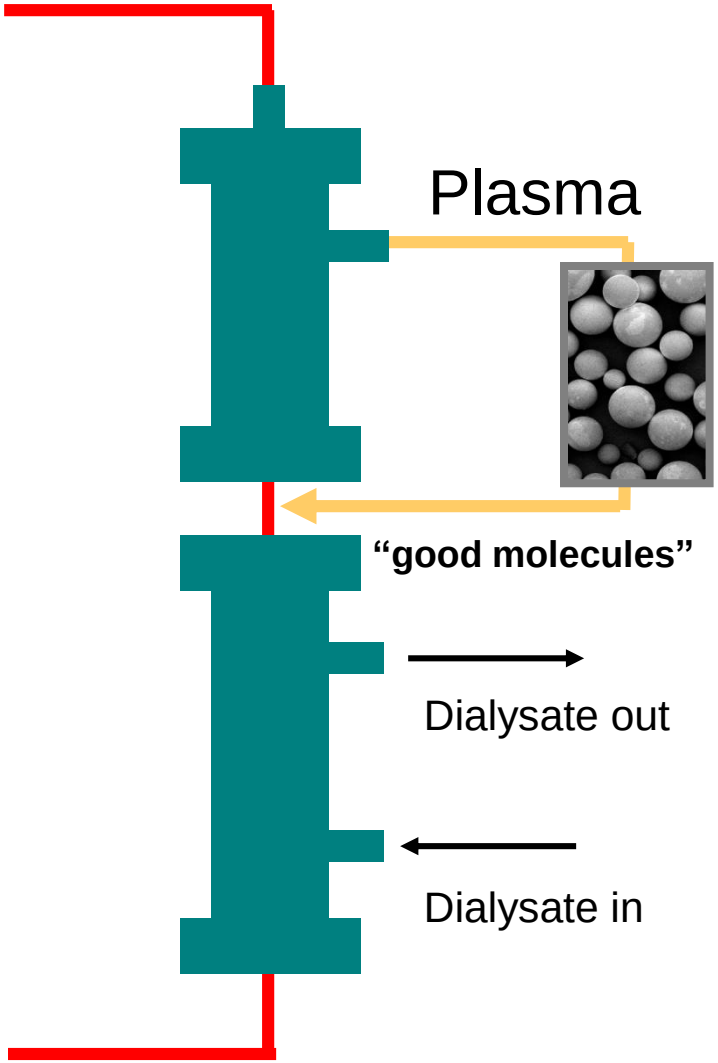
Therapeutic goal

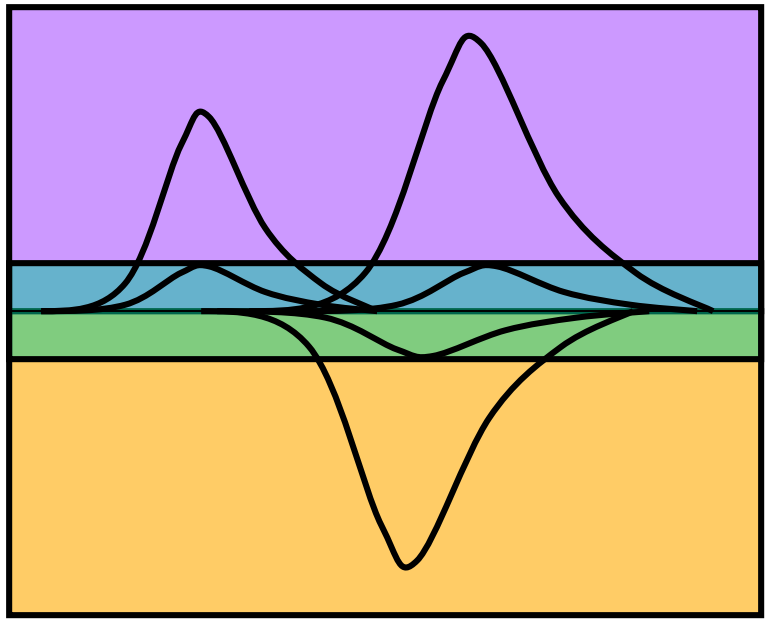
Separate and retain "toxins"
from a complex mixture





Ideal therapy for sepsis





Sustained Low Efficiency Dialysis (SLED)

- ✓EDD (Extended Daily Dialysis)
- ✓SCD (Slow Continuous Dialysis)
- ✓SLEDD (Slow Extended Daily Dialysis)

Slow Continuous Dialysis (SLD)

- ✓Modified standard hemodialysis machine with controlled ultrafiltration on-line production of bicarbonate dialysate
- ✓Blood flow rate: 100(to200) ml/min
- ✓Dialysate flow rate: 100(to300) ml/min
- ✓Extended daily treatments: 8 to 24 hours
- ✓Urea clearance: 70 to 80 ml/min

SLEDD: Adequacy

	SLEDD	c
Blood flow (ml/min)	100-300	100-200
Dialysateflow(ml/min)	100	15-35
Daily urea clearance (l)	80-90	20-40
Daily Kt/V	2.4	0.9-1.4
Daily dialysis cost (USS)	10	50-100

Schlaefer et al.Kidney Int; 56, Suppl 7: S20-S23

GENIUS® - Dialysis Machines: Central Components

Heparin pump
Circulator (Roller-pump, air sensor)

Electronics + rechargeable battery (max. 8hrs)

Distribution rod with UV- source

external low voltage adaptor

UF-monitor, displays, pressure transducer

Dialysate adaptor

Thermically insulated casing

Glass container (75 l)

Case

- 64-year-old female with a history of hypertension, 3-vessle coronary artery disease, and poor left ventricular function (ejection fraction: 20%).
- She weighs 80 kg
- . The surgery is uneventful but she requires fluids and vasoactive medications (epinephrine and dobutamine) to come off of cardiopulmonary bypass.
- Her admission labs (drawn 24 hours before surgery) showed a serum creatinine of 1.5 mg/dL
- Over the first 24 hours after surgery, she makes 200 mL of urine.
- Her serum creatinine increases to 2.0 mg/dL
- mechanical ventilation and extubated. Her cardiac function remains poor but cardiac index is 2.2 on epinephrine and dobutamine. She has not received any nephrotoxic agents. Urine chemistries and microscopy are consistent with a diagnosis of ATN.

Case

- The following day her serum creatinine increases to 3.0 mg/dL
- and her BUN increases to 65 mg/dL.
- She has made 300 mL of urine in the last 24 hours, and her total fluid intake has exceeded all output by 11L since the surgery.
- Her weight is now 90 kg and she has edema on physical exam.
- Furosemide is administered but she does not respond.
- The next day the creatinine is 4.0 mg/dl
- she is started on continuous veno-venous hemofiltration

Case

- at an ultrafiltration rate of 25 ml/kg/hr based on her admission weight.
- Replacement fluid for 18 hr/day was 34 lit.
- 100 mL of fluid are removed per hour
- Blood flow rate based on patient BP was 100 -150 ml/min
- Heparin adjusted based on ACT time or INR.

- Over the course of the next four days 8L of fluid are removed, and her heart function improves such that all vasoactive medications are discontinued. She is converted to intermittent dialysis and is discharged form the ICU.
- A week later renal function gradually recovers, and one month later her serum creatinine has returned to baseline.