Managing a child with failing kidney

ธวัชชัย ดีขจรเดช

จิตลัดดา ดีโรจนวงศ์

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Acute renal failure

- Definition

  " Abrupt failure of the kidneys to regulate water and electrolytes homeostasis"

- Incidence in ICU

  Vary widely depending on the population studied and the definition used

Incidence of ARF

	Incidence	Mortality
Adult ICU Semin Respir Crit Care Med 2006	3-25%	35-75%
NICU/PICU Pediatr Nephro 2000, An Pediatr 2004	8-30%	30-36%
PICU (prospective, n= 1047) Pediatr Crit Care Med 2007	4.5%	30% (VS 2%)

Revised Definition of ARF

- 1998 Acute renal failure study group
  survey 598 doctors & nurses
  199 different definitions for ARF

- 2004 Acute Dialysis Quality Initiative Group (ADQI workgroup)
  " Acute kidney injury (AKI)"
  3 grades of severity and 2 outcomes

RIFLE Criteria

RIFLE	GFR criteria	Urine Output Criteria
Risk	↑ serum creatinine x 1.5 *or* decrease of GFR > 25%	< 0.5 mL/kg/hr for 6 hrs
Injury	↑ serum creatinine x 2 *or* decrease of GFR > 50%	<0.5 mL/kg/hr for 12 hrs
Failure	↑ serum creatinine x 3 *or* decrease of GFR > 75% *or* serum creatinine ≥ 4mg/dL when there was acute rise > 0.5 mg/dL	<0.3 mL/kg/hr for 12 hrs *or* anuria for 12 hrs
Loss	Complete loss of renal function > 4 wks	
End stage	Need for renal replacement therapy > 3 mos	

Incidence of ARF in King Chulalongkorn Memorial Hosp.

		n	PD	CVVH
PICU	2549	612	2	15
	2550	632	5	9

Incidence of ARF in King Chulalongkorn Memorial Hosp.

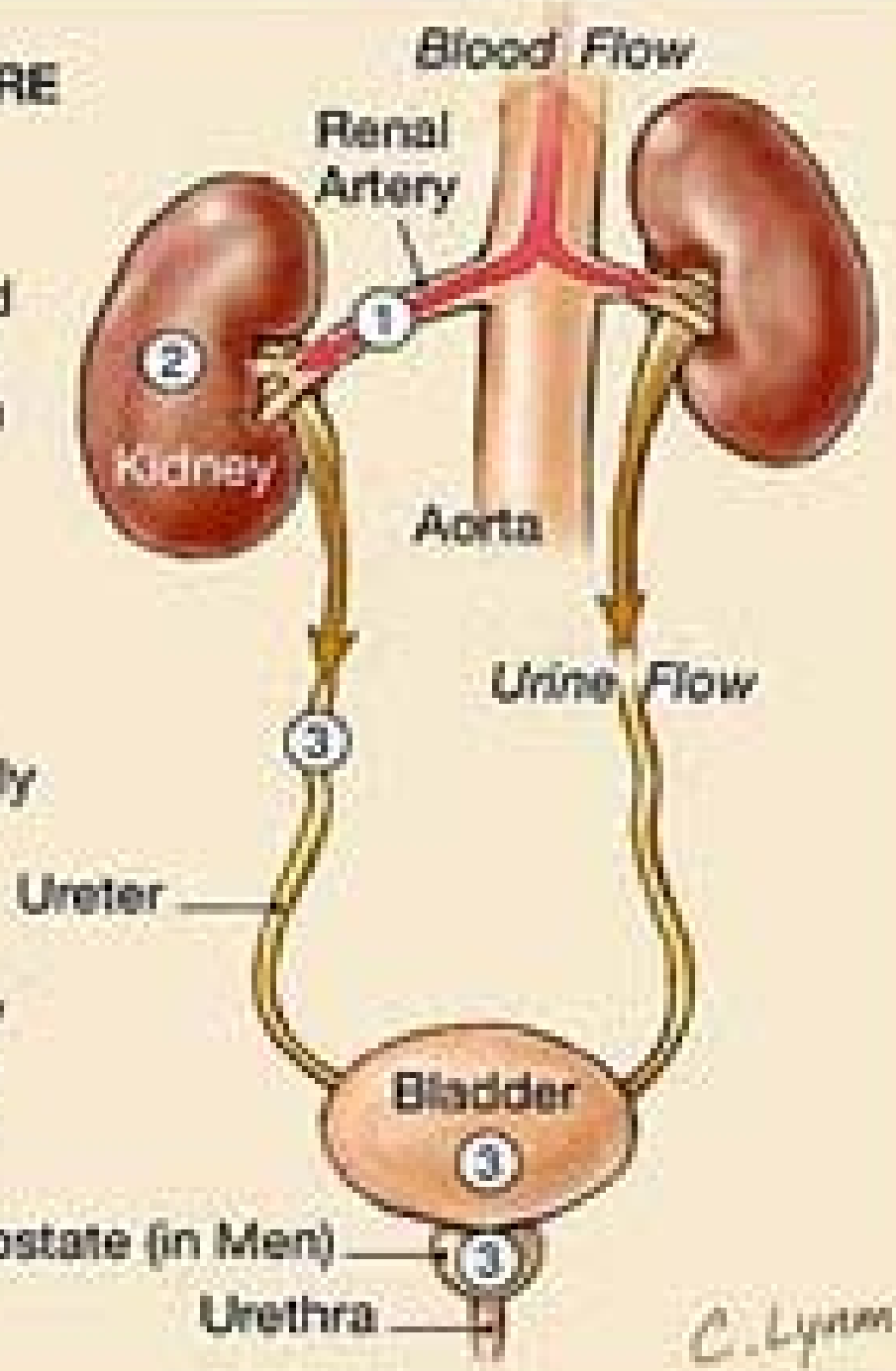
	n	PD	CVVH	HD	No RRT
2549	43	5 (12)	15 (35)	14 (32)	9 (21)
2550	47	6 (13)	9 (19)	22 (47)	10 (21)

CAUSES OF ACUTE RENAL FAILURE

① **Prerenal**
Sudden and severe drop in blood pressure (shock) or interruption of blood flow to the kidneys from severe injury or illness

② **Intrarenal**
Direct damage to the kidneys by inflammation, toxins, drugs, infection, or reduced blood supply

③ **Postrenal**
Sudden obstruction of urine flow due to enlarged prostate, kidney stones, bladder tumor, or injury



Etiology of ARF

Presenting to nephro

- **Unifactorial**
- **On admission**

Causes

- **Immune-mediated renal injury (AGN, vasculitis, etc)**
- **Other medical renal injury**
- **Drugs**
- **Obstructive uropathy**
- **Tropical diseases**

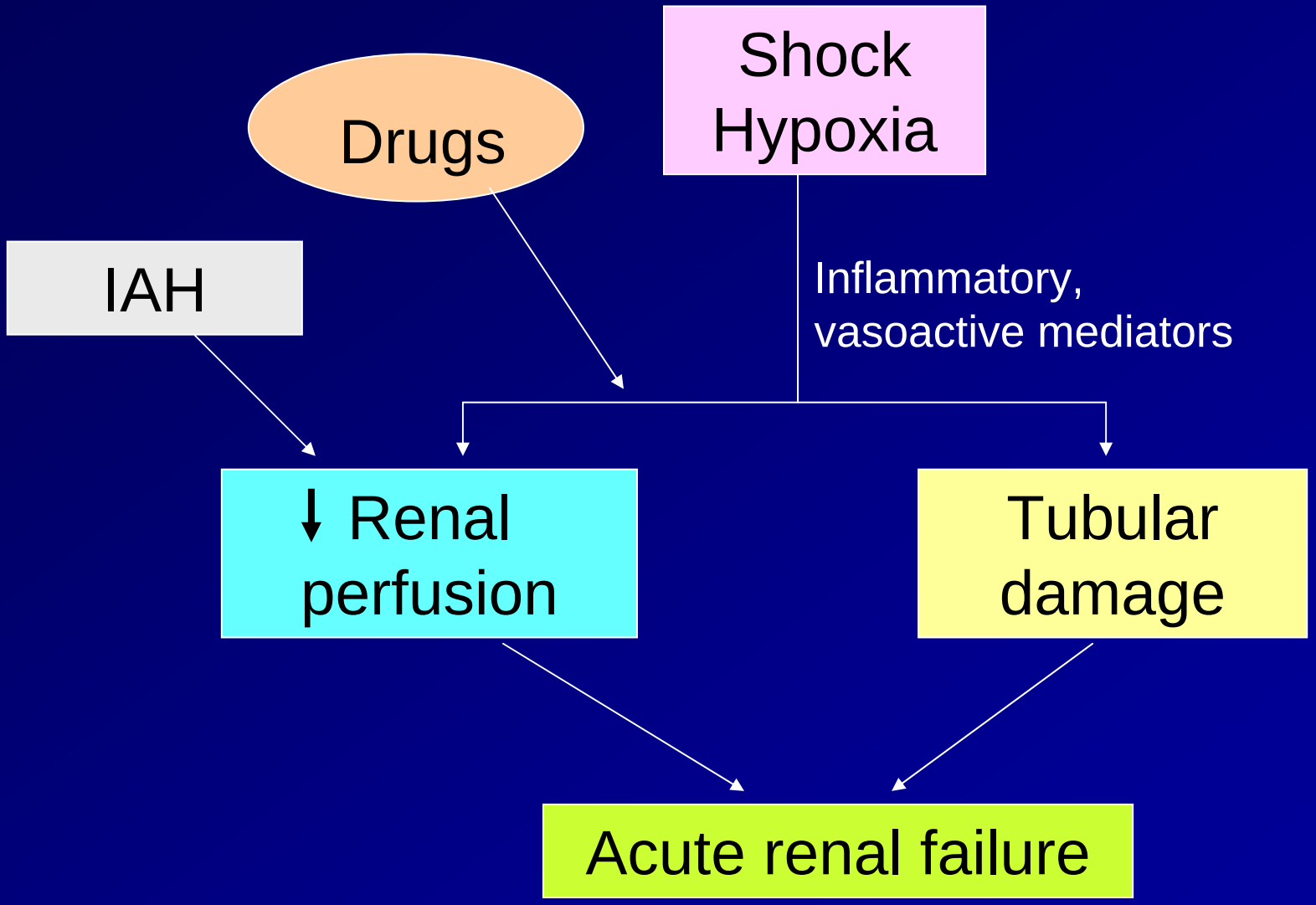
Presenting in ICU

- **Multifactorial**
- **After admission**

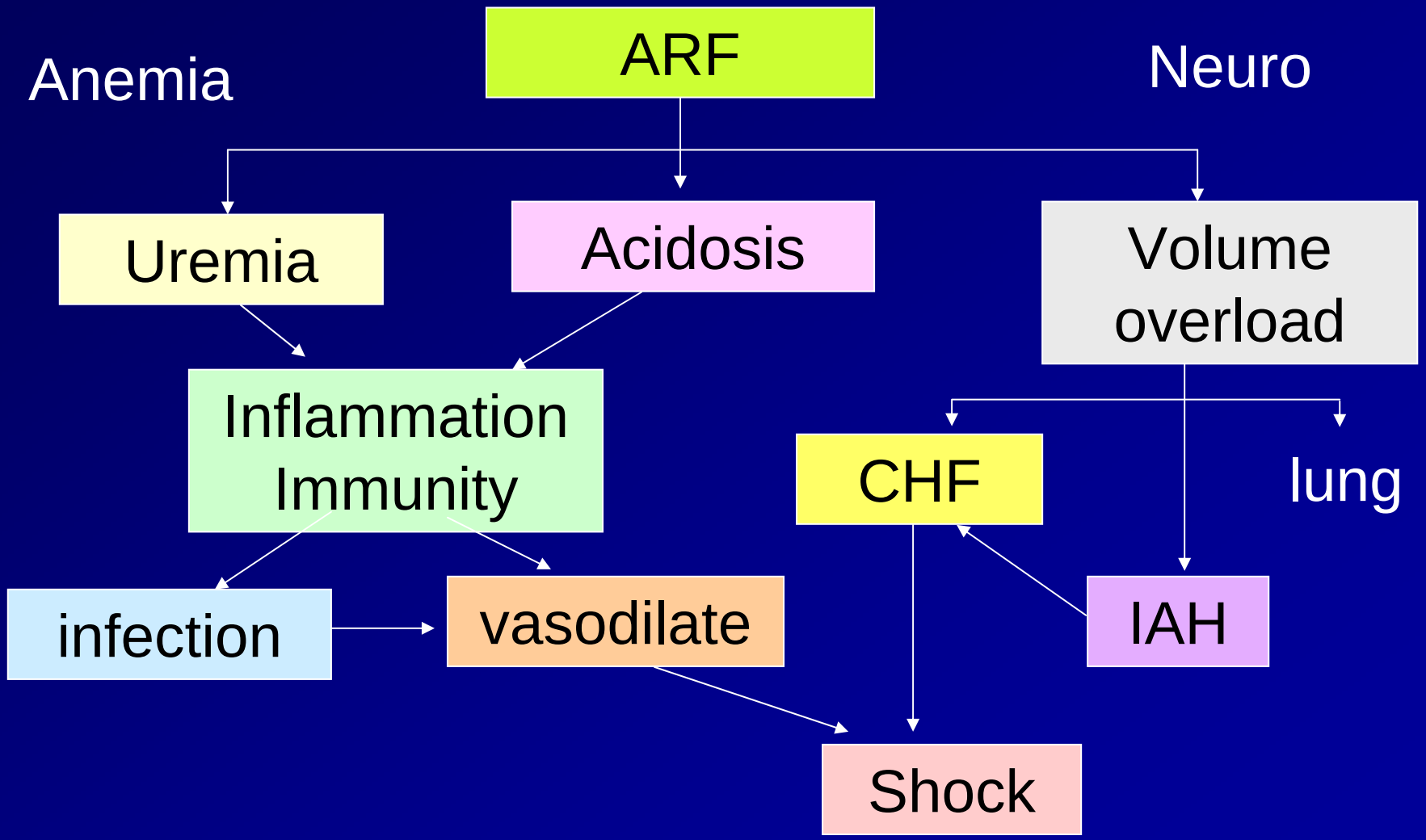
Causes

- **Shock**
- **Sepsis**
- **Postoperative**
- **Posttraumatic**
- **Chronic medical problems (malignancy, CHD, etc)**

AFR in ICU


Shock
Hypoxia
Drugs
IAH
Inflammatory,
vasoactive mediators
↓ Renal
perfusion
Tubular
damage
Acute renal failure

Consequences of ARF



Case

- 8 yrs old boy
- Blunt abdominal injury from car accident
- At hospital

  BP วัดไม่ได้, PR 140/min, RR 30/min, $E_3V_4M_6$
- Distended abdomen, generalized tender and guarding
- Load NSS free flow
- Refer Bureerum Hospital

At Bureerum Hospital

- BP 97/69 mmHg, PR 108/min, RR 28/min

Rx: Blood transfusion, resuscitate fluid

Hct 31% → 37%, BUN/Cr 12/0.8, urine OK

- 12 hours later, restless, RR 60-70/min

Rx: On ET-tube and explore-lap

Hemoperitonium 1,100 mL

Tear liver 5 cm., dept 2 cm.

Renal contusion

Post operation

- Hypoglycemia,
- BP drop to 60/80 mmHg, no urine
- Tritrate dopamine, dobutamine → max
  add adrenaline, hydrocortisone
- Rx- Tienam + cloxacillin
- Stabilized BP but no urine
- BUN/ Cr 22/1.9
- Na 137, K 4.1, Cl 105, HCO_3 19 mEq/L

Assess

- Blunt abdominal injury
- Internal bleeding ⟶ shock
- Renal contusion

- Abrupt failure of kidney function
  - Increased serum creatinine 0.8 ⟶ 1.9
  - Decreased urine output ⟶ anuria

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How to maintain kidney function

- Fluid therapy
- Pharmacologic
- Avoid further damage
- Renal replacement therapy

Fluid therapy

Aim

- Adequate volume
  - deficit
  - maintenance
  - concomitant loss
- Avoid volume overload

Vital sign

Urine output

CVP

Inotropes

Vasoconstrictor

Fluid therapy-Type of fluid

- Crystalloid
  - 1st choice for volume replacement
  - Only 1/3 remain in IVS, 2/3 pass into tissue
- Colloid
  - Larger molecule- better retained in IVS
  - Case with microcirculatory disturbance and increased capillary permeability
- No evidence support the benefit of colloid

B Med J 1998 ,Cochrane Report 2004

Pharmacologic

- Diuretics
  - Furosemide
  - Mannitol
- Vasoactive
  - Dopamine
  - Fenoldopam
- Natriuretic peptides

Furosemide

- Loop diuretic
- Early use may convert oliguric RF to non oliguric RF
  - Flushes out intratubular casts
  - Increases tubular flow
- May help in fluid management
- No evidence support the benefit in
  - Incidence of ARF, need for RRT, mortality

Mehta RL, et al.JAMA 2002,
Uchino S, et al.Crit Care Med 2004

Mannitol

- Osmotic diuresis
  - Flushes out intratubular casts
  - Increases tubular flow
- Improve renal blood flow
- Free-radical scavenger during reperfusion of kidney
- No prospective RCC study to support

Gubern JM, et al. Surgery 1988

Ip-Yam PC, et al. Anesth Analg 1994

Vasopressor

- Low dose dopamine (renal dose)
- 0.5-2 µg/kg/min

Physiologic effect

- Vasodilate - increased renal blood flow
  - increased GFR
- Natriuresis - increased Na excretion

Possible adverse effects of dopamine

- Blunting hypoxic response
  - ↓ventilatory response to hypoxia, hypercarbia
- Endocrine effects
  - ↓prolactin, GH, LH, aggravate sick euthyroid
- Immune suppressive
  - ↓T-lymphocyte proliferative response
- Arrhythmias
  - ↑incidence of atrial fibrillation after cardiac Sx

Low dose dopamine

Kellum JA, Decker JM. Crit Care Med 2001

- Meta-analysis 58 randomized trial on “low dose dopamine for prevent and Rx acute renal failure”

Outcomes

- Mortality 4.7% vs 5.6% (RR 0.83, CI 0.4-1.8)
- ARF 15.3% vs 19.5% (RR 0.79, CI 0.5-1.1)
- Hemodialysis requirement (RR 0.89, CI 0.7-1.2)

Low dose dopamine

Bellomo et al. (ANICS) Lancet 2000

- Multicenter RCT (23 ICU)
- 328 patients with SIR and early renal dysfunction (rising Cr, urine < 0.5ml/kg/hr, 4 hrs)
- Dopamine 2 µg/kg/hr vs placebo

Outcome

- No differences in peak BUN/Cr, urine/hr, need for RRT, duration in ICU, mortality.
- Not increase cardiac arrhythmia

Low dose dopamine

Friedrich et al. Ann Intern Med 2005

- Meta-analysis - 61 studies (3,359 patients)
- Low-dose dopamine (1-5 µg/kg/min- median 2.5)

Result

- Increased urine output, CCr, on 1st day (not $D_{2,3}$)
- No benefit on - requirement of RRT
  - mortality rate
- Not increased adverse effects (arrhythmia, MI)

Fenoldopam

- Selective dopamine-1- receptor agonist
- Animal studies
  - Improve renal perfusion
  - Preserve kidney function
- Study in 12 adults with trauma
  - Increased renal perfusion, urine flow, excretion of Na, K

Murphy MB, et al. N Eng J Med 2001

Anaritide

- Atrial natriuretic peptide
- In animal studies
  - Increase GFR, urine output
- RCT 500 adults with ARF
  - Not improve “dialysis-free” survival

Allgren RL, et al. N Eng J Med 1997

- RCT 61 patients after cardiac Sx
  - Decreased use of dialysis

Sward K, et al. Crit Care Med 2004

How to maintain kidney function

- Fluid therapy
- Pharmacologic
- Avoid further damage
- Renal replacement therapy

Post Op day 2

- No urine
- Bilat alveolar infiltrations on chest X-ray
- BP 120/70 mmHg, on adrenaline, dopamine, dobutamine
- BUN/Cr 57/4.2
- Na 143, K 3.8, Cl 106, HCO_3 13

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What are the targets of RRT?

- Qualitative and quantitative blood purification
- Restoration and maintenance of homeostasis
- Avoidance of complications and good clinical tolerance
- Support of conditions favoring recovery of renal function

Basic Principle

Solute removal across semi-permeable membrane

PD - Peritoneal membrane

HD - Hemodialysis membrane

CRRT - Hemofilter membrane

Renal replacement therapy

- Indication
- Timing of initiation
- Modality
- Dose and adequacy

Indication for RRT in ICU

- Renal
  - Uremia
  - Overload of fluids
  - Electrolyte abnormalities : hyper K, Na abnormalities
  - Acid-base : pH< 7.0
  - Intoxication
- Non renal
  - Allowing administration of fluid and nutrition
  - Hyperthermia
  - Severe hemodynamic instability in sepsis?
  - Elimination of inflammatory mediators in sepsis?

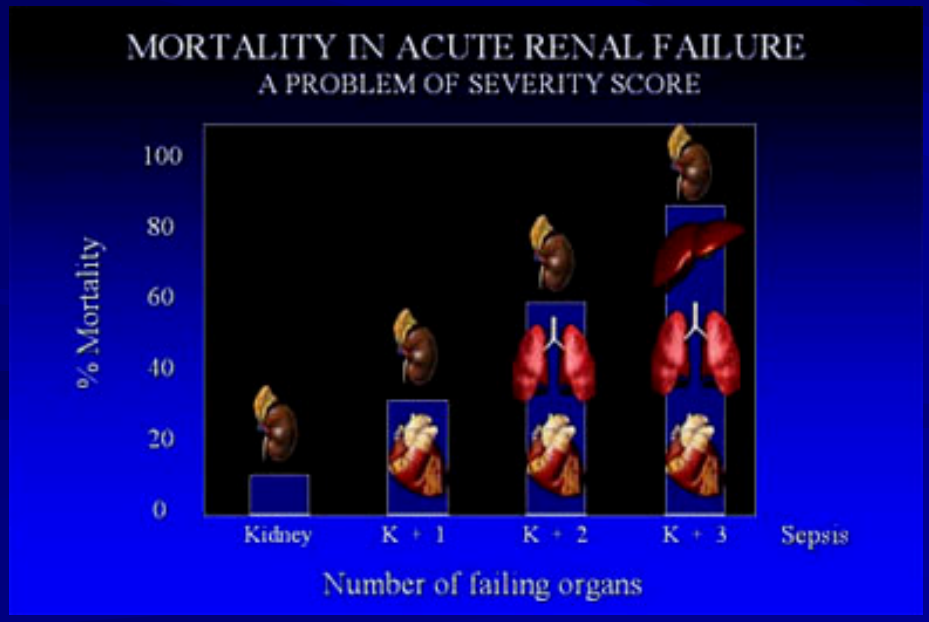
Timing of initiation

	Study design	Clinical setting	Definition of timing	Confounding CRRT factors	Survival advantage early group
Bouman [8]	RCT ($n=105$)	Oliguric ARF and MOF	Early: creatinine clearance <20 ml/min and <12 h after onset of oliguria (<180 ml in 6 h) Late: urea ≥40 mmol/l or severe pulmonary edema[a] after onset of oliguria	No	No
Jiang [28]	RCT ($n=37$)	Severe pancreatitis renal function is not reported	Early: <48 h after onset of abdominal pain Late: >96 h after onset of abdominal pain	No	Yes
Gettings [31]	Retrospective ($n=100$)	Post trauma	Early: urea <60 mg/dl[b] Late: urea ≥60 mg/dl	Various CRRT modes Dose not reported	Yes
Piccini [32]	Retrospective ($n=80$)	Sepsis with oliguric ARF and ALI	Early: <12 h after ICU admission Late: urea >35 mmol/l or creatinine >600 μmol/l	Dose early >> dose late	Yes
Elahi [30]	Retrospective ($n=64$)	Post cardiac surgery	Early: oliguria <100 ml in 8 h Late: urea >30 mmol/l or sCr >250 μmol/l	Dose not reported	Yes
Demirkilic [29]	Retrospective ($n=61$)	Post cardiac surgery	Early: oliguria <100 ml in 8 h Late: sCr >5 mg/dl[c]	Dose not reported	Yes

Current Opinion in Critical Care 2007, 13:656–661

Timing of initiation

- Early initiation :
  - better survival
  - may hasten renal recovery
  - should be considered in multiple organ failure

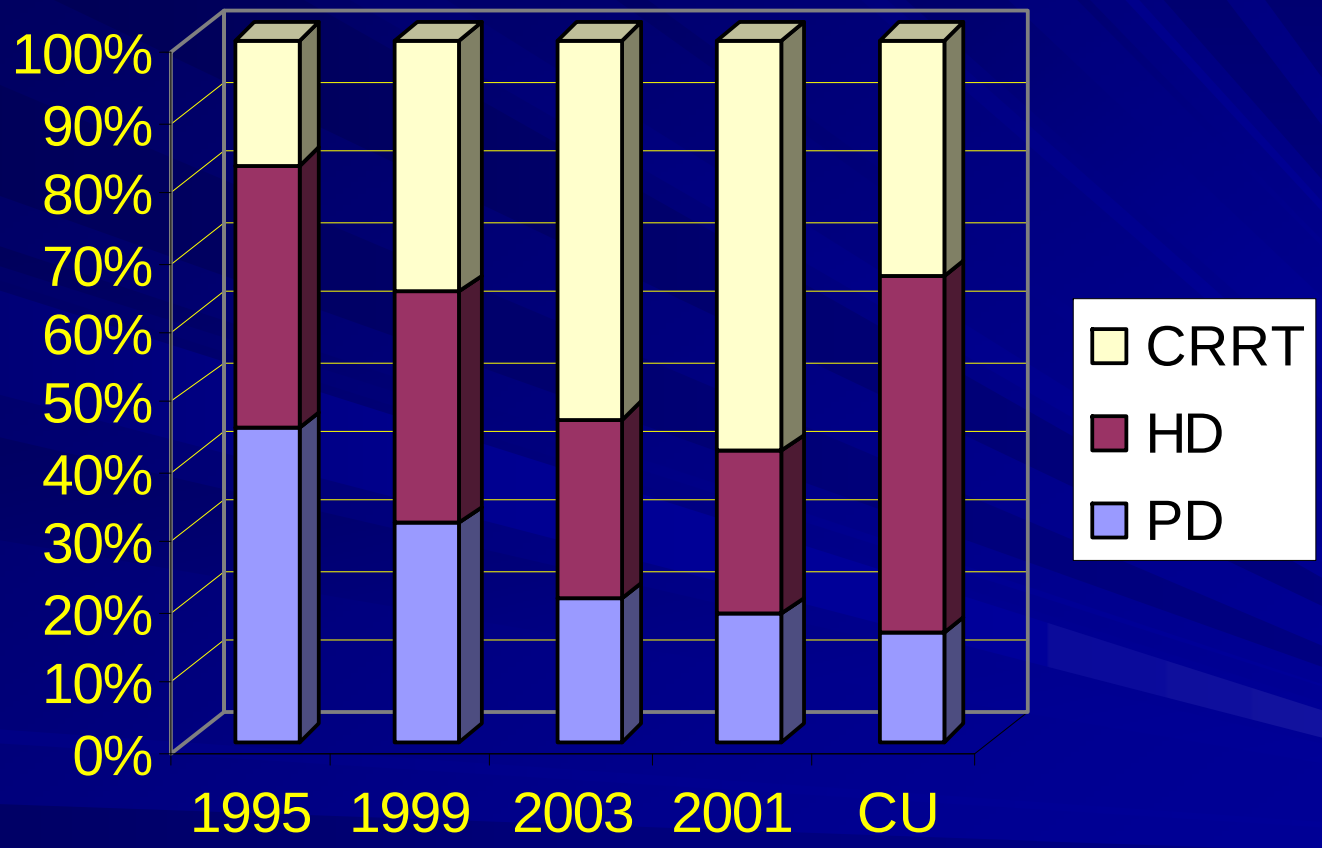


Achra Sumboonnanonda 2001
N = 59
Number of organ dysfunction
Survivors 2.2 ± 1.6
Non survivors 4 ± 1.6

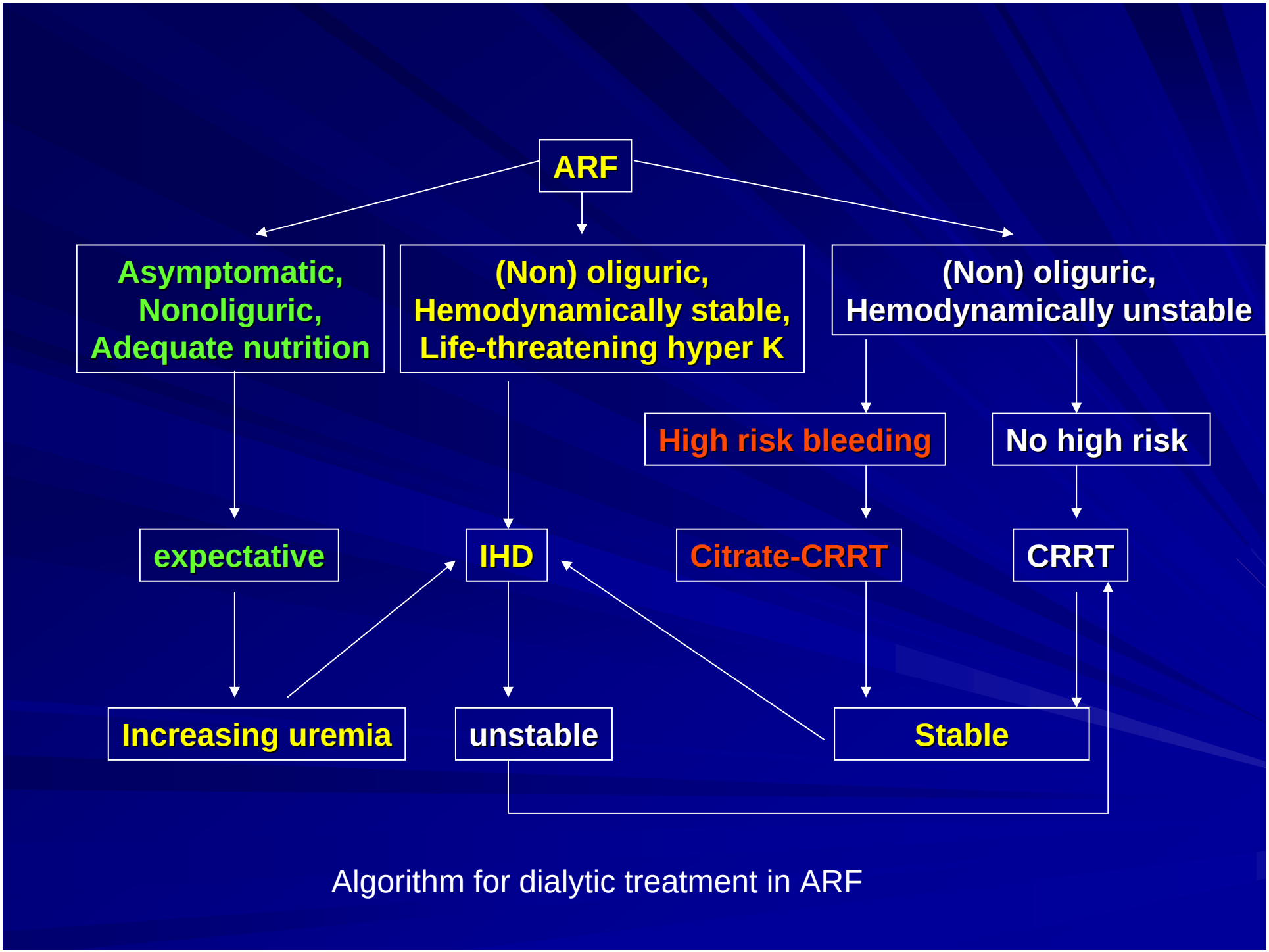
Modality

- Clinical condition of patient
- Available resources
- Expertise of the physician
- Pros and Cons of each option

Dialysis modality : survey results



Warady BA. Pediatr Nephrol 2000
Ronco C. Nephrol Dial Transplant 2001



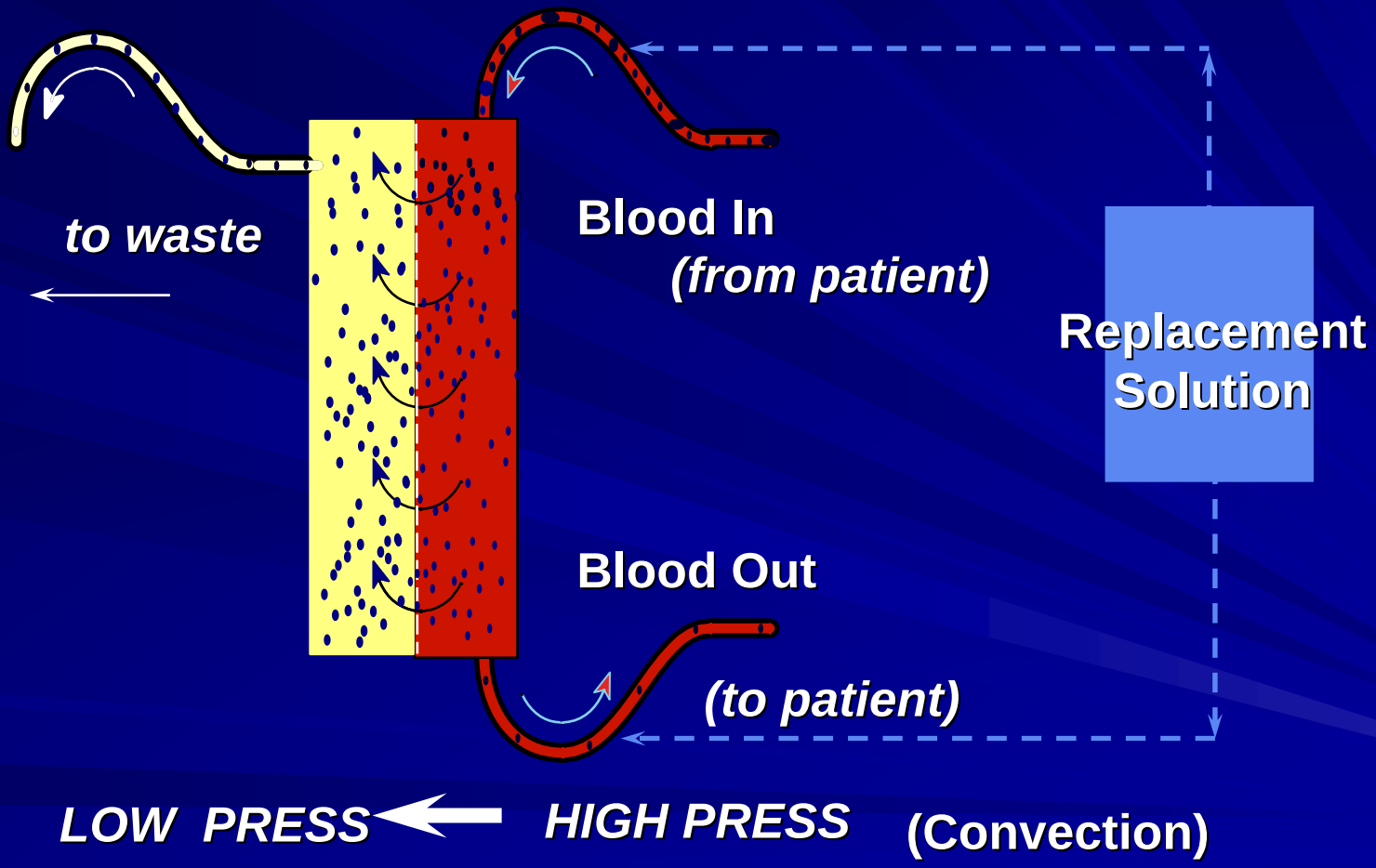
Algorithm for dialytic treatment in ARF

Recommendation of initial choice

Indication	Clinical settings	Modality
Uncomplicated ARF	Drug nephrotoxicity	IHD, PD
Fluid removal	Cardiogenic shock	SCUF, CVVH
Uremia	Complicated ARF	CRRT, IHD
Increased ICP	Hepatorenal syndrome	CVVH, CVVHDF
Shock	Sepsis, ARDS	CVVH, CVVHDF
Nutrition	Burns	CRRT
Poisons	Theophylline, barbiturates	Hemoperfusion, IHD, CVVHD
Electrolyte abnormal	Marked hyperkalemia	IHD, CVVHD

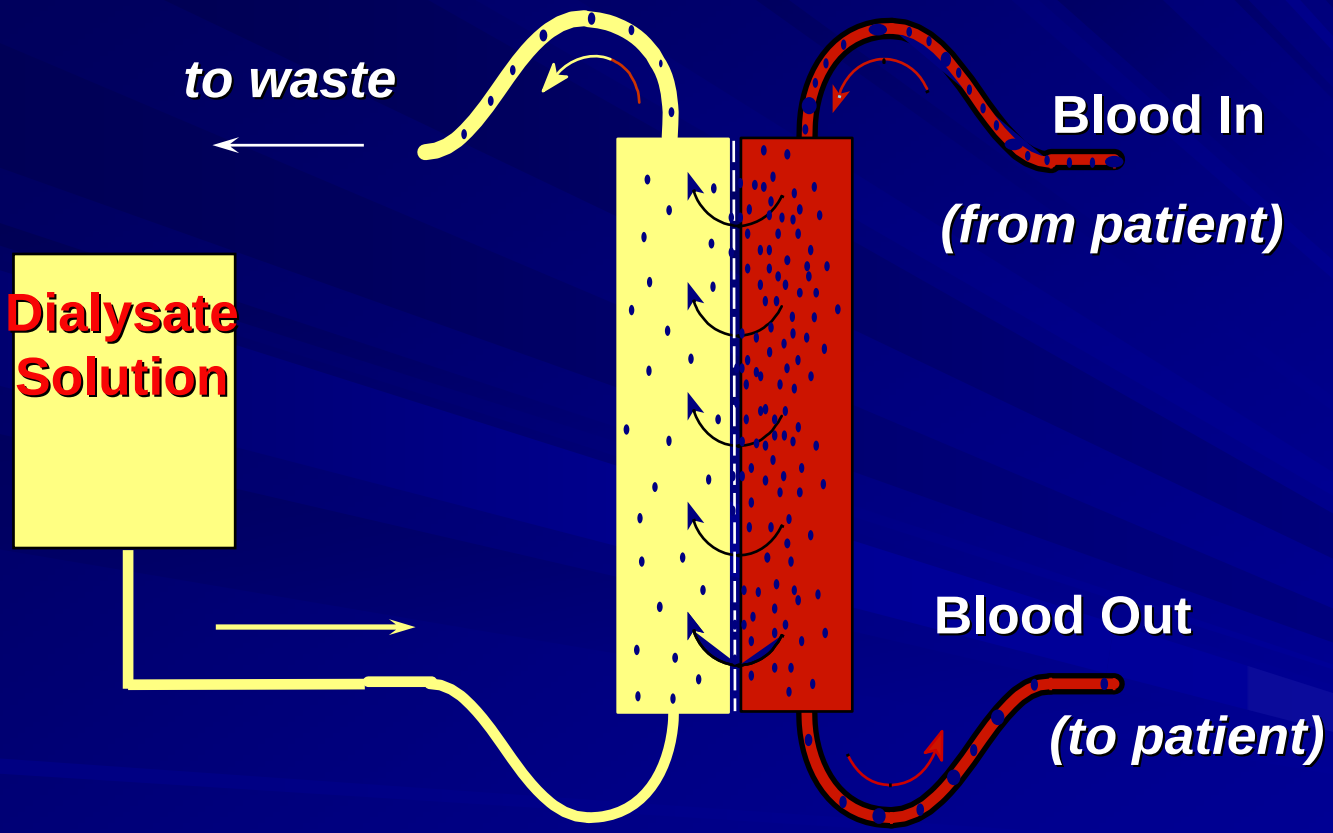
CVVH

Continuous Veno-Venous Hemofiltration



CVVHD

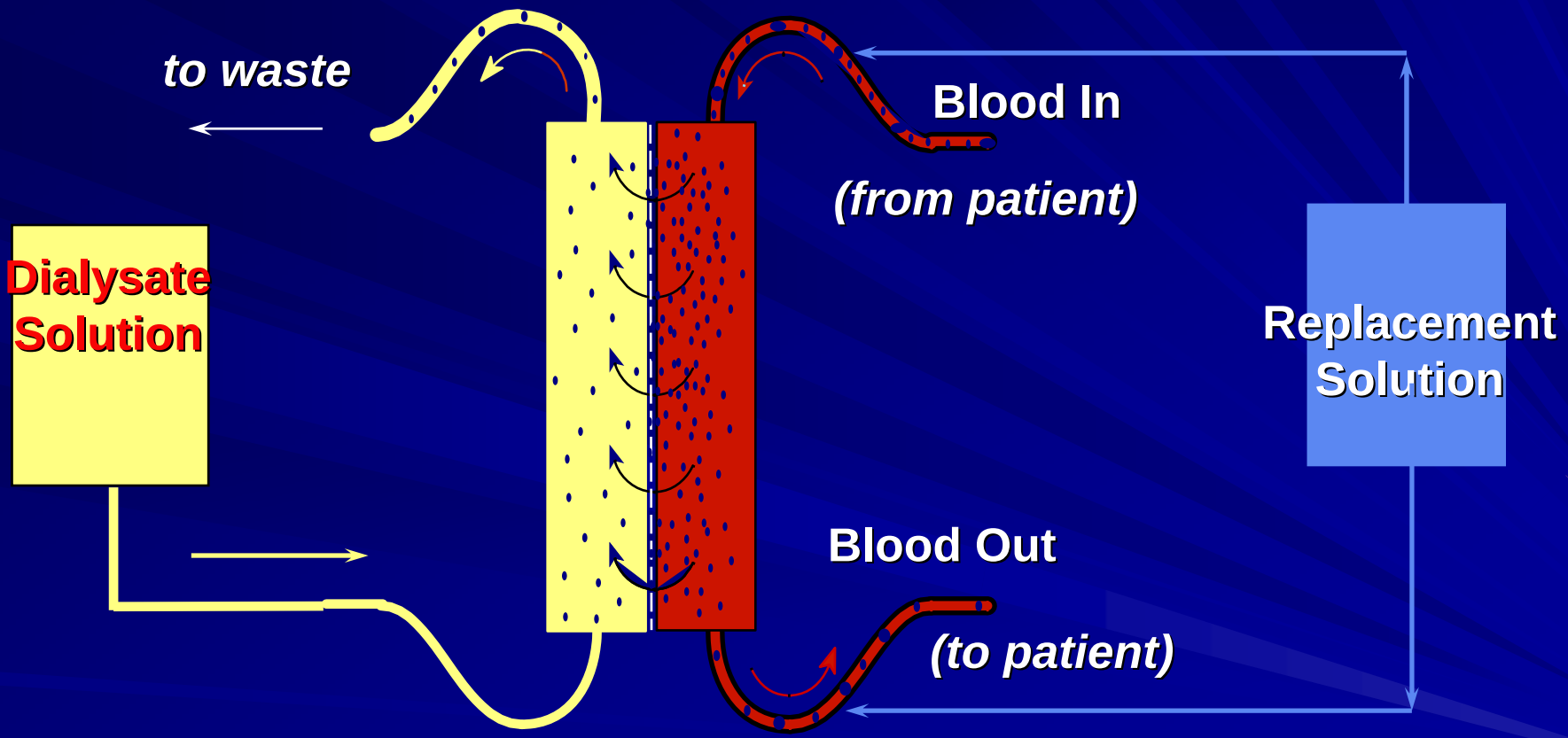
Continuous Veno-Venous Hemodialysis



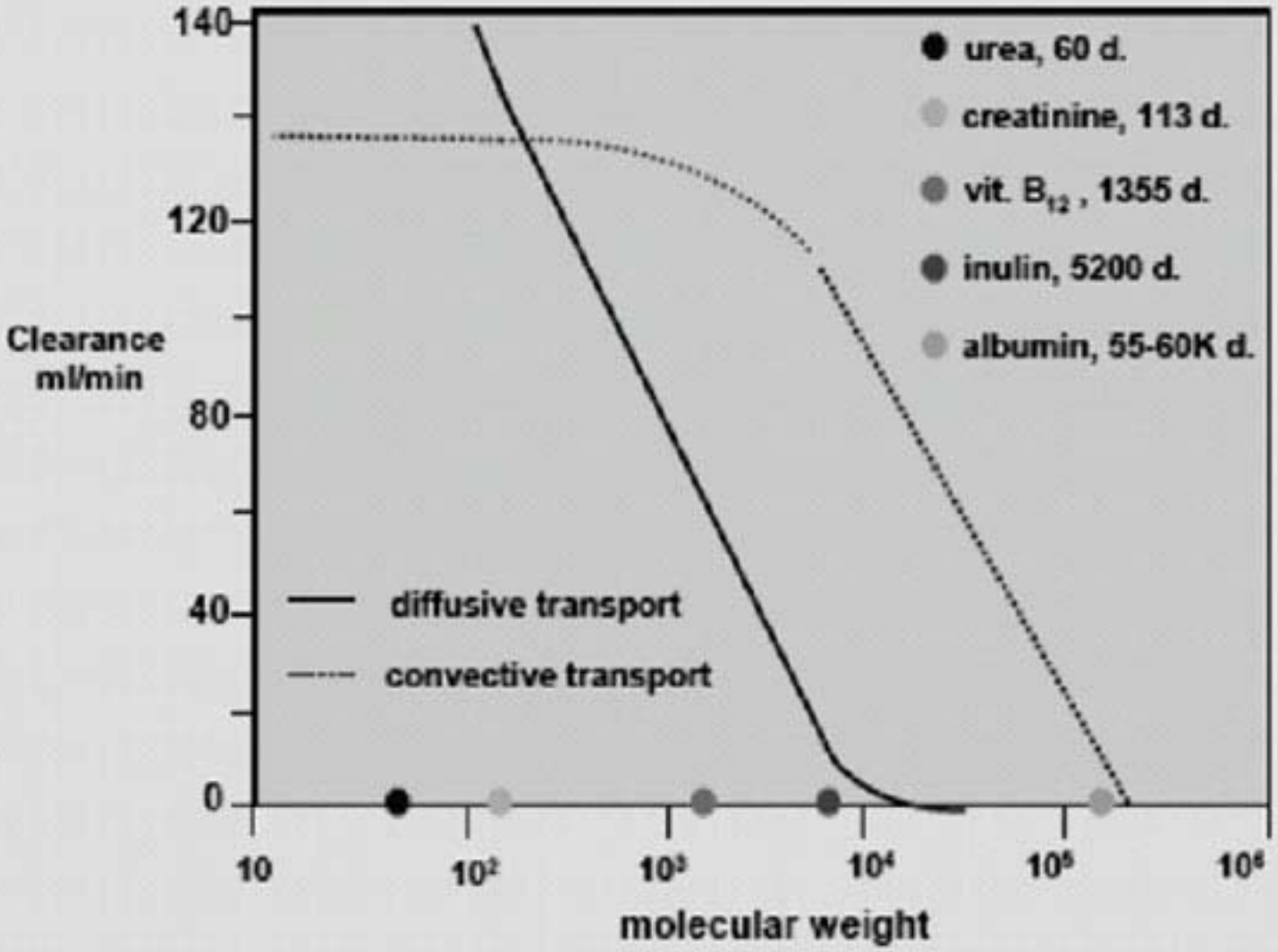
LOW CONC ← *HIGH CONC* (Diffusion)

CVVHDF

Continuous Veno-Venous Hemodiafiltration



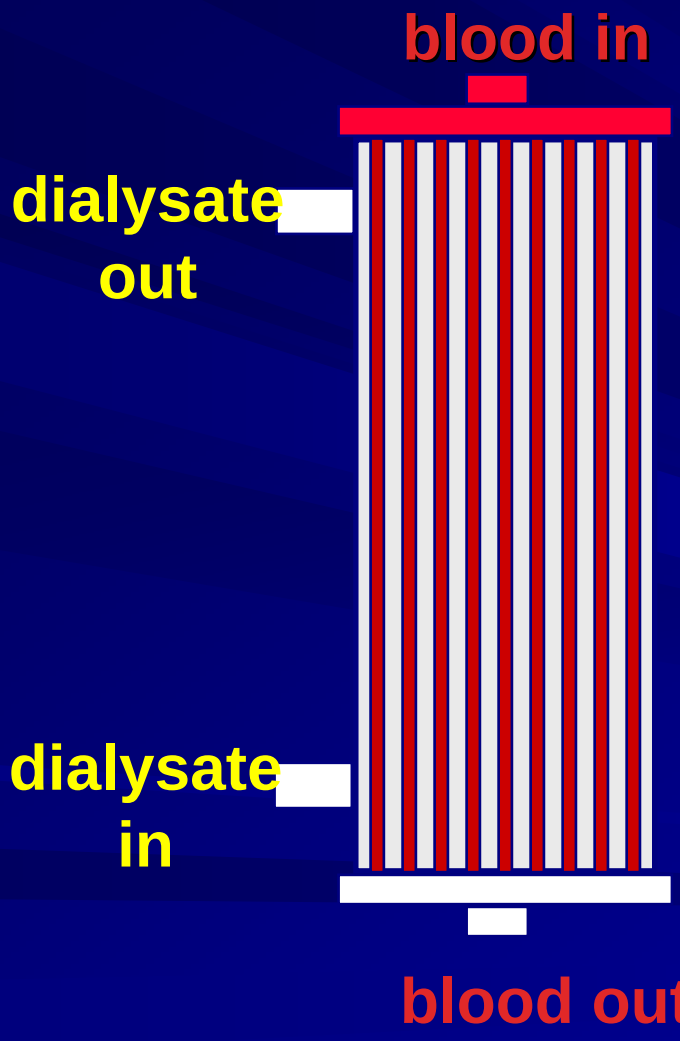
Diffusive vs. Convective Transport



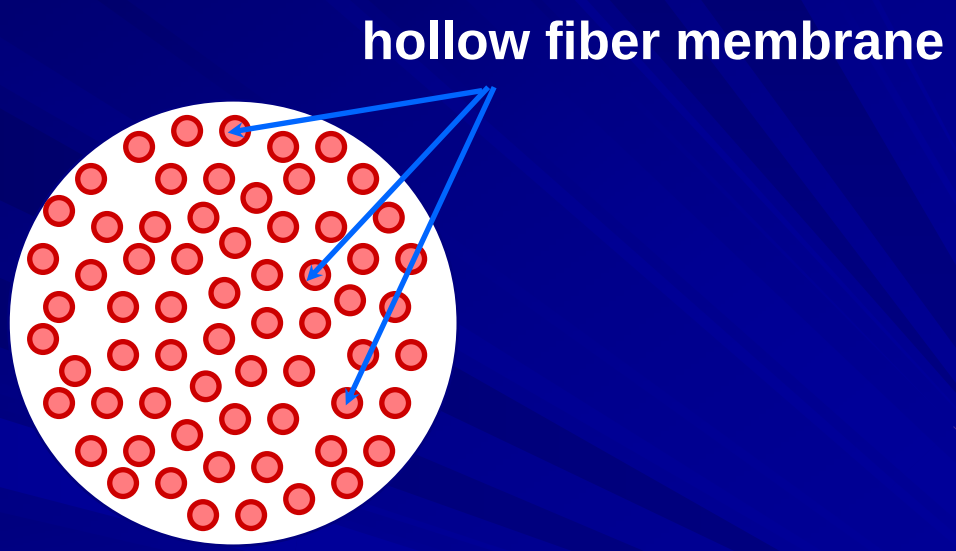
CRRT Circuit

- Hemofilter
- Vascular access and blood line
- Blood pump and infusion pumps
- Anticoagulant
- Replacement fluid and dialysate fluid

Hemofilter



Cross Section



Outside the Fiber (effluent)
Inside the Fiber (blood)

Hemofilter

- High flux, high performance
- Biocompatible
- Size = body surface area

Hemofilter	Surface area	Priming volume	UFR ml/h/mmHg
Aquamax HF03	0.3 m^2	32 ml	16
Aquamax HF07	0.7 m^2	54 ml	33
Aquamax HF12	1.2 m^2	73 ml	51

Vascular access

- Ideal : easy insertion, permits adequate BFR without vascular damage, minimal technical flaws (kinking, high recirculation rate)
- Shorter and larger catheters
- Minimum 30 to 50 ml/min to minimize access and filter clotting

Vascular access

- Match catheter size to patient size and anatomical site
- Dual- or triple-lumen uncuffed catheters
- Sites
  - femoral
  - internal jugular
  - avoid subclavian vein if possible

Vascular access

Patient size	Catheter size	Site of insertion
Newborn	Single lumen 5 Fr Dual lumen 7 Fr	Femoral vein
3-6 kg	Dual lumen 7 Fr	Internal jugular v. Femoral vein
6-15 kg	Dual lumen 8 Fr	Internal jugular v. Femoral vein
15-30 kg	Dual lumen 9 Fr	Internal jugular v. Femoral vein
>30 kg	Dual lumen 10 Fr	Internal jugular v. Femoral vein

Blood line

Manual : Blood line (Kawasumi^{R})

Patient size	Type	Internal Volume (ml)	Internal diameter (mm)
< 30 kg	pediatric	48	6
> 30 kg	adult	88	8