HOW TO MEASURE RENAL INJURY AND WHEN CONSIDER RRT

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Acute kidney injury: not just acute renal failure any more?

- Acute renal injury: acute (hours –days) decline in kidney function (ranging from minor changes of renal function to need of RRT) secondary to structural of functional changes in the kidney;

Table 1: Classifications to define AKI.

(a) RIFLE classification [11]

RIFLE category	SCr/GFR criteria	Urine output criteria
Risk	↑ SCr ≥150–200% (1.5–2 fold) OR decrease of GFR >25%	Urine output <0.5 mL/kg/hour for 6 hours
Injury	↑ SCr >200–300% (>2-3 fold) OR decrease of GFR >50%	Urine output <0.5 mL/kg/hour for 12 hours
Failure	↑ SCr >300% (>3 fold) from baseline OR decrease of GFR >75% OR serum creatinine ≥4 mg/dL with an acute rise of ≥44 μmol/L	Urine output <0.3 mL/kg/hour for 24 hours OR anuria for 12 hours
Loss	Complete loss of renal function for >4 weeks	
End stage kidney disease	Need for RRT for >3 months	

(b) AKI Network classification [12]

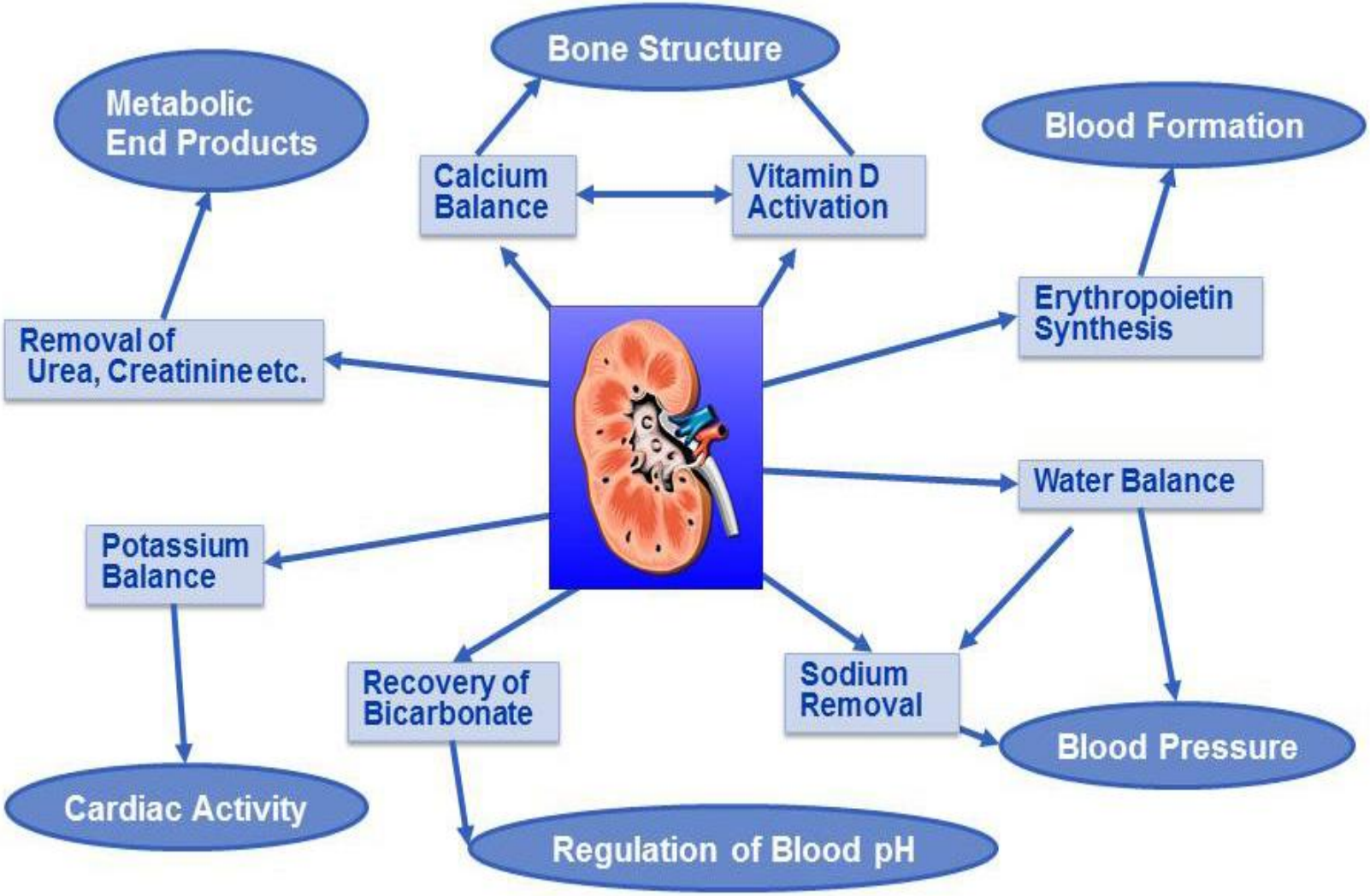
AKIN stage	Serum creatinine criteria	Urine output criteria
1	↑ SCr ≥26.4 μmol/L in ≤48 hours OR ↑ SCr ≥150–200% (1.5–2 fold) from baseline	<0.5 mL/kg/h for >6 h
2	↑ SCr >200–300% (>2–3 fold) from baseline	<0.5 mL/kg/h for >12 h
3	↑ SCr >300% (>3 fold) from baseline OR SCr ≥354 μmol/L with an acute rise of ≥44 μmol/L OR treatment with RRT	<0.3 mL/kg/h for 24 h OR anuria for 12 h

(c) KDIGO classification [3]

Stage	Serum creatinine criteria	Urine output criteria
1	1.5–1.9 times baseline OR ≥0.3 mg/dL (>26.5 μmol/L) in ≤48 hours	<0.5 mL/kg/h for 6–12 hours
2	2–2.9 times baseline	<0.5 mL/kg/h for ≥12 hours
3	≥3 times baseline OR increase in SCr to ≥4.0 mg/dL (353.6 μmol/L) OR initiation of RRT	<0.3 mL/kg/h for ≥24 hours OR anuria for ≥12 hours

Abbreviations: GFR: glomerular filtration rate; RRT: renal replacement therapy; SCr: serum creatinine.
Only one criterion needs to be met to be classified as AKI; if both are present, the criterion which places the patient in the higher stage of AKI is selected.

Kidney functions



Bedside: manifestations of AKI

- Azotemia progressing to uremia;
- Oligo-anuria;
- Hyperkaliemia;
- Metabolic acidosis;
- Volume overload;
- Hyperphoshatemia;
- Accumulations and toxicity of medications excreted by the kidney;

AKI: diagnosis and "quantitative" assessment

- Suggestive clinical features;
- Urine analysis;
- Renal indices;

First recognise the at-risk patient

- **Reduced renal reserve:**

  Pre-existing CRF, age > 60, hypertension, diabetes
- **Reduced intra-vascular volume:**

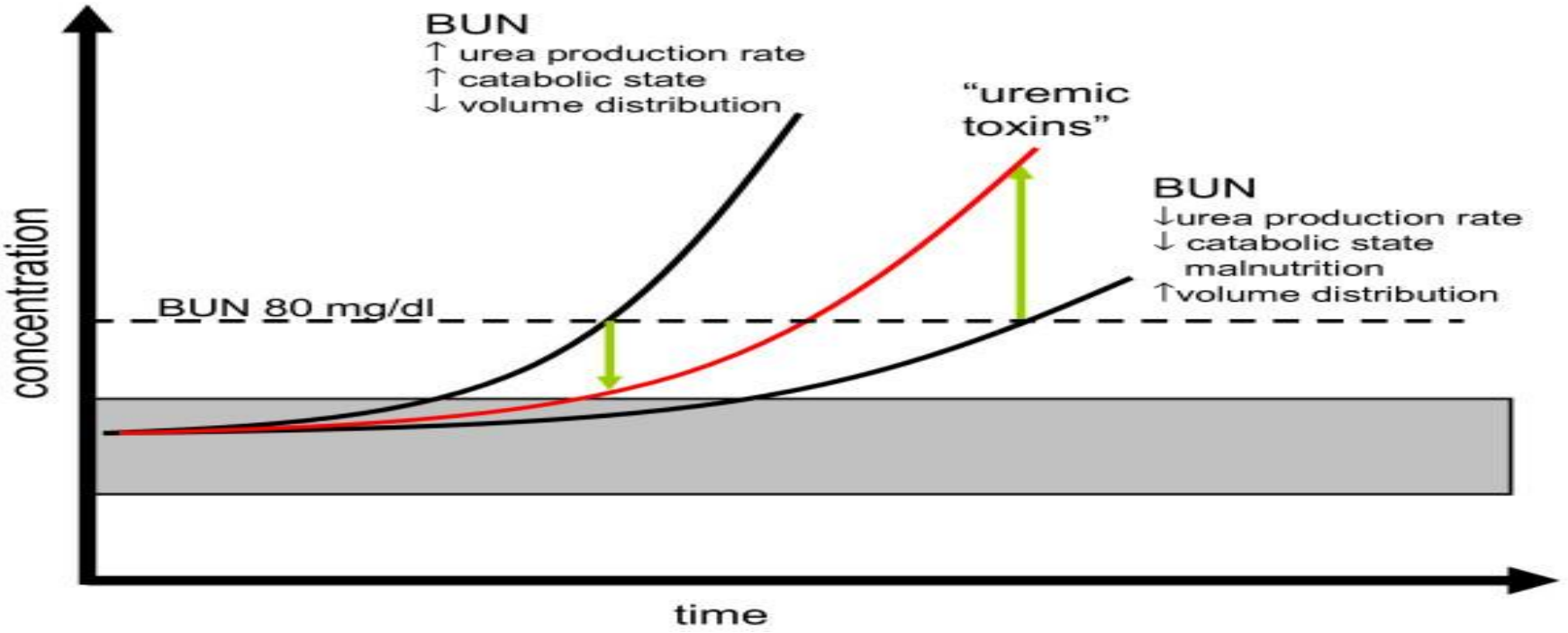
  Diuretics, sepsis, cirrhosis, nephrosis
- **Reduced renal compensation:**

  ACE-I's (ATII), NSAID's (PG's), CyA

Conventional markers of acute kidney injury

Marker	Normal value	Source	Information	Limitations
Urea	8-20 mg/dL	Serum	By-product of protein metabolism, used as a marker indicating solute retention and elimination	Affected by diet, critical illness, burns, gastrointestinal bleeding, and trauma; production rate not constant
Creatinine	0.7-1.5 mg/dL	Serum	Derived from creatine, excreted through filtration in glomerulus	Critically ill patients not in a steady state, may not reflect severity of renal injury; serum value influenced by patient's age, sex, dietary intake, and muscle mass, as well as drugs

Relation of blood urea nitrogen to uremic toxins



INTERPRETATION OF BUN VALUES MUST RELY ON CHANGES OVER TIME MORE THAN ON ABSOLUTE VALUE

Serum Creatinine (sCr)

- Changes in sCr may occur indipendently of GFR through changes in volume status, altered production, **reduced muscle mass** or by drug effects on tubular excretion of creatinine;
- **Serum creatinine concentration does not change until around 50% of kidney function is lost;**
- **The lag time between injury and the resulting loss of function which results in an elevation of sCr is a missed therapeutic opportunity;**

Creatinine Clearence

$$\text{CrCl (ml/min)} = \frac{\text{Urine [Cr](mg/dl) x volume(ml/min}}{\text{Plasma [Cr] (mg/dl)}}$$

1) The most widely used method to assess renal function and estimate GFR;
2) But we need a 2-24-h urine collection (uCr and volume urine);
3) **In AKI creatinine clearence may overstimate GFR;**

Creatinine Clearence Cockroft Gault

Creatinine Clearance. Normal creatinine clearance is 120 $ml min^{-1}$. A crude estimation of the creatinine clearance may be obtained by the following formula.

$$CrCl\ (ml/min) = \frac{(140\text{-age}) \times weight(kg)}{72 \times serum\ Cr\ (mg/dl)}$$

Urinary output

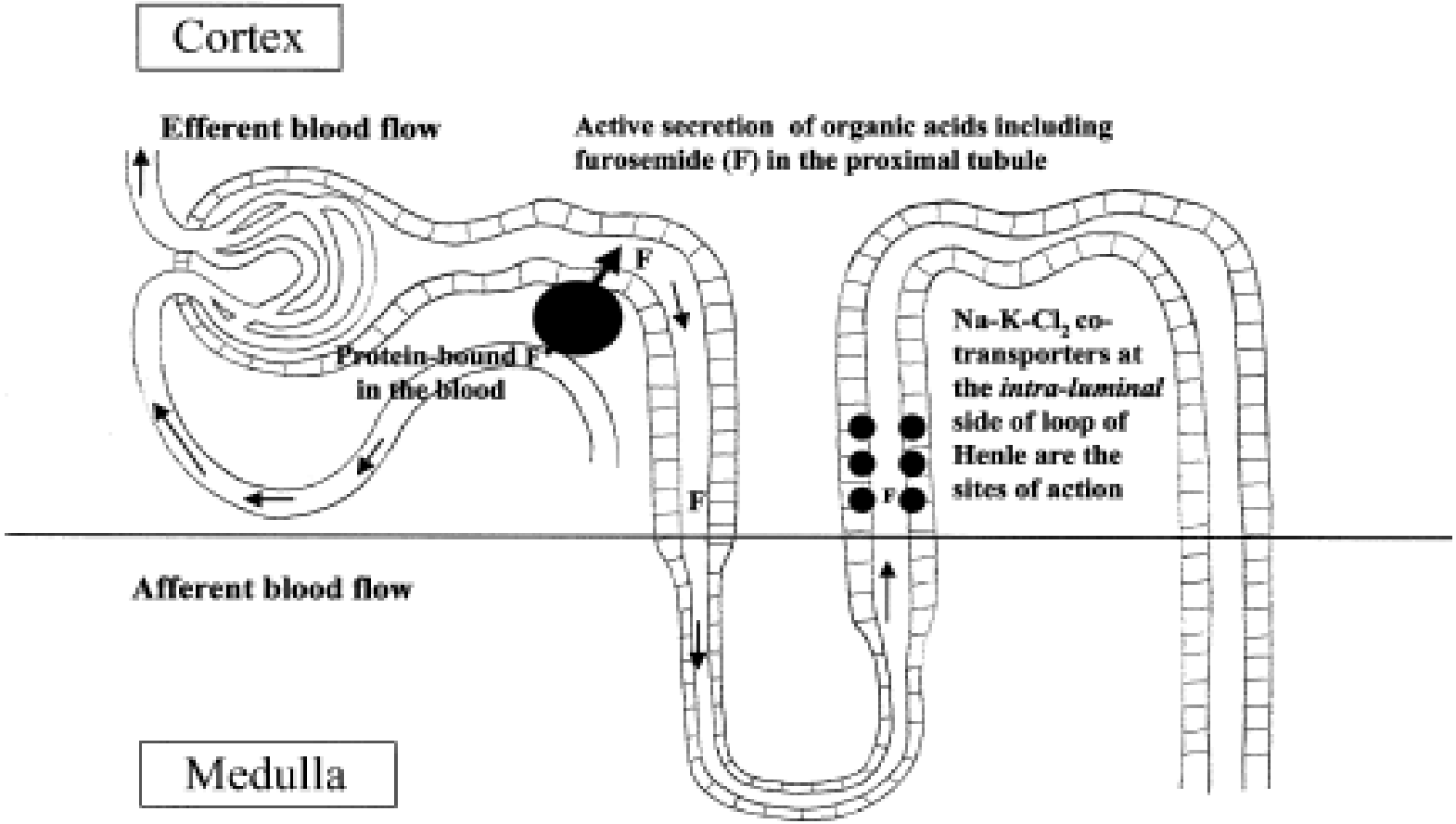
- Oliguria is defined as a urine output of less than 400-500 ml/day or 0.5mg/kg/hr; it can represent a functional adaptation or more often AKI;
- Anuria is defined as less than 50-100ml/day;
- Oligo-anuria may be a feature of AKI but non oliguric AKI is not uncommon;

How to cope with that?

- LOOP DIURETICS **can increase urine output without improving the creatinine clearence and renal function : the drug doesn't change the course of AKI;**

DON'T DELAY DIAGNOSTIC AND THERAPEUTICAL PROCESS TARGETING CAUSE OF AKI

Method of action of loop diuretics



"Forced" urine output

- The diuretic effect of loop diuretics depends on renal blood flow and on proximal tubule and Henle loop function (its effect depends on degree of renal function);

HIGHER DOSE OF LOOP DIURETICS ARE NEEDED TO INDUCE URINE OUTPUT IN SEVERE vs MILD AKI

Potential roles of Furosemide

- Furosemide can increase the urinary escretion of water, sodium, potassium and calcium in patients who are still responsive to furosemide:

USEFULL IN TREATING AKI COMPLICATIONS (hyperkaliemia, acidosis, and fluid overload);

Urine analysis

- Parameters that are commonly measured are urine specific gravity (urine stick), urine osmolarrity, urinary concentration of sodium (statim or 2hr sample) and urine concentration of creatinine;

- Urinary electrolyte analysis became useless once furosemide is administered !!!

Urine electrolytes

- When kidney perfusion is decreased, Na+ readsorption increases and escretion decreases, and urine Na<20meq/L results. This may occours in hypovolemia (PRERENAL AKI);

- When on the contrary there is a renal injury (ATN) Na+ readsorption is impaired and there is an increase in escretion (urinaryNa+>20-40meq/L) (RENAL AKI);

The fractional escretion of sodium

Fractional Excretion of Sodium

$$\text{Fe Na} = \frac{\text{Urine [Na] / plasma [Na]}}{\text{Urine [Cr] / plasma [Cr]}} \times 100$$

Fe Na<1% occour in prerenal injury (functioning tubules reabsorb lots of filtered Na)

Fe Na>2% in renal injury (damaged tubules can't reabsorb Na)

Calculating FeNa after Patient has gotten Lasix...

- Caution with calculating FeNa if pt has had Loop Diuretics in past 24-48 h
- Loop diuretics cause natriuresis (increase urinary Na excretion) that raises U Na-even if pt is prerenal;
- So if FeNa >1%, you don't know if this is because pt is euvolemic or because Lasix increased the U Na
- **So helpful if FeNa still <1%, but not if FeNa >1%**

Investigations to help differentiate prerenal and renal causes of AKI

Investigation	Pre renal	Renal
Urinary sodium ($meqL^{-1}$)	< 20	> 40
Fractional excretion of sodium (%)	< 1	> 2
Urine osmolarity ($mosmL^{-1}$)	>400	250 – 300
Specific gravity	>1020	1010
Urine output	oliguria	oliguria or not

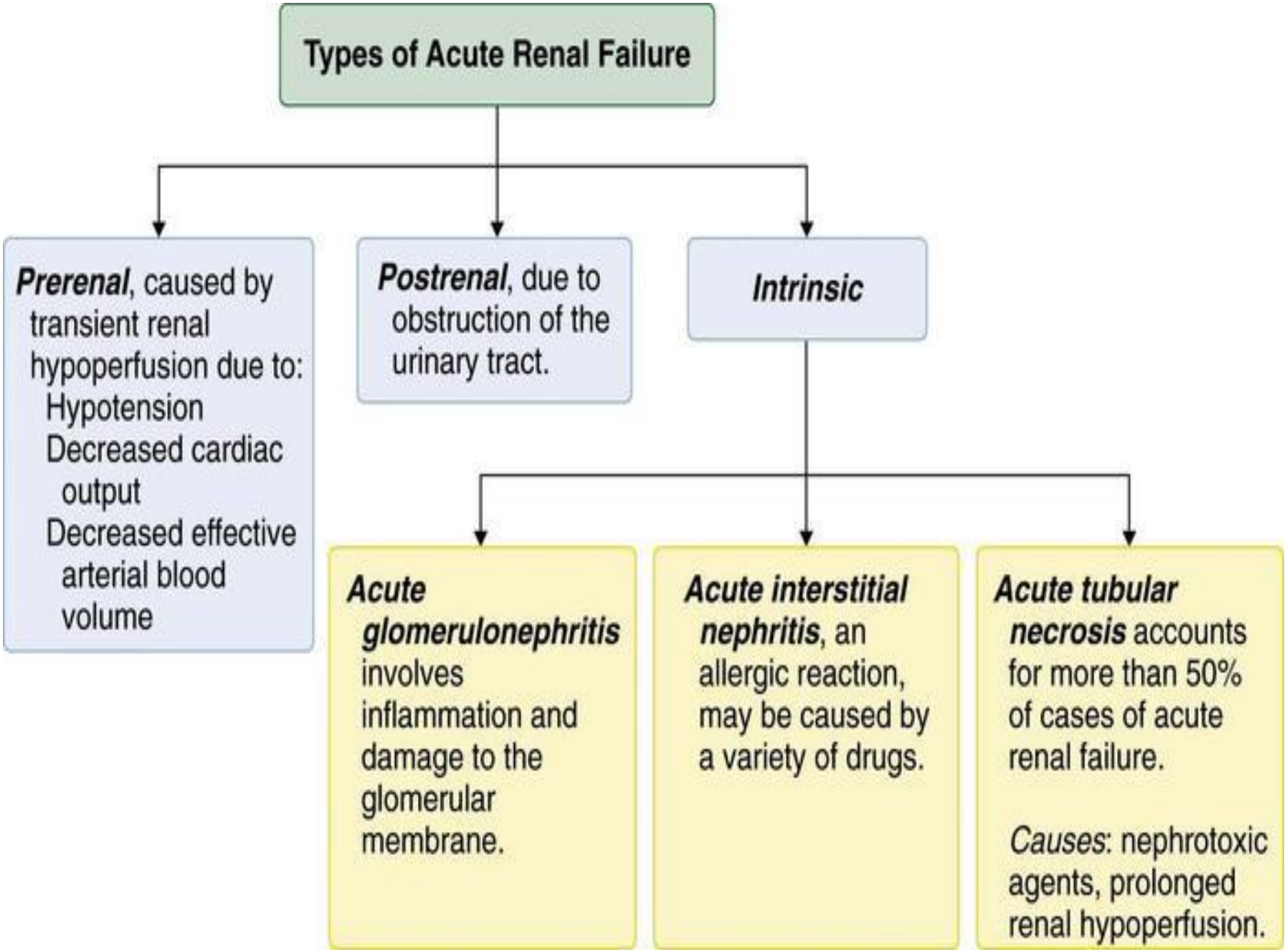

Types of Acute Renal Failure
Prerenal, caused by transient renal hypoperfusion due to:
Hypotension
Decreased cardiac output
Decreased effective arterial blood volume
Postrenal, due to obstruction of the urinary tract.
Intrinsic
Acute glomerulonephritis involves inflammation and damage to the glomerular membrane.
Acute interstitial nephritis, an allergic reaction, may be caused by a variety of drugs.
Acute tubular necrosis accounts for more than 50% of cases of acute renal failure.
Causes: nephrotoxic agents, prolonged renal hypoperfusion.

Table - 2[4] : Causes of oliguria

Pre renal	Renal	Post Renal
Hypovolemia Hypotension Poor cardiac output Pre existing renal damage Renal vascular disease Renal vasoconstriction Sepsis	Hypoxia From pre renal causes Renal vein thrombosis Nephrotoxins Aminoglycosides Amphotericin Chemotherapeutic agents NSAIDS Contrast media (beware in diabetes and multiple myeloma) Tissue injury Haemoglobinuria Myoglobinuria Uric Acid (tumour lysis) Inflammatory nephritides Glomerulonephritis Interstitial nephritis Polyarteritis Myeloma	Bladder neck obstruction Blocked drainage system Pelvis surgery Prostatic enlargement Raised intra-abdominal pressure Renal or ureteric Calculi Clots Necrotic papillae

Approachto the Patientwith AKI

1. Recognize AKI;

2. Treat lifethreatening conditions;

3. Assess contributing cause of AKI :

3a. Is there a pre-renal cause?

3b. Could this be obstruction?

3c. Is intrinsic renal disease probable?

4. Therapyto reverse or prevent worseningof AKI

How to do a diagnosis?

3a. Isthere a pre-renal cause?
CHECK VOLUME STATUS/BP-CARDIAC PUMP

3b. Could this be obstruction?
CHECK BLADDER, CATHETER and ULTRASOUND

3c. Is intrinsic renal disease probable?
CHECK URINANALYSIS

Box 2: Evaluation of Patients With Acute Renal Failure

1. Review records, perform history and physical examination

- Findings that suggest prerenal causes:
  - Volume depletion
  - Congestive heart failure
  - Severe liver disease or other edematous states
- Findings that suggest postrenal causes:
  - Palpable bladder or hydronephrotic kidneys
  - Enlarged prostate
  - Abnormal pelvic examination
  - Large residual bladder urine volume
  - History of renal calculi, perform ultrasound to screen for urinary tract obstruction)
- Findings that suggest intrinsic renal disease:
  - Exposure to nephrotoxic drugs or hypotensive
  - Recent radiographic procedures with contrast

2. Examine the urine sediment

- If no abnormalities: suspect prerenal or postrenal azotemia
- If eosinophils: suspect acute interstitial nephritis
- If red blood cell casts: suspect glomerulonephritis or vasculitis
- If renal tubular epithelial cells and muddy brown casts: suspect acute tubular necrosis

3. Calculate urinary indices

- Findings that suggest prerenal azotemia or glomerulonephritis:
  - Urinary sodium concentration <20 mEq/L
  - Urine : plasma creatinine ratio >30
  - Renal failure index <1
  - Renal failure index = (urinary sodium concentration × plasma creatinine concentration)/urinary creatinine concentration
  - Urine osmolality >500 mOsm/kg
- Findings that suggest acute tubular necrosis or postrenal azotemia:
  - Urinary sodium concentration >40 mEq/L
  - Urine:plasma creatinine ratio <20
  - Renal failure index >1
  - Urine osmolality <100 mOsm/kg

How to treat?

3a. Is there a pre-renal cause?
CHECK VOLUME STATUS/BP-CARDIAC PUMP
➔VOLUME REPLETION/INOTROPIC SUPPORT

3b. Could this be obstruction?
CHECK BLADDER, CATHETER and ULTRASOUND
➔NEPHROSTOMY or URETERAL STENT

3c. Is intrinsic renal disease probable?
CHECK URINANALYSIS
➔GENERAL SUPPORTIVE CARE (fluid mng, drug dosing…..)

What we can ask to the kidney?

Demand	Capacity	Example	Action
High	Normal	Catabolic state Nutritional loading Poisoning	Reduce demand Monitor for adding renal support
High	Low	Decreased GFR from AKI	Add capacity Reduce demand
Normal	Low	CKD Noncatabolic AKI	Add additional capacity to maintain steady state
Low	Low	Malnutrition and wasting; CKD	Assess for nutritional state and add capacity

GFR, glomerular filtration rate; AKI, acute kidney injury.

WHETER OR NOT TO PROVIDE RENAL REPLACEMENT SUPPORT?

CLASSIC AND POTENTIAL RRT INDICATIONS

UREMIA

- Azotemia (Blood urea >30mmol/l o >100mg/dl);

OVERLOAD OF FLUIDS

- Suspected uremic organic involvment;
- Non obstructive oliguria or anuria (UO<200ml or <50ml/12h);
- Diuretic resistant volume overload;

ELECTROLYTE

- Iperkaliemia (K+>6.5 mmol/l or rapidlyraisingK+);
- Progressive severe dysnatremia (Na+>160 or <115 mmol/l);

ACID-BASE

- Severe acidemia (pH<7.1) due to metabolic acidosis;

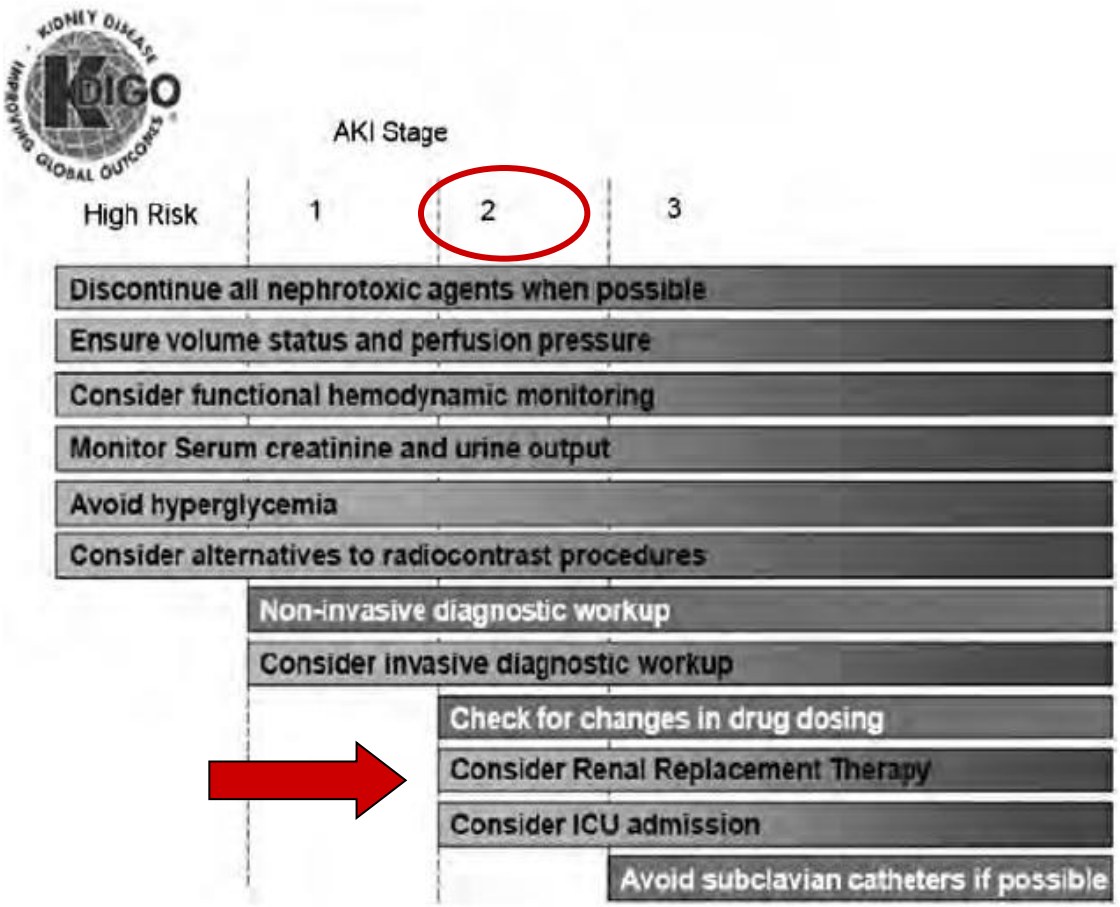
INTOXICATION

- Overdose with dialyzable drug;

NONRENAL

- Distrupted fluid balance (cardiacfailure or MOF);
- Immunomodulation (sepsis);
- Hyperthermia;
- Increased catabolic state (eg. Rhabdomyolysis);
- Electrolytes abnormalities;

KDIGO Clinical Practice Guideline for Acute Kidney Injury



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WHAT ARE THE INDICATIONS FOR RRT IN (CRITICALLY ILL) PATIENTS WITH AKI?

IS STILL LACKING AN OPERATIVE DEFINITION OF ARF IN WHICH RRT IS INDICATED.

KDIGO Clinical Practice Guideline for Acute Kidney Injury

5.1.1: Initiate RRT emergently when life-threatening changes in fluid, electrolyte, and acid-base balance exist. (*Not Graded*)

5.1.2: Consider the broader clinical context, the presence of conditions that can be modified with RRT, and trends of laboratory tests—rather than single BUN and creatinine thresholds alone—when making the decision to start RRT. (*Not Graded*)

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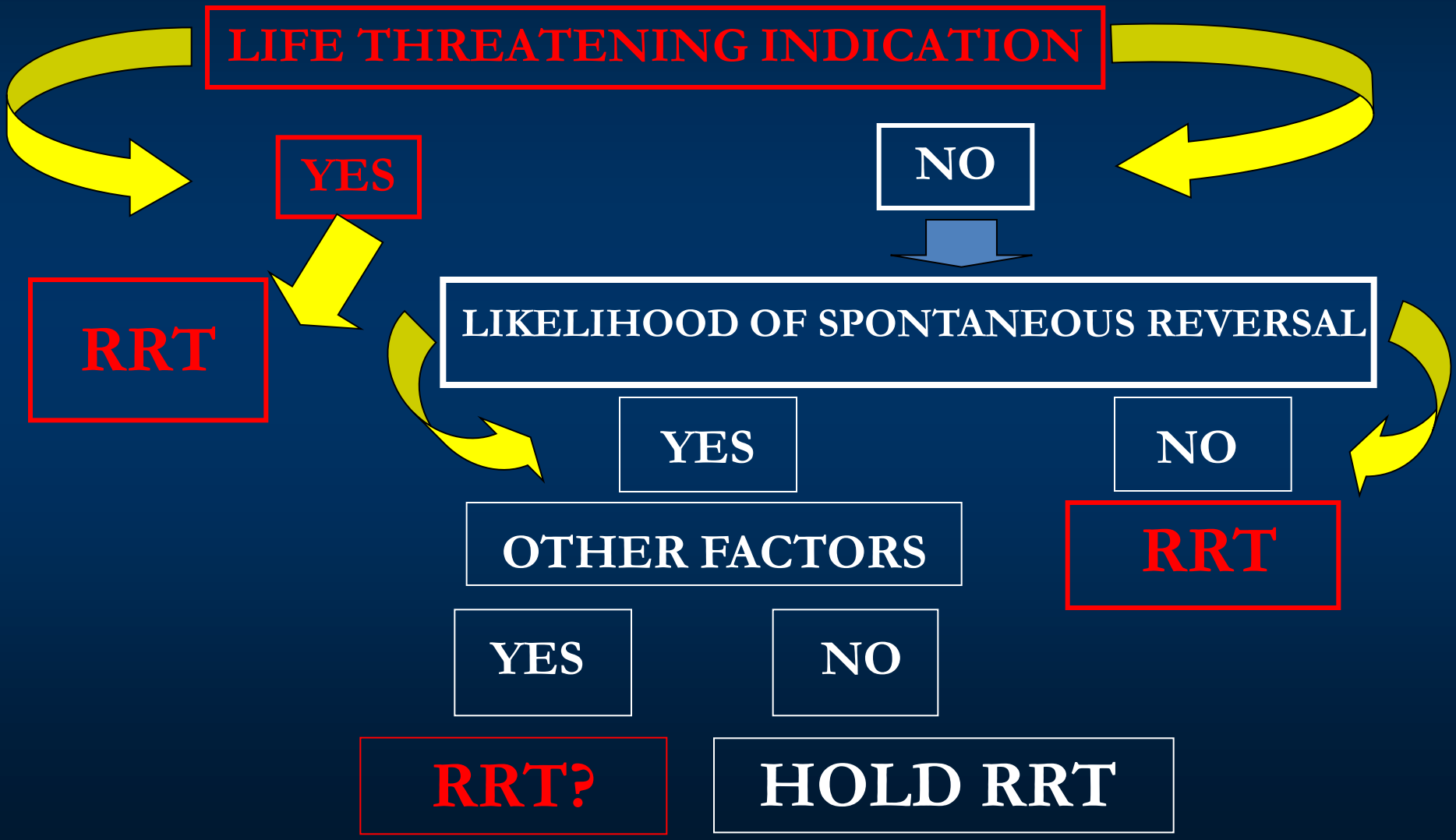
DECISION PROCESS FOR INITIATION OF RRT IN ICU

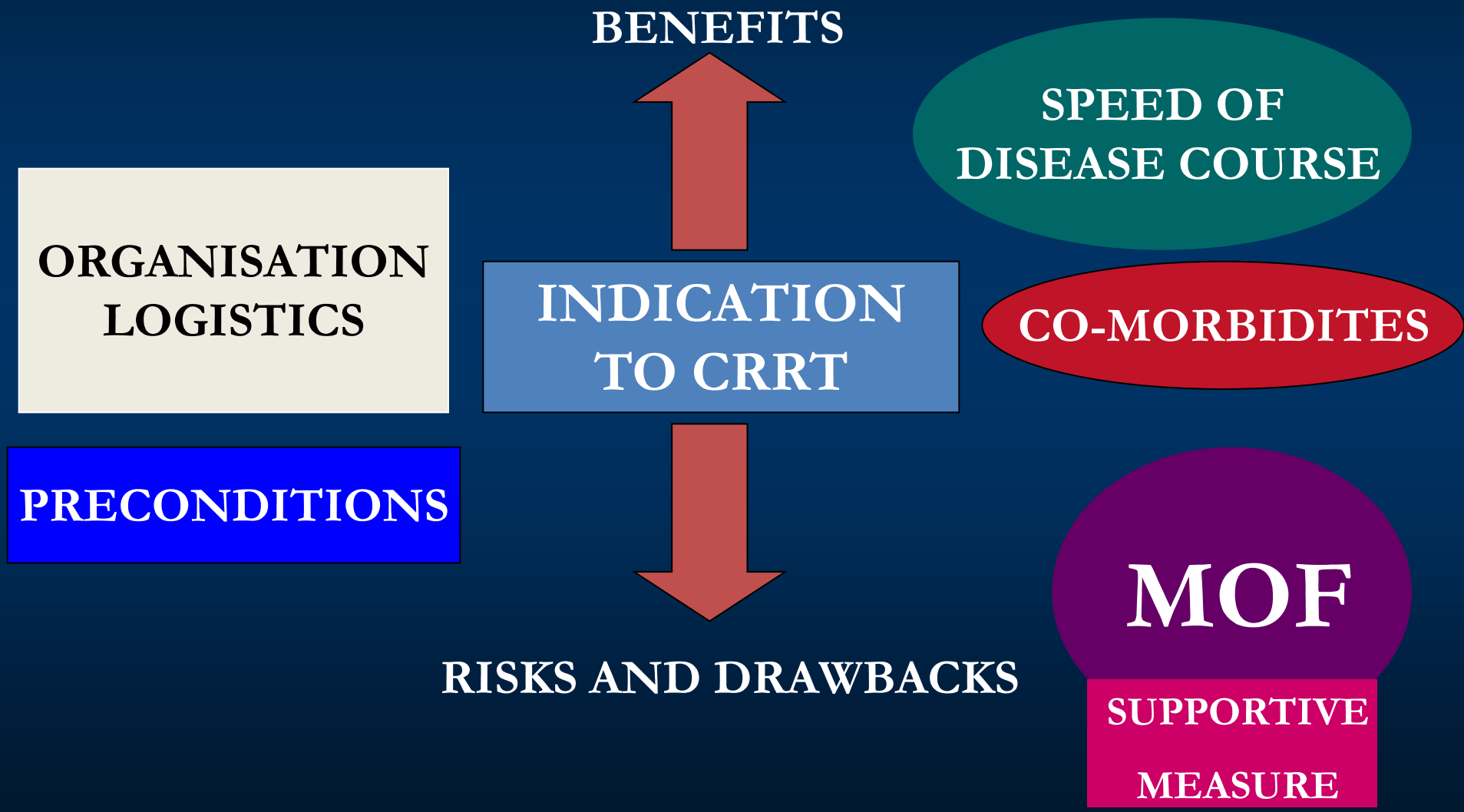


Factors to assess likelihood of spontaneous reversal of renal dysfunction in AKI

Factor	Influence
Nature and timing of renal insult	Both nature and timing well defined, e.g. antibiotic nephrotoxicity (20%) Possible knowledge of insult and timing, e.g. postoperative ARF (50%) Nature and timing unknown, e.g. multiorgan failure (50%)
Presence of oliguria	Affected by diuretic use Inaccurate marker for estimating level of renal function Unreliable as an indicator for recovery
Change in BUN and creatinine	Affected by multiple factors Imprecise in detecting impending recovery May lag behind recovery
Underlying disease	Is ARF an epiphenomenon? Does ARF contribute to outcome?
Other factors	Demand exceeds renal excretory capacity, e.g. volume resuscitation Intensivist demand Logistics

"LIMITED" APPROACH

WHAT PATIENT AND/OR CLINICAL ENVIROMENTAL CHARACTERISTIC MAKE CRRT DESIDERABLE?



STRATEGIES FOR MANAGEMENT OF AKI

	AKI	ESRD
GOALS OF THERAPY	Improve organ failure	Ameliorate uremia
DESIRED OUTCOME	Survival, renal recovery	LT survival, QL
DETERMINING FACTOR	Other organ support	Renal process
INDICATION RRT	Renal support until recovery	Renal replacement

RRT DECISION IN ICU: A "WIDE" APPROACH

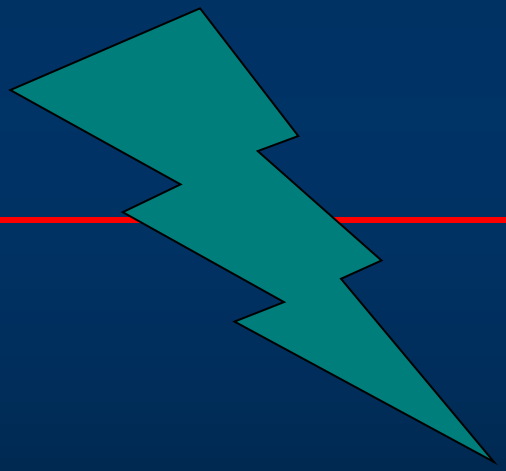
RENAL REPLACEMENT

Life-threatening indications

Regulation of acid-base electrolyte status

Fluid removal

Solute control



RENAL SUPPORT

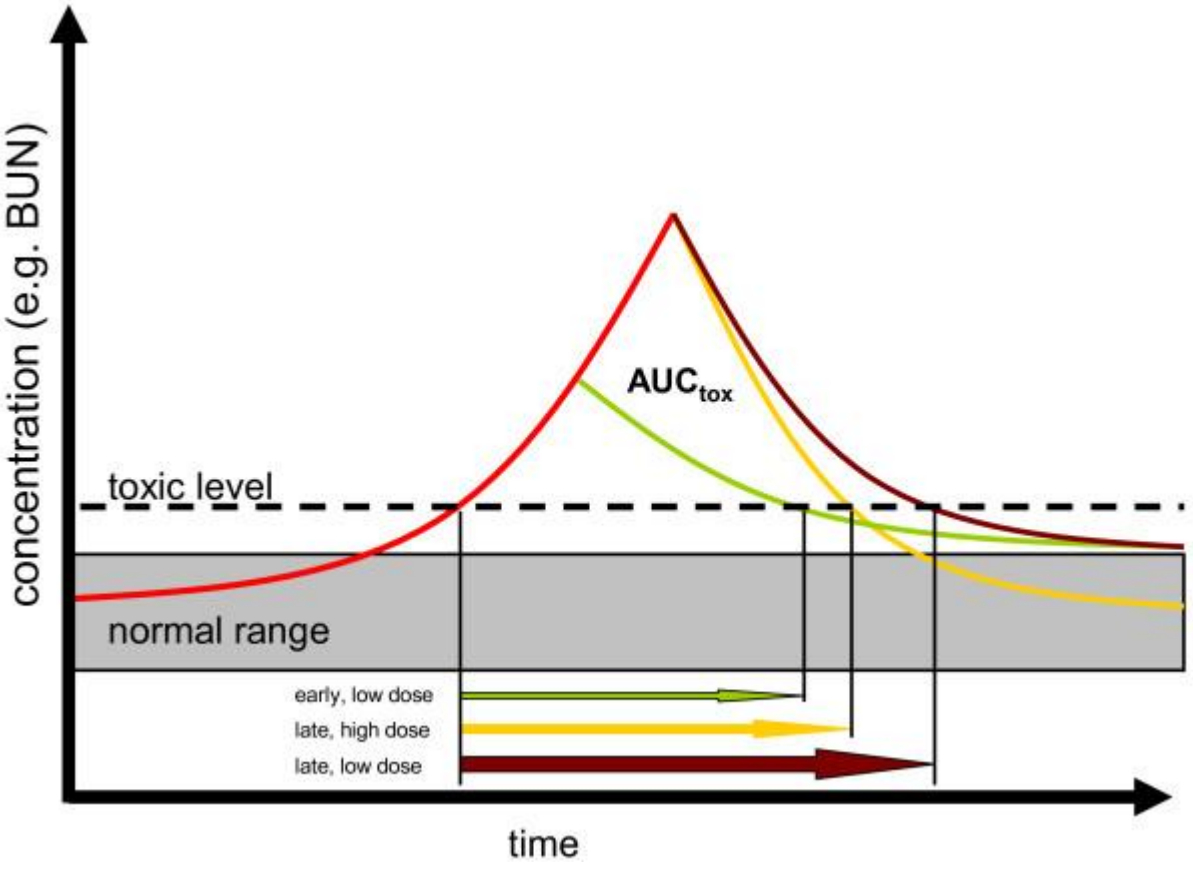
Nutrition

Fluid removal in CHF

Cytokine manipulation in sepsis

Fluid management in MOF

Influence of time and dosing on exposure to uremic toxins



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ULTRAFILTRATION IN CHF

WHY ?

HOW ?

WHEN ?

RATIONALE FOR THE USE OF UF IN HF

- Reduction of extravascular volume/ restoration intravascular volume
- Solute regulation
- Restoration of urine output and diuretic responsivity
- Reset neurohormonal axis

UF IN CHF: WHEN

CLINICAL INDICATION TO UF IN CHF

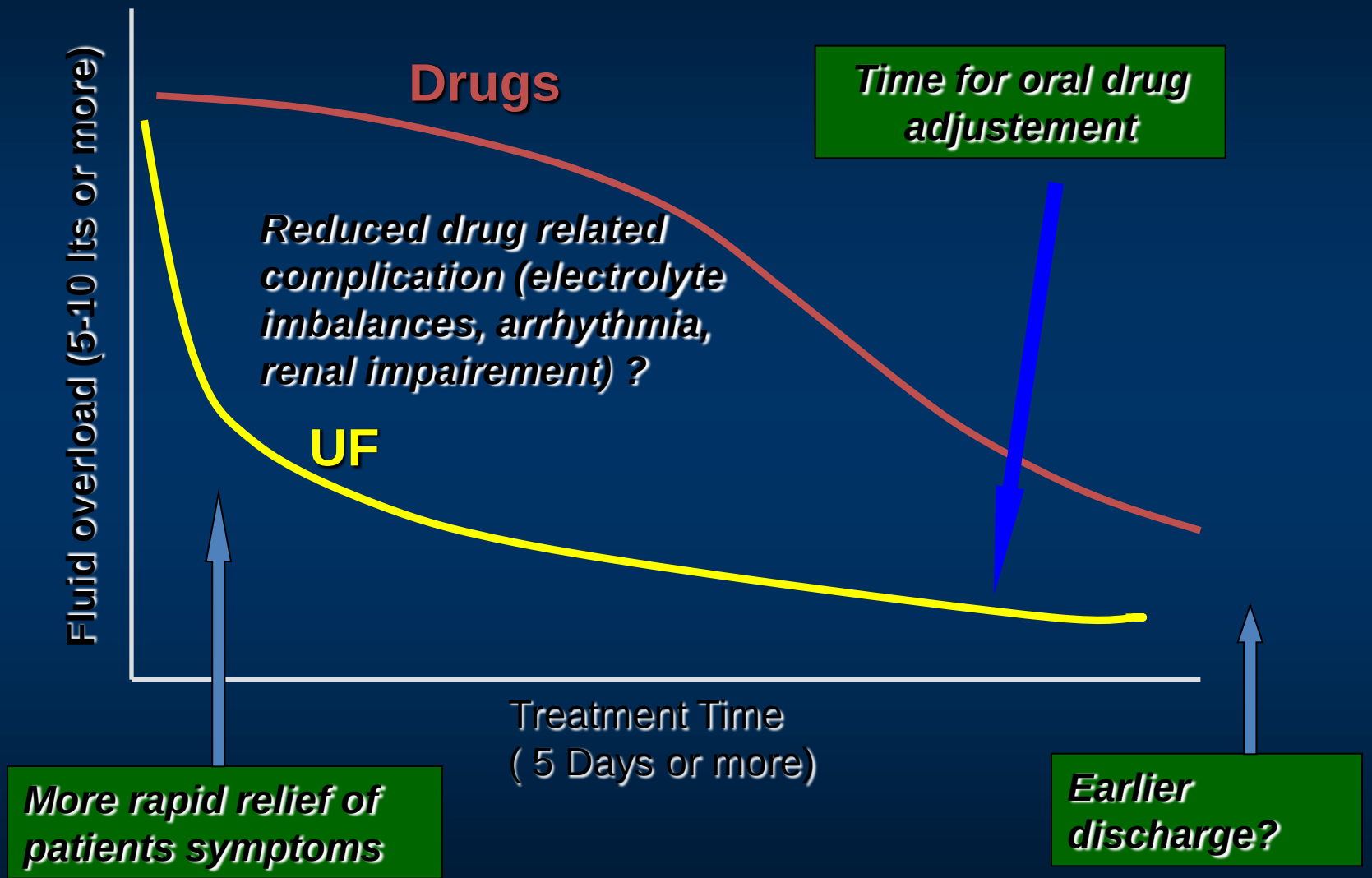
1. Acute decompensation of previously compensated CHF (emergency procedure)

2.Temporary treatment for patients awaiting for TX

3. Long term treatment in CHF resistant to conventional therapy

ULTRAFILTRATION AS A COMPLEMENTARY STRATEGY

STRATEGY OF COMPLEMENTARY MANAGEMENT IN CHF



Clark et al J Artif Organs 2004

UF IN CHF: WHEN?

ACUTE EXACERBATION IN WRF

Canaud 1998
Marenzi 2001
Sheppard 2004

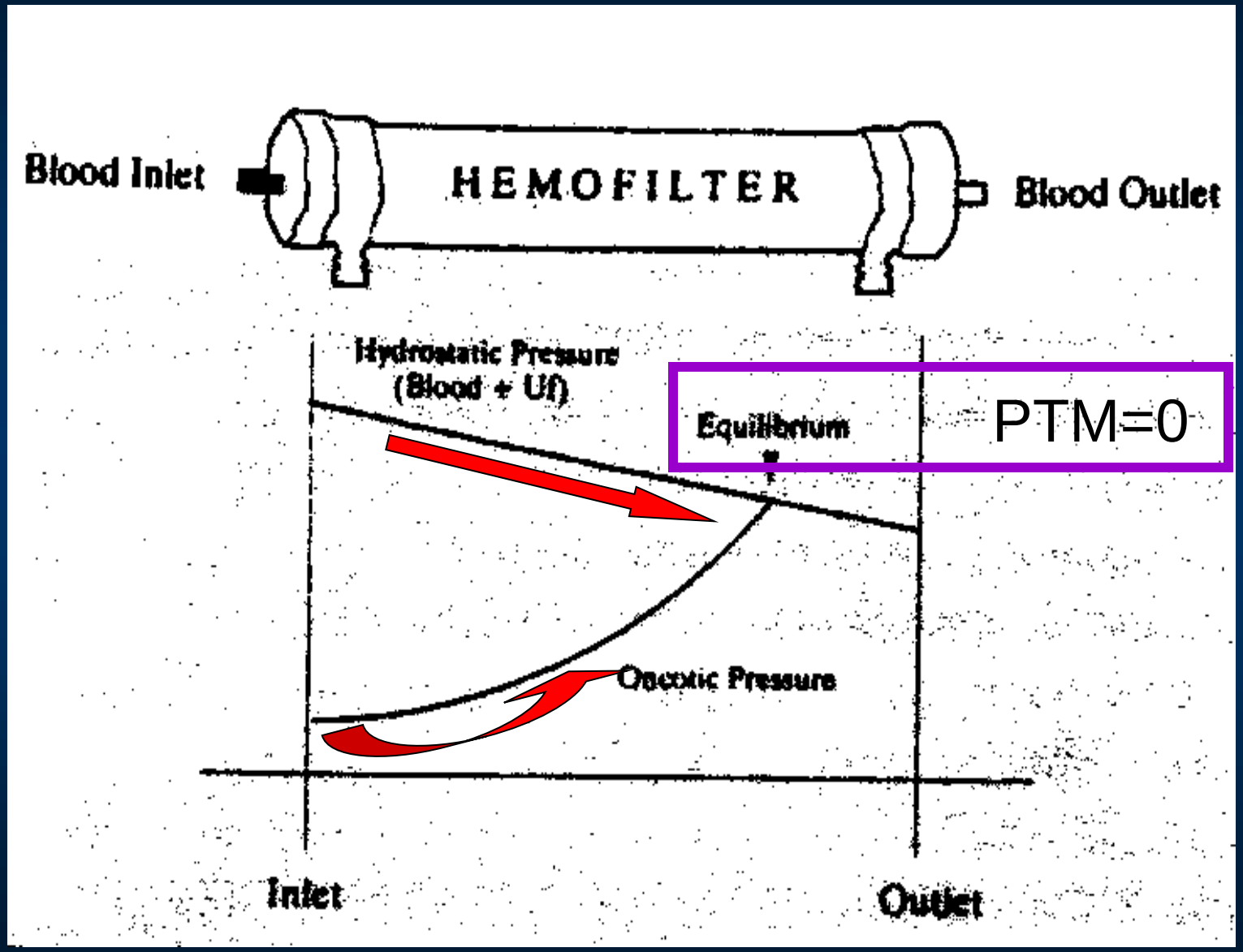
?

FUTURE ISSUE

- UF seems to improve quality of life, reduce hospital admission and length of stay in H in CHF patients.
- More studies (RT) are needed:

- To better define the criteria of CHF patients that could benefit from UF as chronic support therapy;
- To establish the ability of UF to prolong survival.

MANIPULATION OF ULTRAFILTRATION



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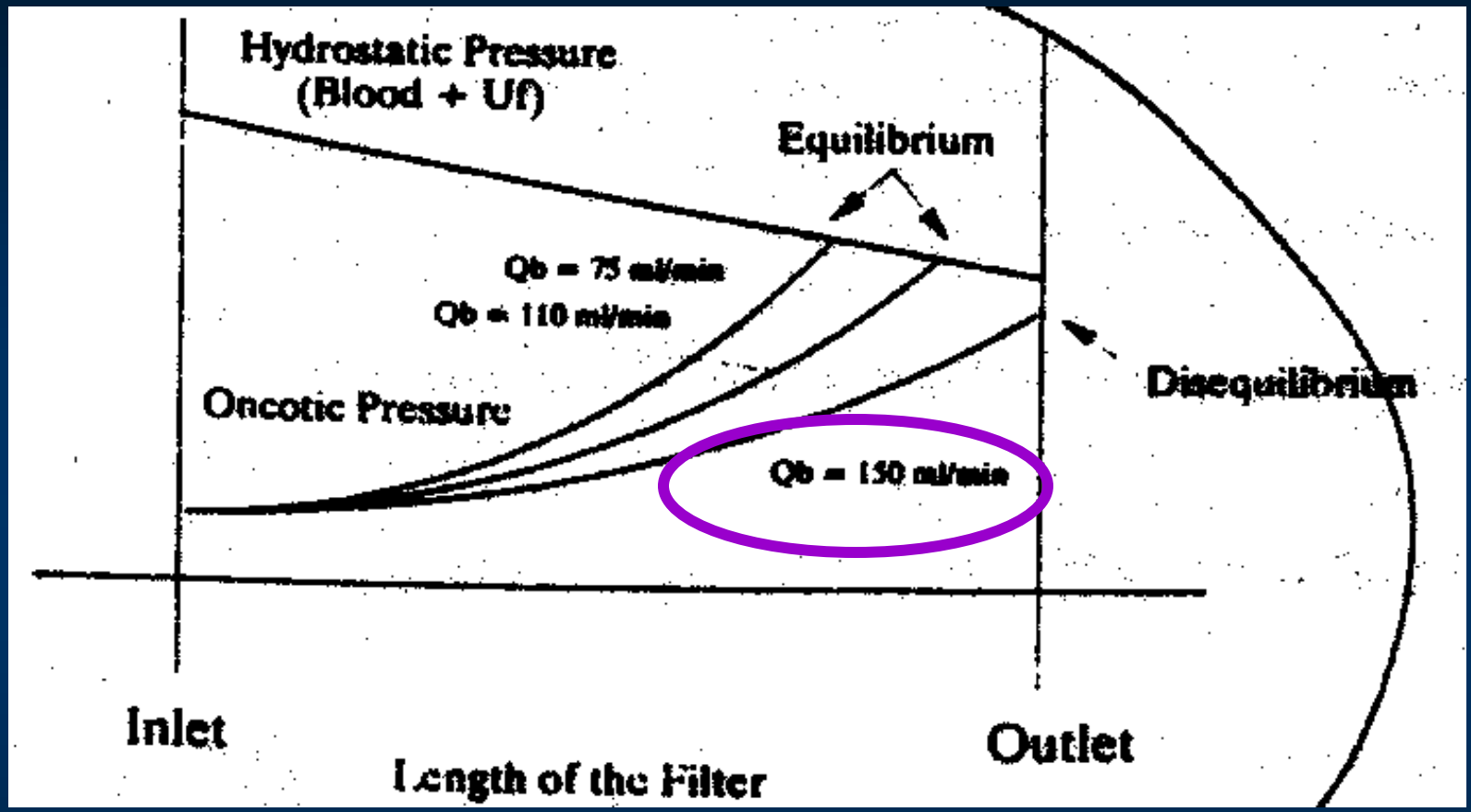

L'AUMENTO Qb INDUCE UN AUMENTO Quf grazie ad una ralativa riduzione dell'effetto della P oncotica. NB. Oltre certi valori la Quf non aumenta.