Acute kidney injury

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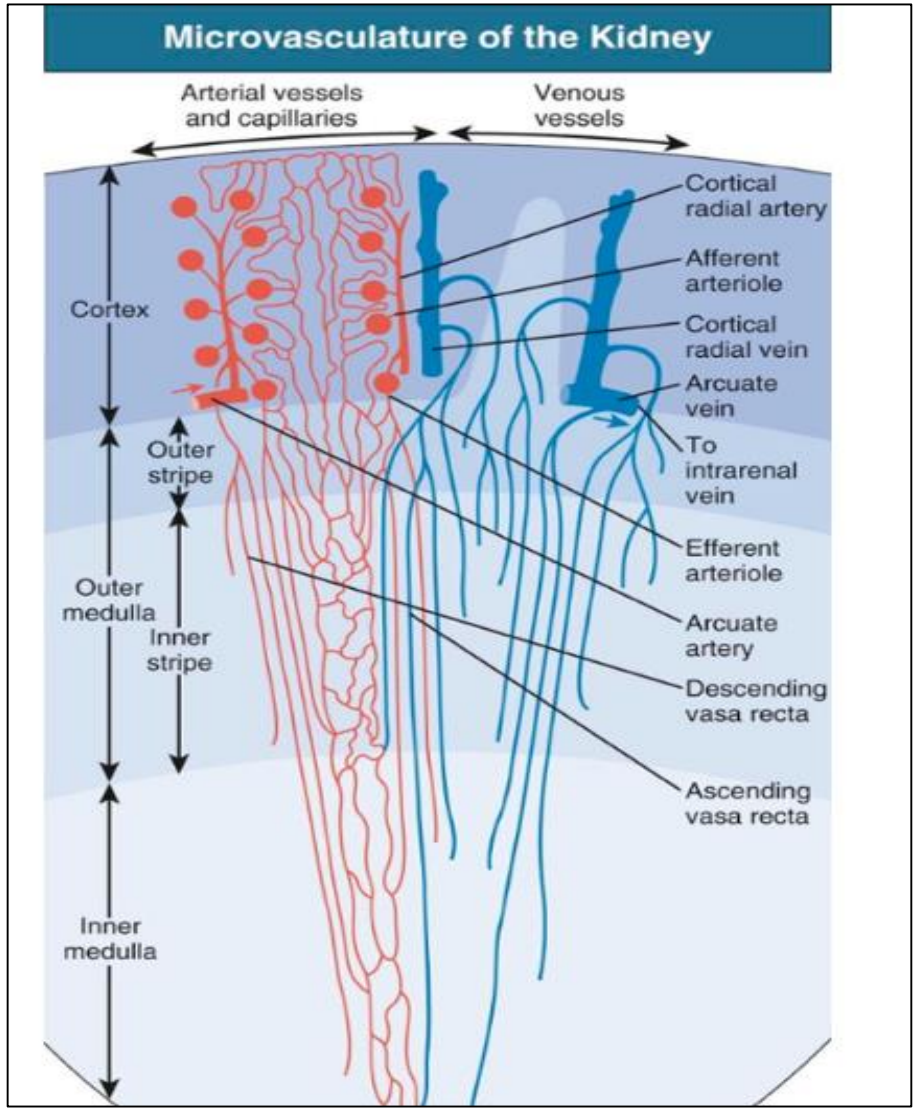
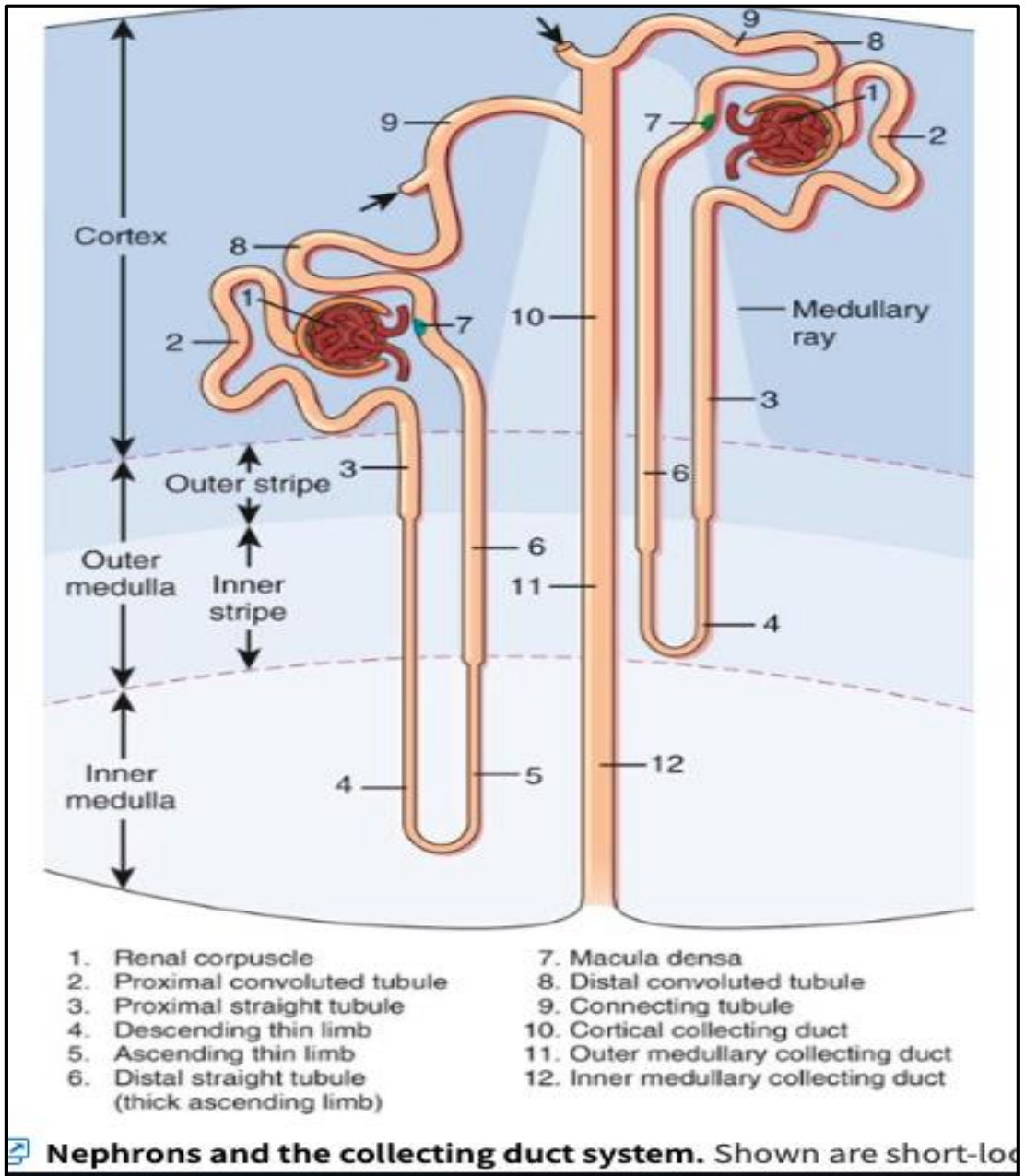
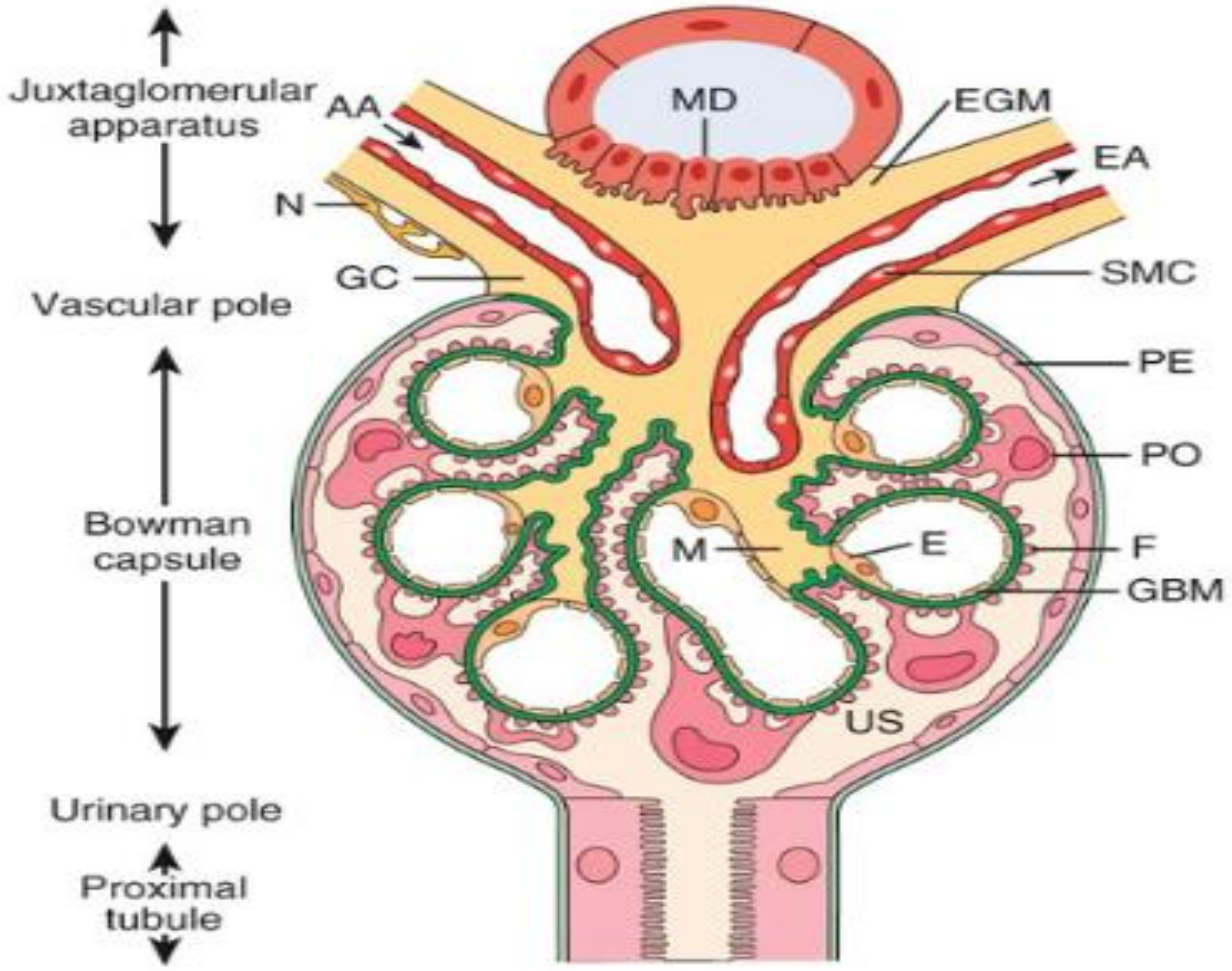
Nephrons and the collecting duct system



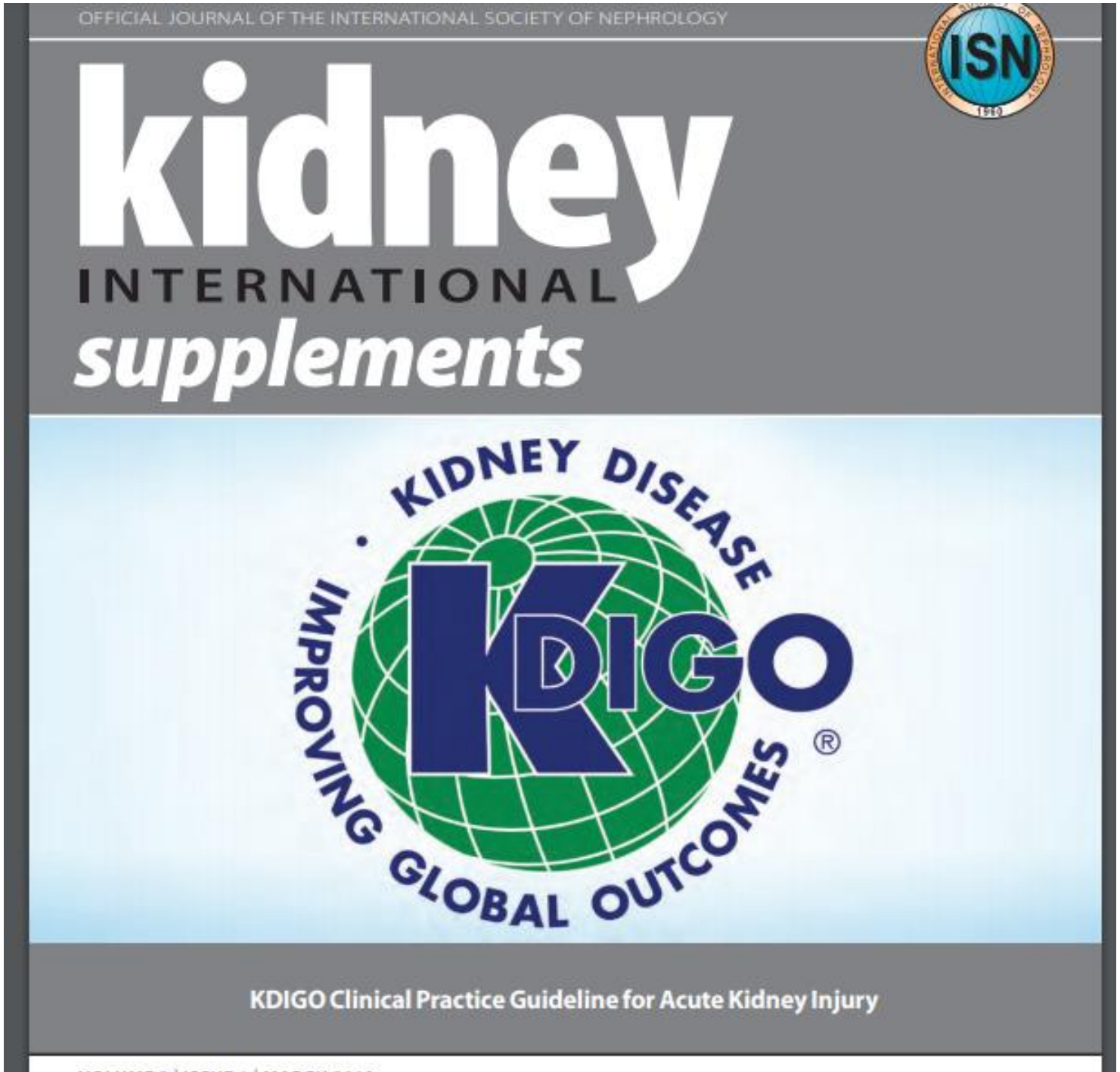


Nephrons and the collecting duct system. Shown are short-loc

Renal Corpuscle and Juxtaglomerular Apparatus



AA	Afferent arteriole
MD	Macula densa
EGM	Extraglomerular mesangium
EA	Efferent arteriole
N	Sympathetic nerve terminals
GC	Granular cells
SMC	Vascular smooth muscle cells
PE	Parietal epithelium
PO	Podocyte
M	Mesangium
E	Endothelium
F	Foot process
GBM	Glomerular basement membrane
US	Urinary space



AKI

- Clinical syndrome
- Abrupt decline in GFR
- Insufficient to eliminate waste products
- AKI replaced previously used term acute renal failure (ARF)

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Section 2: AKI Definition

2.1.1: AKI is defined as any of the following (*Not Graded*):

- **Increase in SCr by ⩾0.3 mg/dl (⩾26.5 μmol/l) within 48 hours; or**
- **Increase in SCr to ⩾1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or**
- **Urine volume <0.5 ml/kg/h for 6 hours.**

2.1.2: AKI is staged for severity according to the following criteria (Table 2). (*Not Graded*)

Table 2 | Staging of AKI

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ⩾0.3 mg/dl (⩾26.5 μmol/l) increase	<0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ⩾12 hours
3	3.0 times baseline OR Increase in serum creatinine to ⩾4.0 mg/dl (⩾353.6 μmol/l) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/h for ⩾24 hours OR Anuria for ⩾12 hours

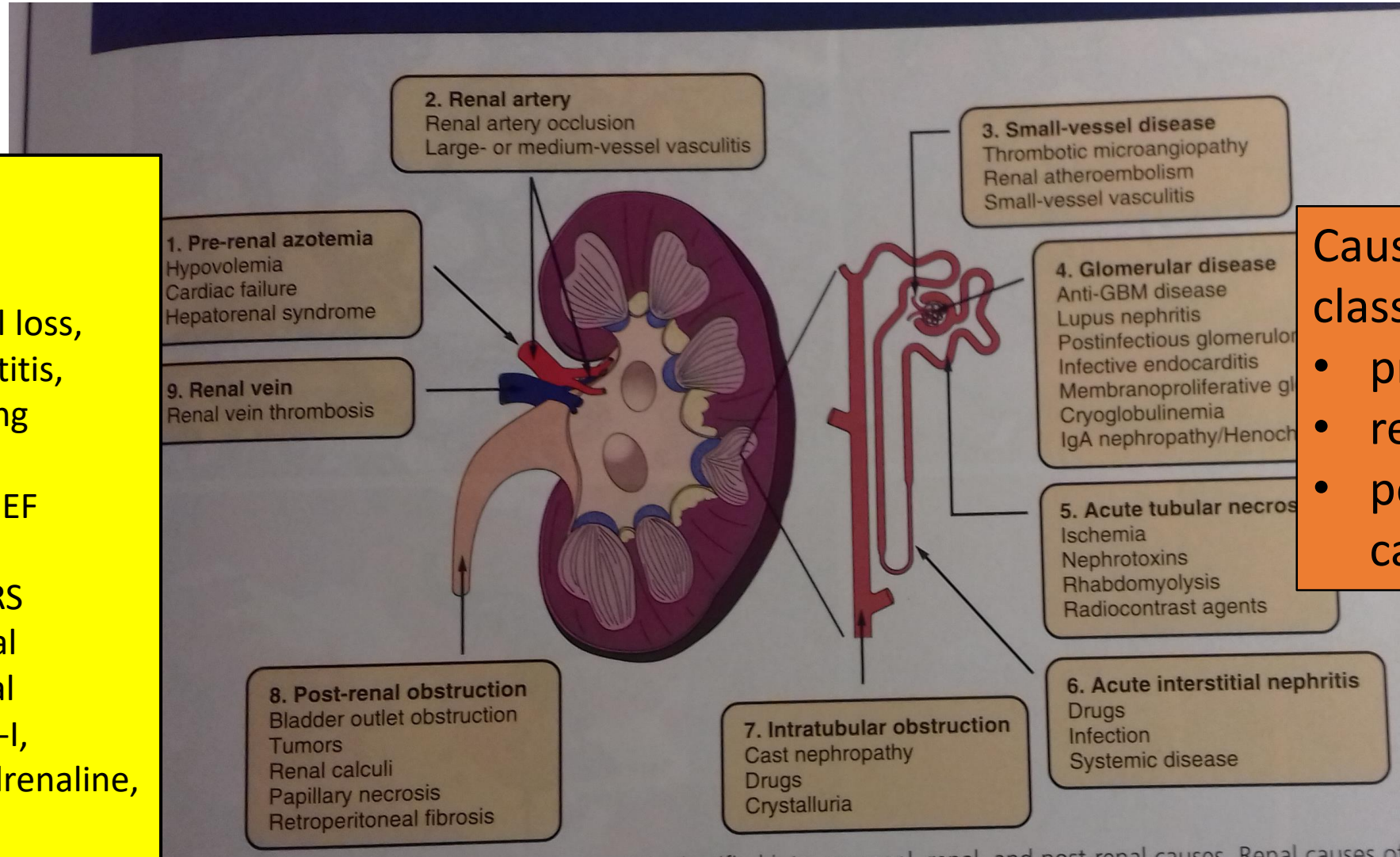
Table 3 | Comparison of RIFLE and AKIN criteria for diagnosis and classification of AKI

AKI staging	Urine output	RIFLE	
Serum creatinine	(common to both)	Class	Serum creatinine or GFR
Stage 1 Increase of more than or equal to 0.3 mg/dl (⩾26.5 μmol/l) or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 ml/kg/h for more than 6 hours	Risk	Increase in serum creatinine × 1.5 or GFR decrease >25%
Stage 2 Increased to more than 200% to 300% (>2- to 3-fold) from baseline	Less than 0.5 ml/kg per hour for more than 12 hours	Injury	Serum creatinine × 2 or GFR decreased >50%
Stage 3 Increased to more than 300% (>3-fold) from baseline, or more than or equal to 4.0 mg/dl (⩾354 μmol/l) with an acute increase of at least 0.5 mg/dl (44 μmol/l) or on RRT	Less than 0.3 ml/kg/h for 24 hours or anuria for 12 hours	Failure	Serum creatinine × 3, or serum creatinine >4 mg/dl (>354 μmol/l) with an acute rise >0.5 mg/dl (>44 μmol/l) or GFR decreased >75%
		Loss	Persistent acute renal failure=complete loss of kidney function >4 weeks
		End-stage kidney disease	ESRD >3 months

Note: For conversion of creatinine expressed in SI units to mg/dl, divide by 88.4. For both AKIN stage and RIFLE criteria, only one criterion (creatinine rise or urine output decline) needs to be fulfilled. Class is based on the worst of either GFR or urine output criteria. GFR decrease is calculated from the increase in serum creatinine above baseline. For AKIN, the increase in creatinine must occur in <48 hours. For RIFLE, AKI should be both abrupt (within 1–7 days) and sustained (more than 24 hours). When baseline creatinine is elevated, an abrupt rise of at least 0.5 mg/dl (44 μmol/l) to >4 mg/dl (>354 μmol/l) is sufficient for RIFLE class Failure (modified from Mehta *et al.*[23] and the report of the Acute Dialysis Quality Initiative consortium[22]).

AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; ESRD, end-stage renal disease; GFR, glomerular filtration rate; RIFLE, risk, injury, failure, loss, and end stage; RRT, renal replacement therapy. Reprinted from Endre ZH. Acute kidney injury: definitions and new paradigms. Adv Chronic Kidney Dis 2008; 15: 213–221 with permission from National Kidney Foundation[46]; accessed http://www.ackdjournal.org/article/S1548-5595(08)00049-9/fulltext

Pre-renal:
1. Hypovolemia
(GI loss, skin loss, renal loss, trauma, burn, pancreatitis, peritonitis, third-spacing sequestration)
2. Cardiac failure– low EF
3. Systemic arterial vasodilation-Sepsis, HRS
4. Disturbances of renal autoregulation (general anesthesia, COX-I, ACE-I, hypercalcemia, CNI, adrenaline, amphotericin B)
5. Renal artery thrombosis/stenosis



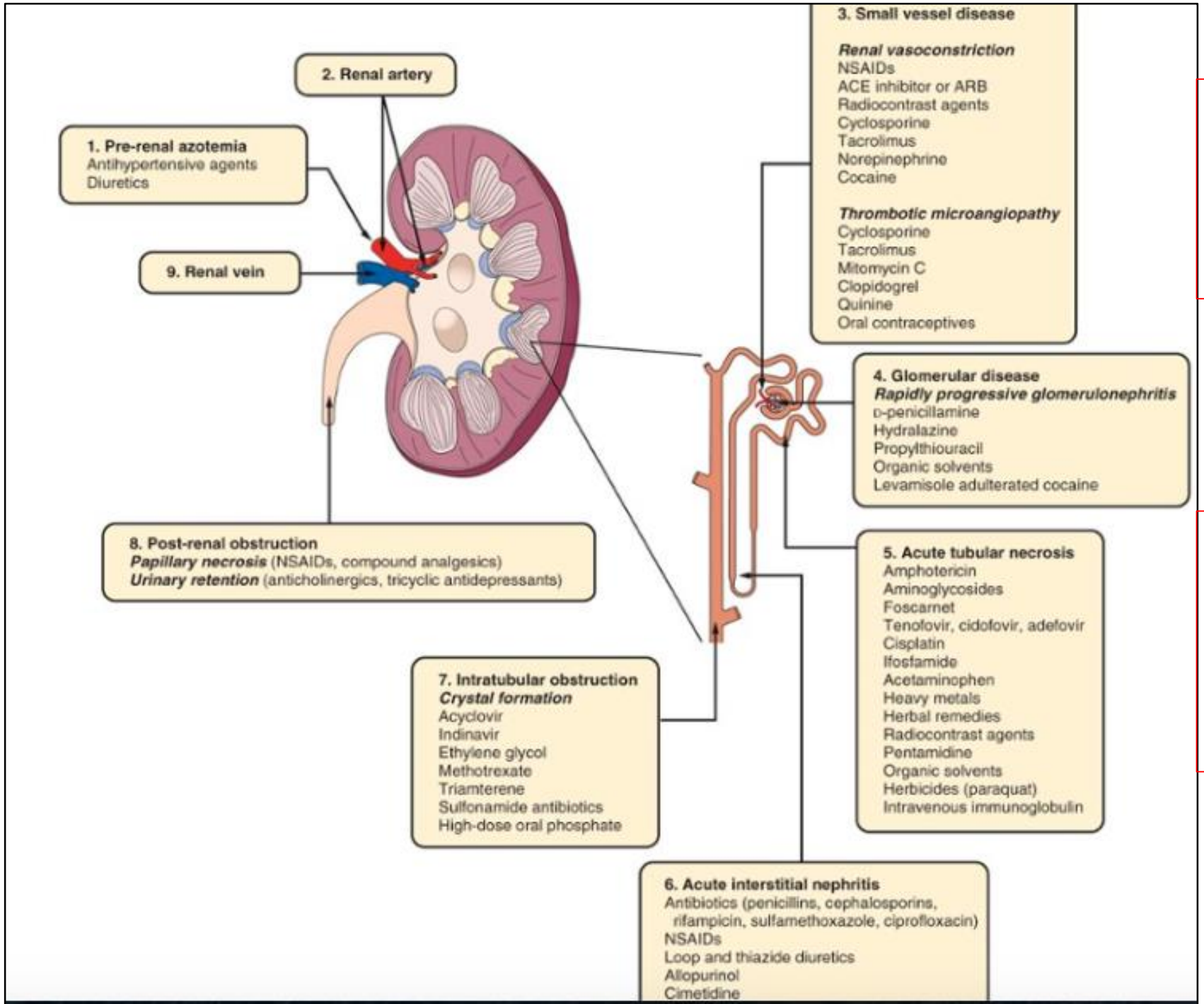
Causes of acute kidney injury (AKI). AKI is classified into pre-renal, renal, and post-renal causes. Renal causes of AKI should be conside
fferent anatomic components of the kidney (vascular supply; glomerular, tubular, and interstitial disease). *GBM,* Glomerular basem

forms of AKI are divided into intratubular and extrarenal. Tub

Causes of AKI are classified into
- pre-renal
- renal
- post-renal causes

TABLE 7-3 Major causes of extracellular fluid volume depletion

Major Causes of Extracellular Fluid Volume Depletion	
Renal	**Extrarenal**
Diuretic use	Gastrointestinal losses
Tubular disorders	Vomiting
Genetic	Gastrointestinal suctioning
Bartter and Gitelman syndromes	Diarrhea
Pseudohypoaldosteronism type 1	Ileostomy/colostomy secretions
Acquired tubular disorders	Dermal losses
Acute kidney injury	Sweat
Recovery phase of oliguric kidney injury	Exudative skin disease
Release of urinary tract obstruction	Third-space sequestration
Hormonal and metabolic disturbances	Ascites
Mineralocorticoid deficiency or resistance	Pleural effusion, hydrothorax
Primary adrenal insufficiency (Addison disease)	Intestinal obstruction
Hyporeninemic hypoaldosteronism	Retroperitoneal collection
Diabetes mellitus	Hemorrhage
Chronic interstitial renal diseases	Internal
Solute diuresis	External
Renal water loss	
Diabetes insipidus	

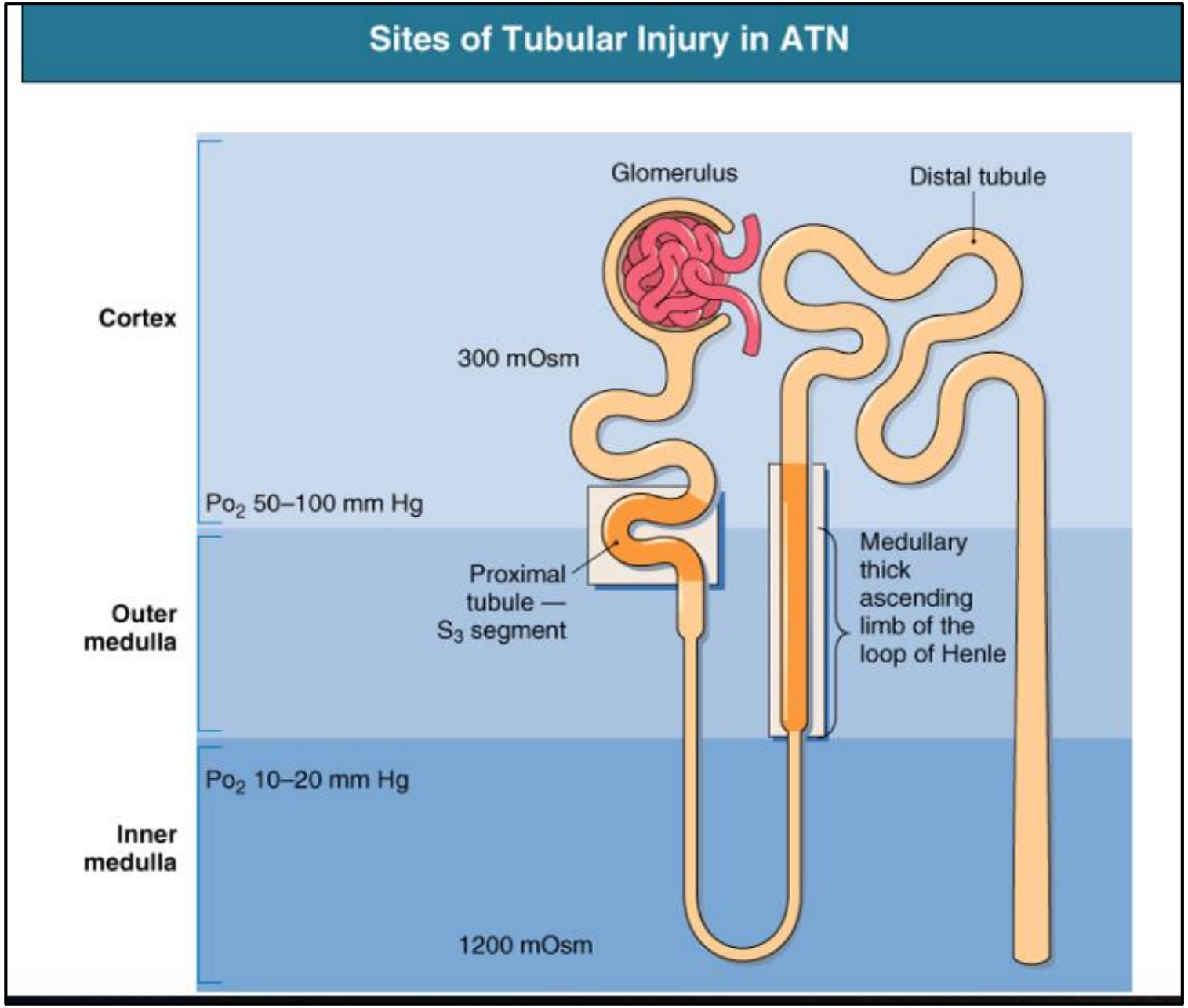


Autoregulation of renal perfusion
If systolic BP<80 mmHg

- RAAS
- Reflex stimulation of sympathetic nervous system

In renal hypoperfusion glomerular filtration pressure is maintained by

- afferent arteriolar vasodilatation (eicosanoids)
- efferent arteriolar vasoconstriction (AgII)



- Borderline oxygen supply/ high metabolic demand
- High tubular energy requirements
- Impaired renal autoregulation – ischemic injury

Ischemia+nephrotoxins=ATN

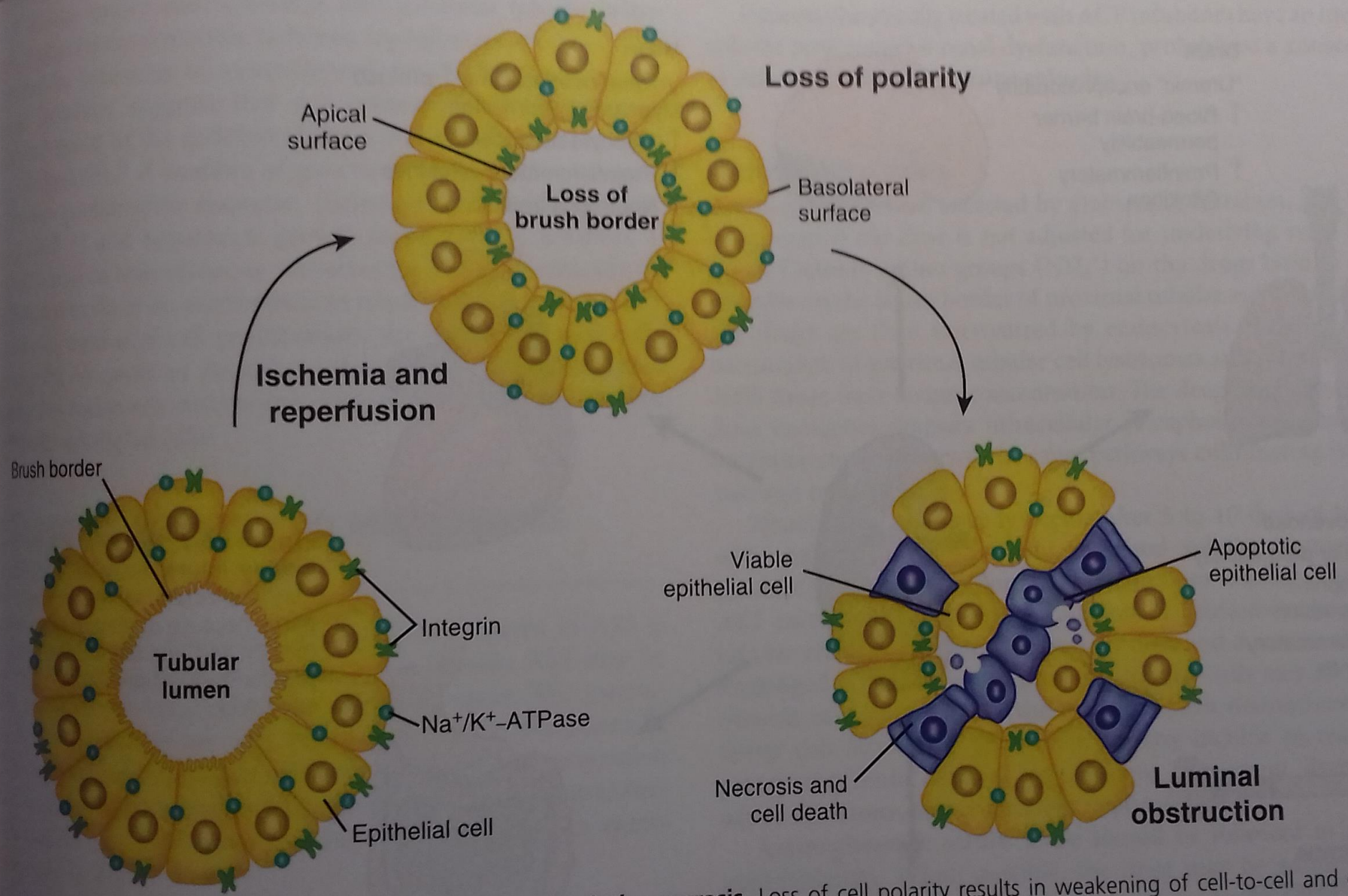


Figure 69-6 Tubular factors in the development of acute tubular necrosis. Loss of cell polarity results in weakening of cell-to-cell and cell matrix adhesion, resulting in cast obstruction and backleak of tubular fluid. *(Modified from reference 31.)*

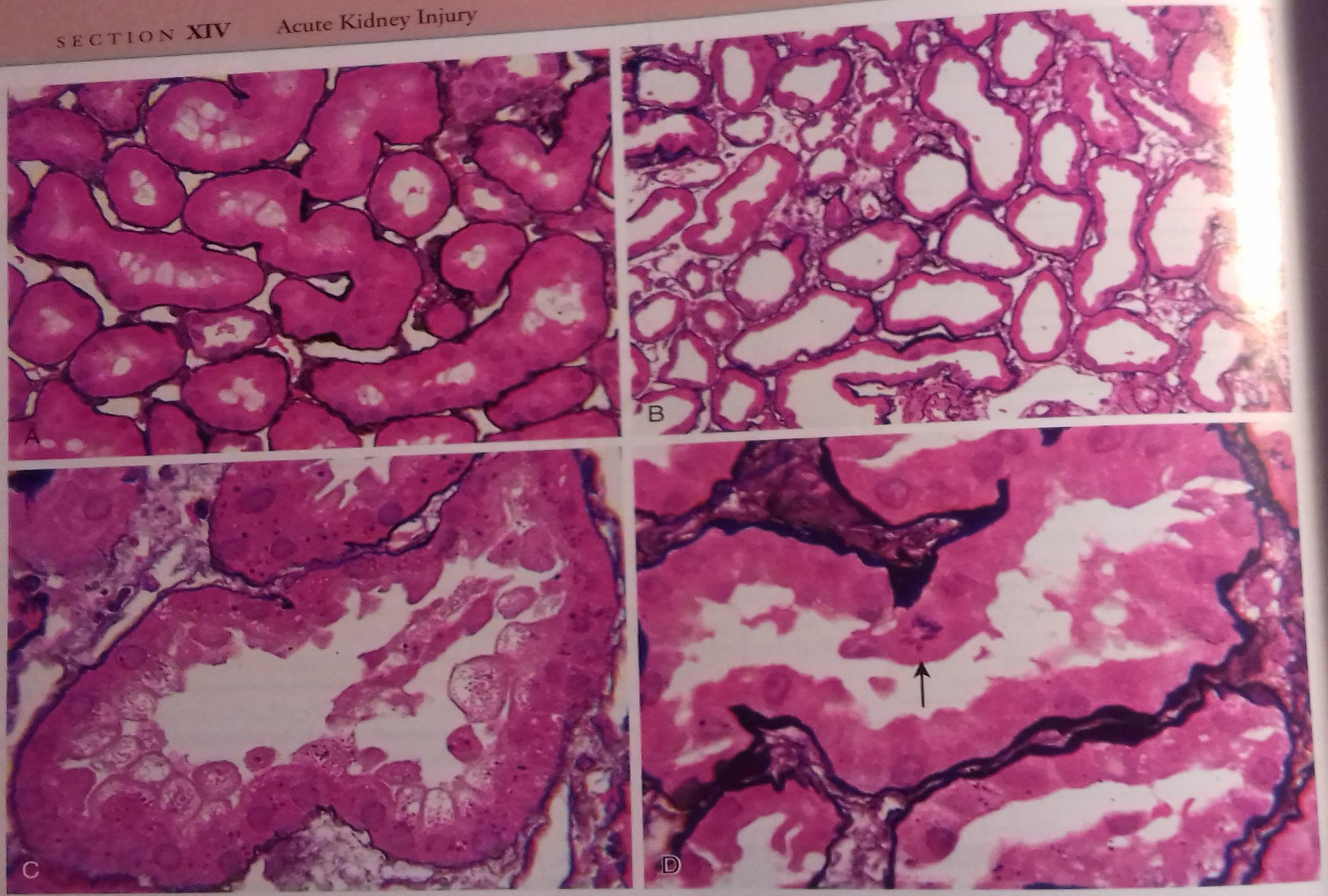
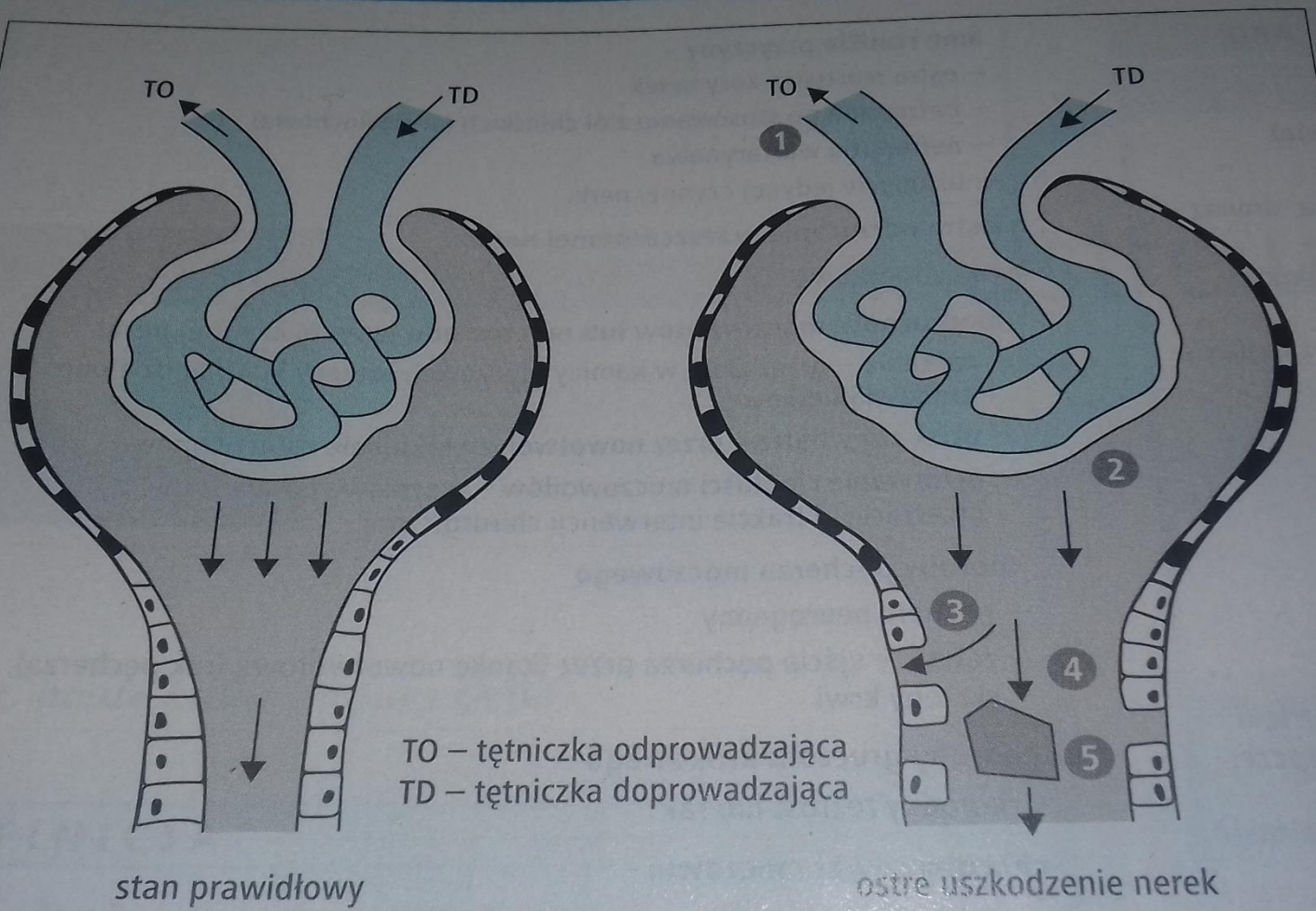


Figure 69-3 Renal pathology in acute tubular necrosis (ATN). A, Normal cortical renal tubules. **B** and **C,** ATN. Note the flattened epithelium, bare basement membranes, and intraluminal cellular debris. **D,** Recovering ATN showing a tubular epithelial cell mitotic figure *(arrow)*. *(Courtesy Erika Bracamonte, MD, University of Arizona.)*

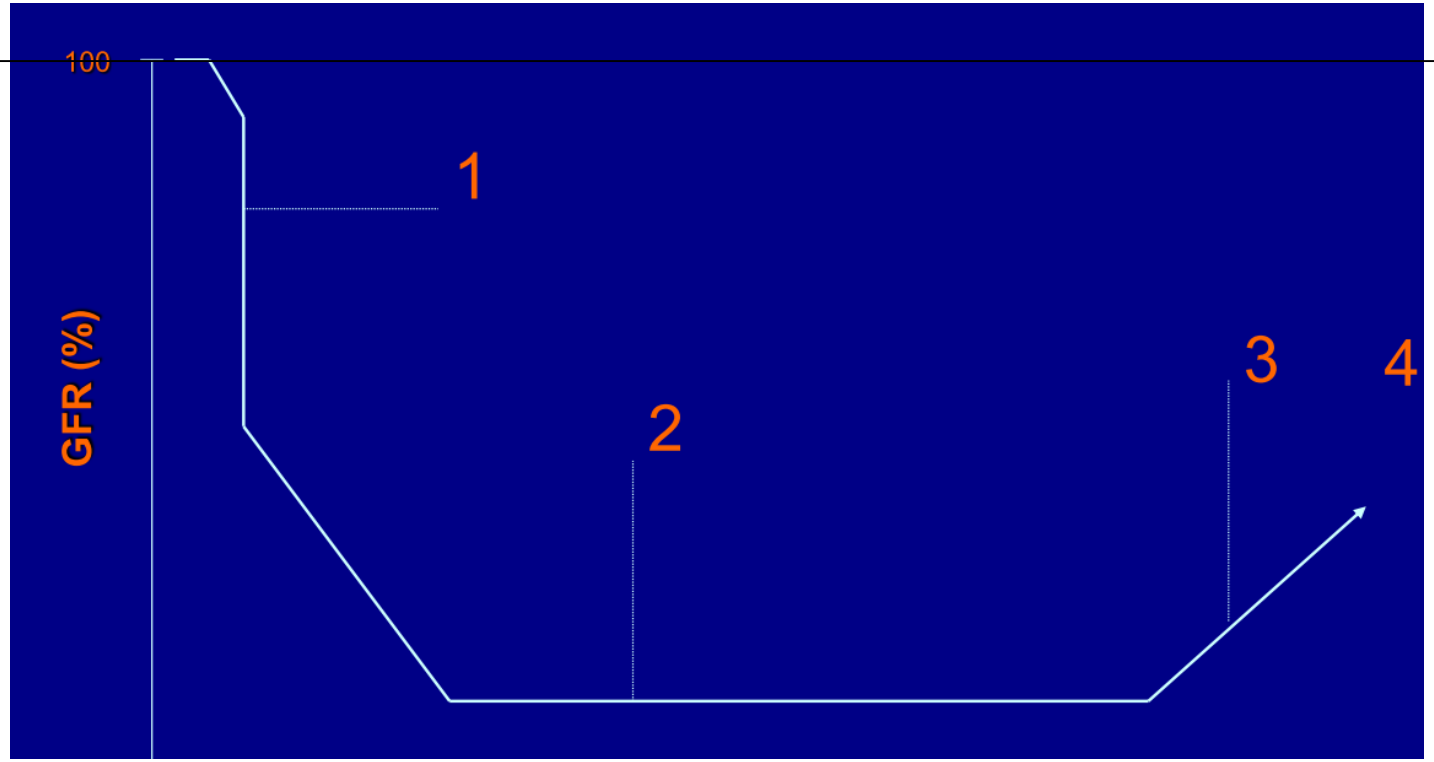


Ryc. V.C-1. Schemat mech
nych ostrego uszkodzenia
rzenie tętniczki odprowad
filtracyjnego w kłębuszk
szenie powierzchni filtru
wite wchłanianie zwrot
ki śródmiąższowej nerk
cewek nerkowych, 5 –
złuszczone komórki n

1. dilation of the efferent arteriole, decreased glomerular pressure
2. mesangial contraction, reduction of filtration surface
3. total filtrate reabsorption, interstitial edema
4. acute tutbular injury/necrosis
5. tubular obstruction, cellular debris, bare TBM

AKI- phases

1. preliminary phase – minutes or hours
2. anuria/oliguria - 10-14 days in 50%, the rest experience non-oliguric AKI. Parenchymal AKI- daily SCr increase 0,5-1 mg/dl
   if >2 mg/dl – catabolism, crush syndrome, rhabdomyolisis. Pre-renal AKI – SCr fluctuations depend on renal flow
3. polyuria – few weeks
4. recovery – few months



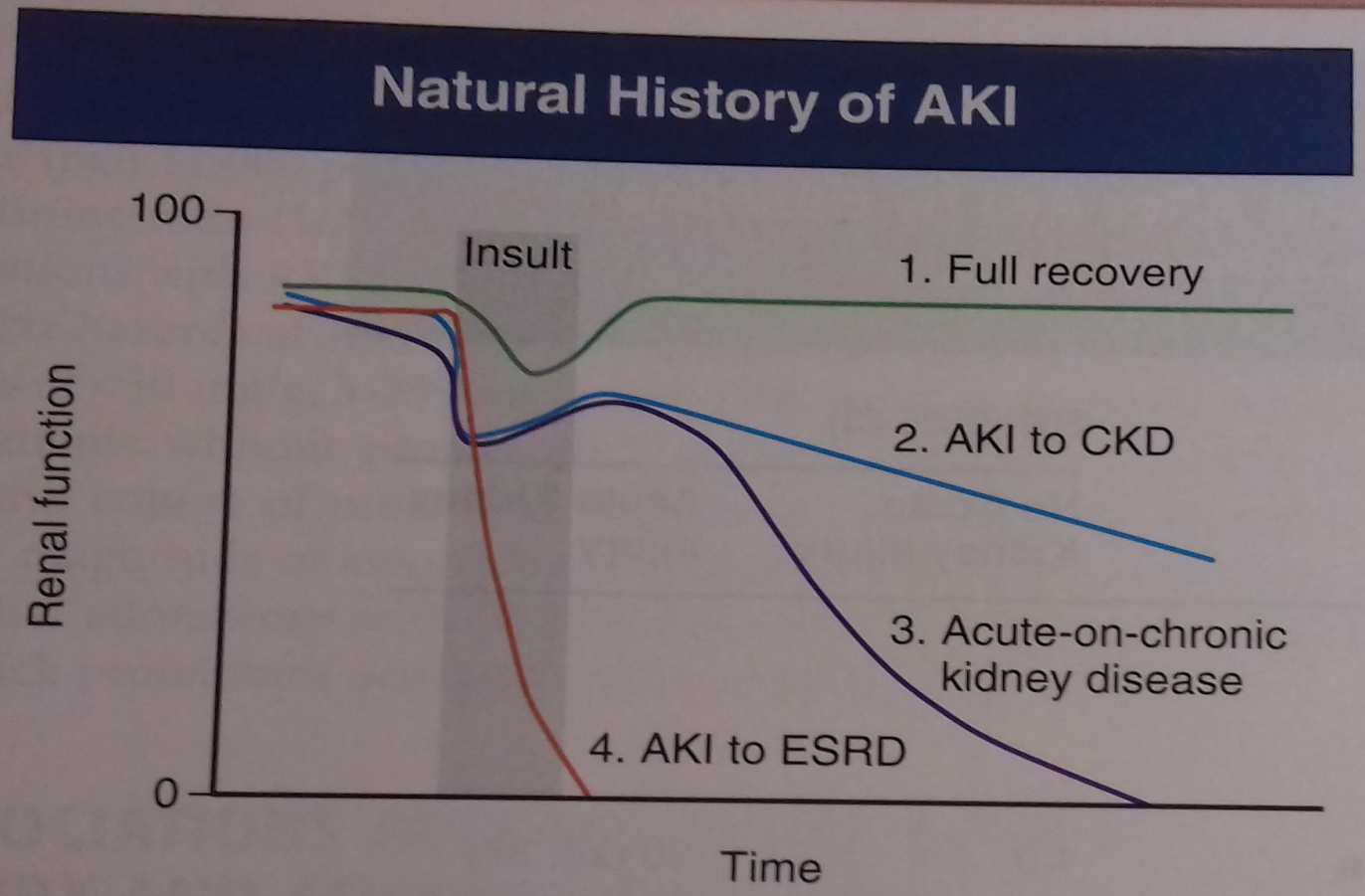


Figure 72-4 Natural history of acute kidney injury (AKI). Patients who develop AKI may experience (1) complete recovery of renal function, (2) development of progressive chronic kidney disease (CKD), (3) exacerbation of the rate of progression of preexisting CKD, or (4) irreversible loss of kidney function and evolution to end-stage renal disease (ESRD). *(From reference 21.)*

Health Care Costs

Most studies describing the
United States. A U.S. study
strated a direct relationship
hospital length of stay and
dl (26-μmol/l) increase in
incremental total hospitali
creatinine was associated
of specific populations o
ings; the average excess
surgery ranges from $90
In multivariable analysis,
tive complication for these
portion of resource use
Another study of 5875
necessitating dialysis was
complication, with an esti
tures of $28,359 compare
course, and resulted in al
a cardiac arrest. However
impact of CKD on AKI

Epidemiology of AKI

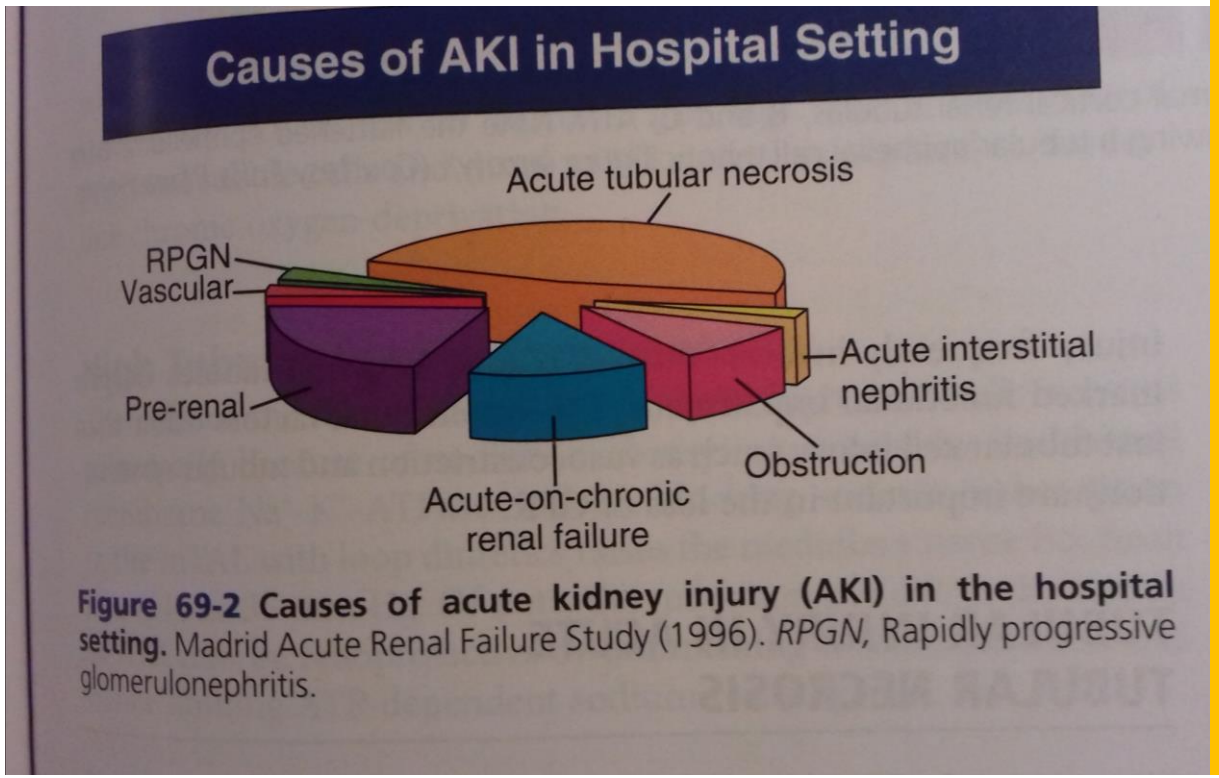


Figure 69-2 Causes of acute kidney injury (AKI) in the hospital setting. Madrid Acute Renal Failure Study (1996). *RPGN,* Rapidly progressive glomerulonephritis.

- The incidence of AKI 3000/mln/year
- 8% of medical pts
- 40% critically ill pts
- 50% connected to operations or trauma
- 10% pregnancy or childbirth
- mortality 20-50% (30%)
  - mostly due to comorbidities
  - 80% multiorgan failure

- 10% RRT
- 70% full recovery

AKI - symptoms

- Urine output – anuria<100ml/d
  oliguria<400ml/d in 50%

- 20% with polyuria! >2500ml/d

If GRF 10 ml/min =14l/24h of primary filtrate
If injured tubules reabsorb only half of it, urine output is preserved

AKI physical examination

- BP, HR, volume depletion
- Rash, purpura – vasculitis, immune complex disease, HUS, DIC, cryoglobulinemia
- Livedo reticularis – SLE
- Abdomen – acites, collateral circulation (*caput medusae*), spleen enlargement, liver cirrhosis - HRS

- Bladder enlargement in urine obstruction

Lab tests

- SCr, urea, electrolytes Na, K
- Urea acid >15mg/dl → gout or AKI
- CPK, LDH ↑ → rhabdomyolisis
  - ↑LDH→DIC, HUS
  - ↑aPTT, ↓fibrinogen, ↓PLT →DIC
  - thrombocytopenia if aPTT i PT normal → TMA
  - ↑PT→ liver disease
  - monoclonal protein, FLC → monoclonal gammapathy
  - ANA, ANCA, anty-GBM, APLA → autoimmune disease
  - C3, C4 → complement-mediated disease, immune complex

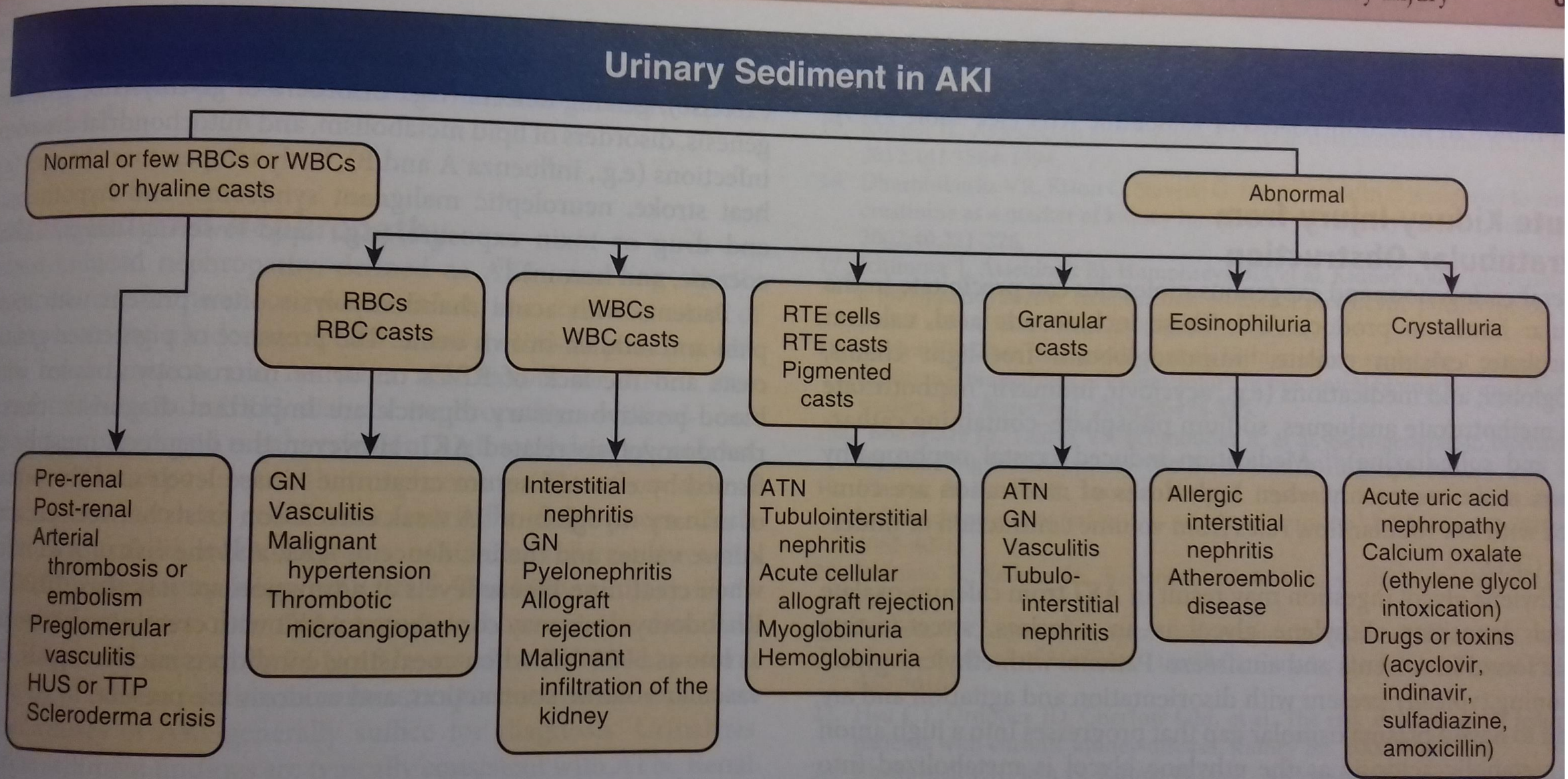


Figure 71-4 Urinary sediment in acute kidney injury (AKI). *ATN,* Acute tubular necrosis; *GN,* glomerulonephritis; *HUS,* hemolytic uremic syndro *RBC,* red blood cell; *RTE,* renal tubular epithelial; *TTP,* thrombotic thrombocytopenic purpura; *WBC,* white blood cell.

Lab test

- Urinalysis and urine microscopy – RBC and proteinuria
- Urine sediment – „muddy brown” granular casts, renal tubular epithelial cells indicated ATN-related AKI
- Urinary eosinophiles – are neither highly-sensitive nor specific, drug-induced AKI
- Uric acid cristals accompanying high serum phosphorus level – tumor lysis syndrome

Clinical and Laboratory Variables in the Differential Diagnosis Between Pre-renal and Renal Acute Kidney Injury (AKI)		
	Pre-renal	**Renal**
History	GI, urinary, skin volume loss, blood loss, or third spacing	Drugs or toxin exposure, hemodynamic change
Clinical presentation	Hypotension or volume depletion	No specific symptoms or signs
Laboratory studies		
BUN/S_{Cr}	>20	<20
Sediment	Normal to few casts	"Muddy brown" casts
U_{osm} (mmol/kg)	>500	<350
Proteinuria	None to trace	Mild to moderate
U_{Na} (mmol/l)	<20	>40
FE_{Na} (%)	<1	>1
FE_{Urea} (%)	<35	>35
Novel biomarkers	None	KIM-1, cystatin C, NGAL, CYR61, others

Fractional Excretion of Sodium and Urea

The urine-serum concentrations of sodium in relation to the urine-serum concentrations of creatinine (fractional excretion of sodium [FE_{Na}]) has been used to approximate renal tubular function:

$$\mathbf{FE_{Na}} = \frac{[\mathrm{U/S}]_{\mathbf{Na}}}{[\mathrm{U/S}]_{\mathbf{Cr}}} \times 100\,\%$$

where U = urine, S = serum, Na = sodium, and Cr = creatinine.

The basic premise is that renal tubular cells will reabsorb sodium in the pre-renal setting, whereas tubules damaged by ATN will not.[33] FE_{Na} below 1% is consistent with pre-renal AKI, and FE_{Na} above 3% is typical of ATN. However, many exceptions to these cutoffs have been discovered since FE_{Na} was first introduced into clinical practice in 1976. FE_{Na} may be less than 1% despite the presence of ATN in the setting of sepsis, hemoglobinuria or myoglobinuria, radiocontrast exposure, nonoliguria, heart failure, and advanced cirrhosis. Underlying CKD, diuretic use, recent intravenous fluid administration, glucosuria, bicarbonaturia, and salt-wasting disorders may be associated with elevated FE_{Na} despite the presence of pre-renal AKI.[33] Therefore FE_{Na} has significant limitations in the setting of hospital-acquired AKI, where confounders abound, yet may be helpful in differentiating pre-renal AKI from ATN in specific patient populations with oliguria. Urea reabsorption, primarily occurring in proximal tubules, is less affected by loop and thiazide diuretics, and the

Differential Diagnosis by Pathophysiologic Classification of Acute Kidney Injury (AKI)	
Cause	**Comments**
Pre-renal	30%-60% of AKI
Volume depletion	Renal losses, GI losses, hemorrhage
Decreased cardiac output	Right- or left-sided heart failure, cardiac tamponade
Systemic vasodilation	Sepsis, anaphylaxis, anesthetics
Afferent arteriolar vasoconstriction	NSAIDs, calcineurin inhibitors, radiocontrast, hepatorenal syndrome, hypercalcemia
Efferent arteriolar vasodilation	ACE inhibitors, ARBs
Intrinsic	Approximately 40% of AKI
Acute tubular injury	
Ischemic	
Nephrotoxic (drug)	Aminoglycosides, lithium, amphotericin, pentamidine, cisplatin, ifosfamide, radiocontrast
Nephrotoxic (pigment)	Rhabdomyolysis, intravascular hemolysis
Acute interstitial nephritis (AIN)	
Drug induced	Penicillins, cephalosporins, NSAIDs, PPIs, allopurinol, rifampin, sulfonamides
Infection related	Pyelonephritis, viral nephritides
Autoimmune diseases	Sjögren syndrome, sarcoidosis, SLE
Malignancy	Lymphoma, leukemia
Intratubular obstruction	
Paraprotein	Immunoglobulin light chains
Crystals	Acute phosphate nephropathy, tumor lysis syndrome, ethylene glycol, acyclovir, indinavir, methotrexate
Acute glomerulonephritis	Postinfectious, cryoglobulinemia, RPGN, SLE
Macrovascular	Increased renal vein pressure from increased intra-abdominal pressure, bilateral renal vein thrombosis, bilateral renal artery emboli
Microvascular	Atheroembolic disease, HUS, TTP, scleroderma renal crisis, malignant hypertension
Post-renal (Obstruction)	Approximately 10% of AKI
Intrinsic	Bilateral ureteral stones, bladder outlet obstruction (prostatic enlargement or blood clot), neurogenic bladder
Extrinsic	Retroperitoneal fibrosis, metastatic cancer

- Pre-renal – 30-60% of AKI
- Renal – 40% of AKI
- Post-renal – 10% of AKI

imaging – ultrasound renal biopsy

Box 6-1
Indications for renal biopsy

Indications for Renal Biopsy

Nephrotic Syndrome

Routinely indicated in adults
In prepubertal children, indicated only if clinical features atypical of minimal change disease

Acute Kidney Injury

Indicated if obstruction, reduced renal perfusion, and acute tubular necrosis have been ruled out

Systemic Disease with Renal Dysfunction

Indicated in patients with small-vessel vasculitis, anti–glomerular basement membrane disease, and systemic lupus
Indicated in patients with diabetes only if atypical features present

Non-nephrotic Proteinuria

Table 13 | Markers of kidney damage in AKD and CKD

Markers	AKD	CKD
Pathology	X	X
Urinary markers		
RBC/casts	X	X
WBC/casts	X	X
RTE/casts	X	X
Fine and coarse granular casts	X	X
Proteinuria	X	X
Blood markers (tubular syndromes)	X	X
Imaging		
Large kidneys	X	X
Small kidneys	—	X
Size discrepancy	—	X
Hydronephrosis	X	X
Cysts	X	X
Stones	X	X
History of kidney transplantation	—	X

Kidney damage is not required for diagnosis of AKI. In the presence of AKI, findings of kidney damage do not indicate a separate diagnosis of AKD.
AKD, acute kidney diseases and disorders; CKD, chronic kidney disease; RBC, red blood cells; RTE, renal tubular epithelial cells; WBC, white blood cells.

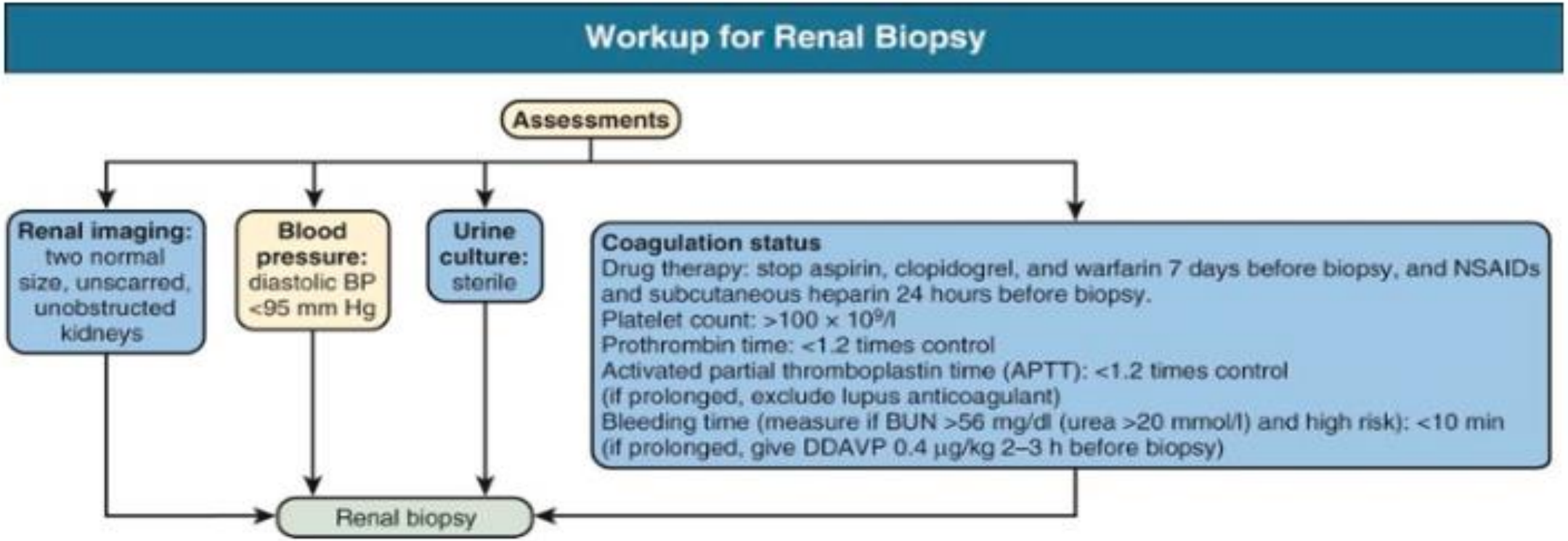


FIGURE 6-1 **Workup for renal biopsy.** *NSAID,* Nonsteroidal anti-inflammatory drug;...

An ultrasound scan should be performed to assess kidney size and to identify significant anatomic abnormalities, such as solitary kidney, polycystic or simple cystic kidneys, malpositioned kidneys, horseshoe kidneys, small kidneys, and hydronephrosis.

FLUIDS

3.1.1: In the absence of hemorrhagic shock, we suggest using isotonic crystalloids rather than colloids (albumin or starches) as initial management for expansion of intravascular volume in patients at risk for AKI or with AKI. (*2B*)

GLYCEMIC CONTROL IN CRITICAL ILLNESS: RENAL EFFECTS AND OUTCOMES

3.3.1: In critically ill patients, we suggest insulin therapy targeting plasma glucose 110–149 mg/dl (6.1–8.3 mmol/l). (*2C*)

3.4.1: We recommend not using diuretics to prevent AKI. (*1B*)

3.4.2: We suggest not using diuretics to treat AKI, except in the management of volume overload. (*2C*)

AKI – symptomatic treatment

- Remove reversible causes of AKI – urine obstruction, infection
- Fluid overload – water intake restrictions, diuretics, optimize volume status
- Fluid depletion – cristalloids than colloids, blood transfusion
- Metabolic acidosis
- Nurition

0.8-1g/kg of protein if not catabolic

total energy intake 20-30kcal/kg/day

AKI - treatment

- The best treatment is to prevent AKI

  (primary and secondary prevention)

TABLE 73-1 Major risk factors for AKI.

Major Risk Factors for Acute Kidney Injury (AKI)		
Patient Factors	**Medications and Agents**	**Procedures**
Older age (>75 years)	Nonsteroidal anti-inflammatory drugs	Cardiopulmonary bypass procedures
Diabetes	Cyclooxygenase-2 inhibitors	Surgery involving aortic clamp
Hepatic failure	Cyclosporine or tacrolimus	Increased intra-abdominal pressure
Chronic kidney disease	Angiotensin-converting enzyme inhibitors	Large arterial catheter placement with risk for atheroembolization
Atherosclerosis	Angiotensin receptor blockers	Liver transplantation
Renal artery stenosis	Iodinated contrast agents	Kidney transplantation
Hypertension	Hydroxyethyl starch (HES)	
Hypotension	Aminoglycosides	
Hypercalcemia	Amphotericin	
Sepsis		
Perioperative cardiac dysfunction		
Rhabdomyolysis		
Tumor lysis syndrome		

TABLE 73-2 Specific risk factors for the development of AKI in common clinical

Hyperkaliemia

ECG Changes in Hyperkalemia		
QRS Complex	Approximate Serum Potassium (mmol/l)	ECG Change
	4–5	Normal
	6–7	Peaked T waves
	7–8	Flattened P wave, prolonged PR interval, depressed ST segment, peaked T wave
	8–9	Atrial standstill, prolonged QRS duration, further peaking T waves
	>9	Sinusoid wave pattern

Electrocardiographic (ECG) changes in hyperkalemia. Progressive hyperk..

TABLE 9-5 Treatment of hyperkalemia

Treatment of Hyperkalemia				
Mechanism	**Therapy**	**Dose**	**Onset**	**Duration**
Antagonize membrane effects	Calcium	Calcium gluconate, 10% solution, 10 ml IV over 10 min	1-3 min	30-60 min
Cellular potassium uptake	Insulin	Regular insulin, 10 U IV, with dextrose 50%, 50 ml, if plasma glucose <250 mg/dl	30 min	4-6 hr
	β_2-Adrenergic agonist	Nebulized albuterol, 10 mg	30 min	2-4 hr
Potassium removal	Sodium polystyrene sulfonate or calcium polystyrene sulfonate (calcium resonium)	30-60 g PO in 20% sorbitol *or* 30-60 g in water, per retention enema	1-2 hr	4-6 hr
	Hemodialysis	—	Immediate	Until dialysis completed

Table 17 | Potential applications for RRT

Applications	Comments
Renal replacement	This is the traditional, prevailing approach based on utilization of RRT when there is little or no residual kidney function.
Life-threatening indications	No trials to validate these criteria.
Hyperkalemia	Dialysis for hyperkalemia is effective in removing potassium; however, it requires frequent monitoring of potassium levels and adjustment of concurrent medical management to prevent relapses.
Acidemia	Metabolic acidosis due to AKI is often aggravated by the underlying condition. Correction of metabolic acidosis with RRT in these conditions depends on the underlying disease process.
Pulmonary edema	RRT is often utilized to prevent the need for ventilatory support; however, it is equally important to manage pulmonary edema in ventilated patients.
Uremic complications (pericarditis, bleeding, etc.)	In contemporary practice it is rare to wait to initiate RRT in AKI patients until there are uremic complications.
Nonemergent indications	
Solute control	BUN reflects factors not directly associated with kidney function, such as catabolic rate and volume status. SCr is influenced by age, race, muscle mass, and catabolic rate, and by changes in its volume of distribution due to fluid administration or withdrawal.
Fluid removal	Fluid overload is an important determinant of the timing of RRT initiation.
Correction of acid-base abnormalities	No standard criteria for initiating dialysis exist.
Renal support	This approach is based on the utilization of RRT techniques as an adjunct to enhance kidney function, modify fluid balance, and control solute levels.
Volume control	Fluid overload is emerging as an important factor associated with, and possibly contributing to, adverse outcomes in AKI.
	Recent studies have shown potential benefits from extracorporeal fluid removal in CHF.
	Intraoperative fluid removal using modified ultrafiltration has been shown to improve outcomes in pediatric cardiac surgery patients.
Nutrition	Restricting volume administration in the setting of oliguric AKI may result in limited nutritional support and RRT allows better nutritional supplementation.
Drug delivery	RRT support can enhances the ability to administer drugs without concerns about concurrent fluid accumulation.
Regulation of acid-base and electrolyte status	Permissive hypercapnic acidosis in patients with lung injury can be corrected with RRT, without inducing fluid overload and hypernatremia.
Solute modulation	Changes in solute burden should be anticipated (e.g., tumor lysis syndrome). Although current evidence is unclear, studies are ongoing to assess the efficacy of RRT for cytokine manipulation in sepsis.

AKI, acute kidney injury; BUN, blood urea nitrogen; CHF, congestive heart failure; SCr, serum creatinine; RRT, renal replacement therapy.

Clinical indication:

- pulmonary odema refractory to diuretics
- Uremic encephalopathy
- Uremic diathesis
- Symptomatic fluid in pericardium
- Hipercatabolism
- Intoxication with substance removing during HD

Biochemical indication

- K>6.5 mmol/l
- Acidosis pH<7.2 HCO3<12 mmol/l
- Urea >200 mg/dl
- Na >155 mmol/l
  Na <120 mmol/l

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*)**

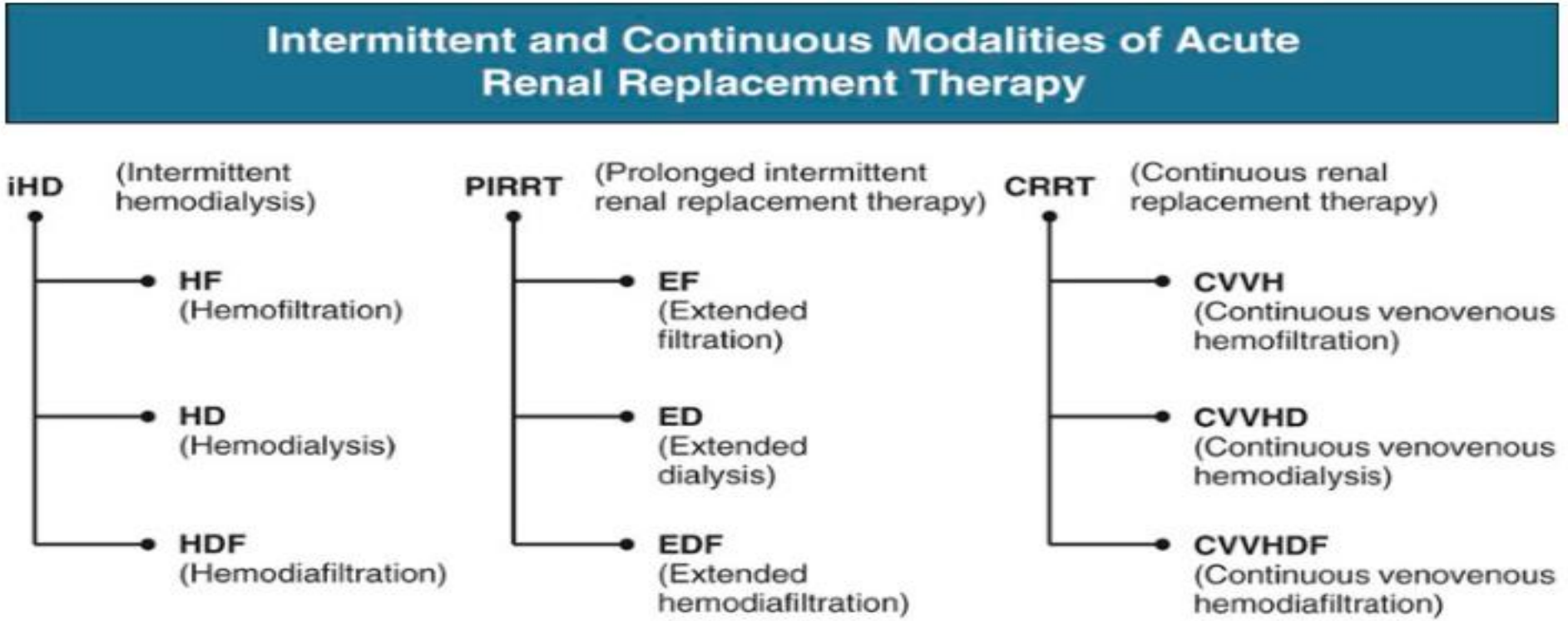


FIGURE 74-1 **Intermittent and continuous modalities of acute renal replacemen...**

Causes of Rhabdomyolysis	
Muscle injury, ischemia	Trauma, pressure necrosis, electric shock, burns, acute vascular disease
Myofiber exhaustion	Seizures, excessive exercise, heat exhaustion
Toxins	Alcohol, cocaine, heroin, amphetamines, ecstasy, phencyclidine, snakebite
Drugs	Statins, fibrates, zidovudine, neuroleptic malignant syndrome, azathioprine, theophylline, lithium, diuretics
Electrolyte disorders	Hypophosphatemia, hypokalemia, excess water shifts (hyperosmolarity)
Infections	Viral (influenza, human immunodeficiency virus [HIV], Coxsackievirus, Epstein-Barr virus), bacterial *(Legionella, Francisella, Streptococcus pneumoniae, Salmonella, Staphylococcus aureus)*
Familial	McArdle disease, carnitine palmitoyl transferase deficiency, malignant hyperthermia
Other	Hypothyroidism, polymyositis, dermatomyositis

Special settings

1. rhabdomyolysis
2. contrast-induced nephropathy
3. warfarin nephropathy
4. HRS
5. Sars-Cov-2-associated AKI

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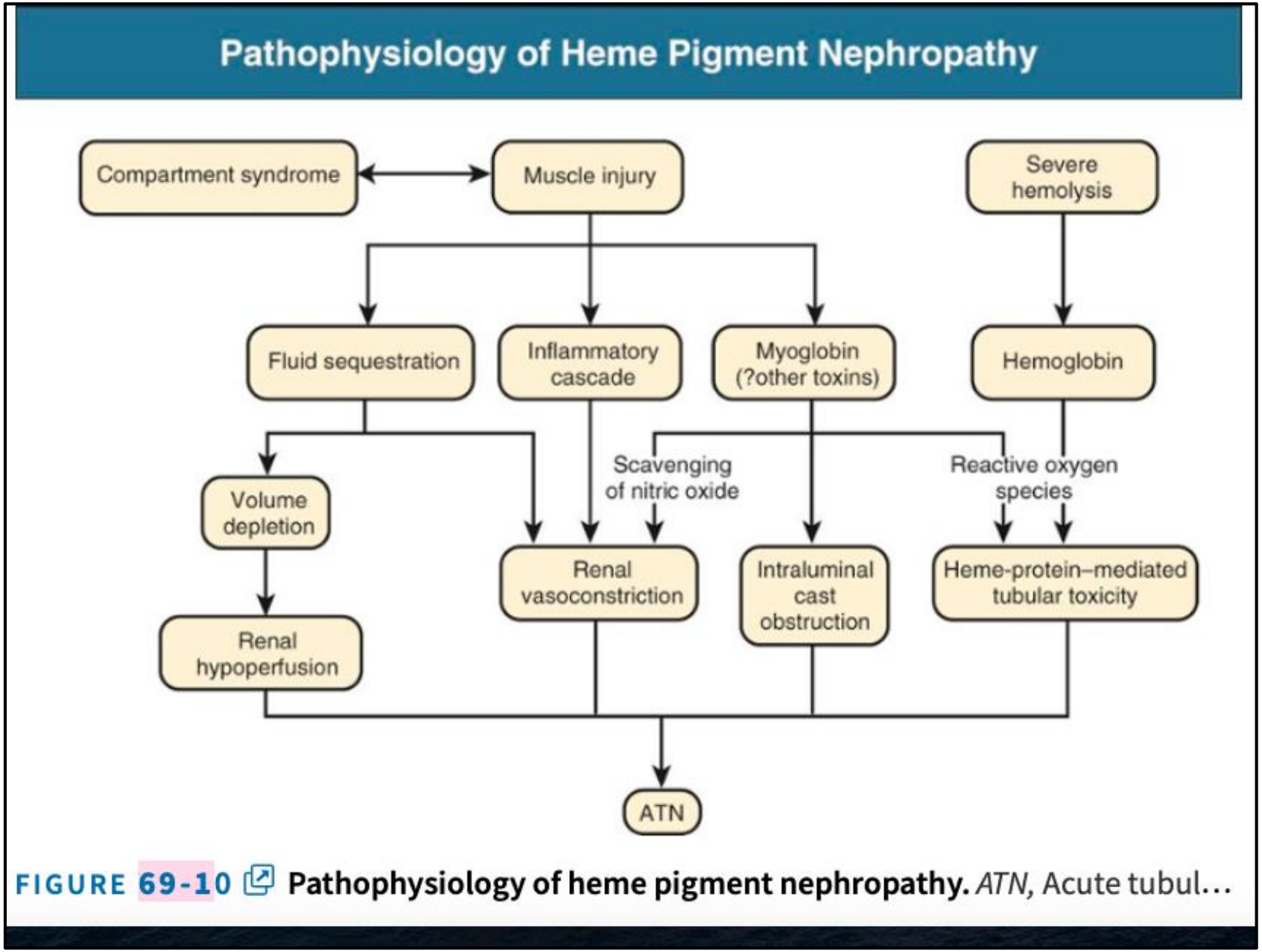

FIGURE 69-10 **Pathophysiology of heme pigment nephropathy.** *ATN,* Acute tubul…

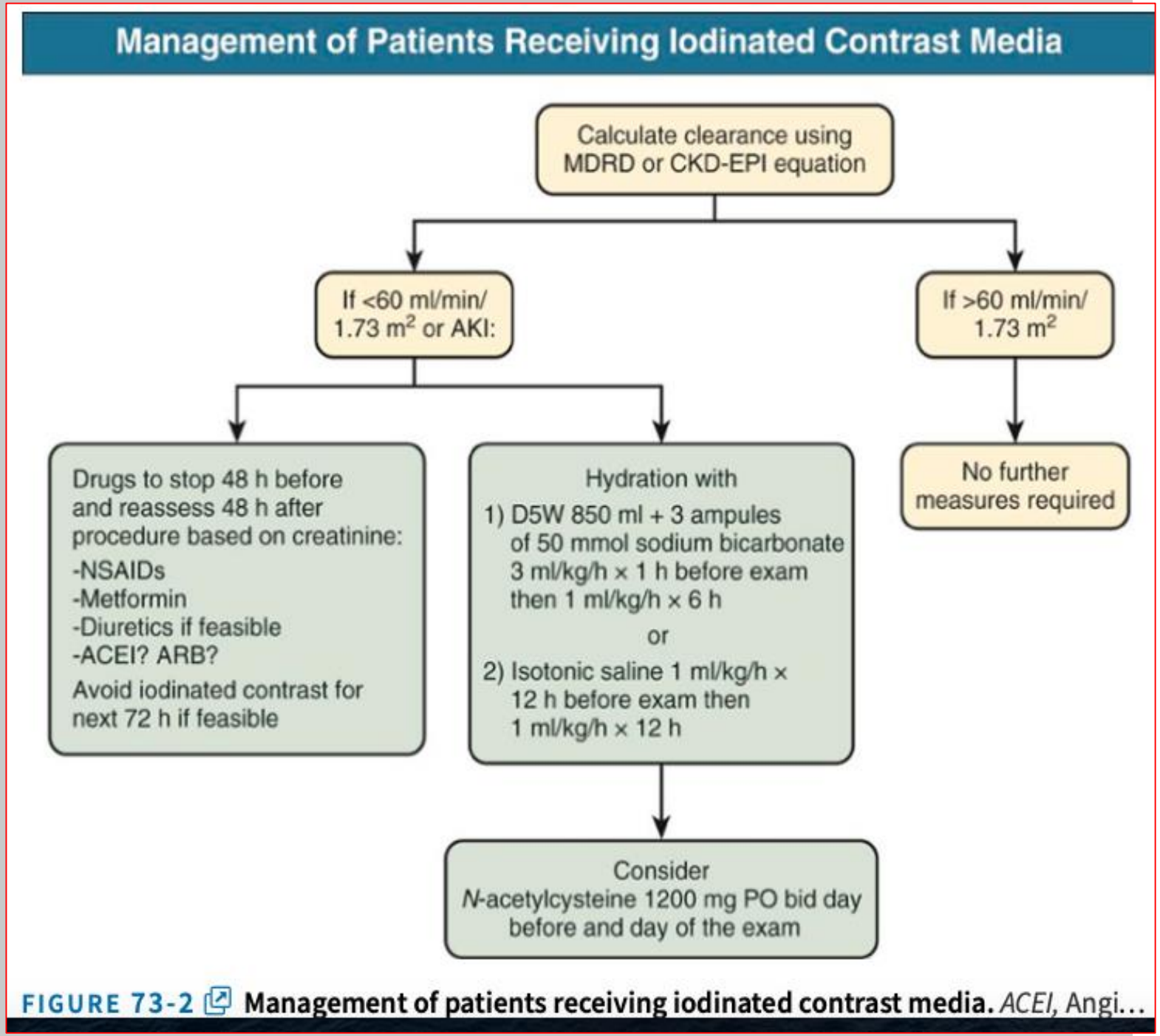

FIGURE 73-2 **Management of patients receiving iodinated contrast media.** *ACEI*, Angi…

CIN

SCr >0.5 mg/dl
or a 25% increase from baseline value assessed at 48h

The Society of Urogenital Radiology – same df but Scr changes within 72h

Management of acute kidney injury in patients with COVID-19

Claudio Ronco, Thiago Reis, Faeq Husain-Syed

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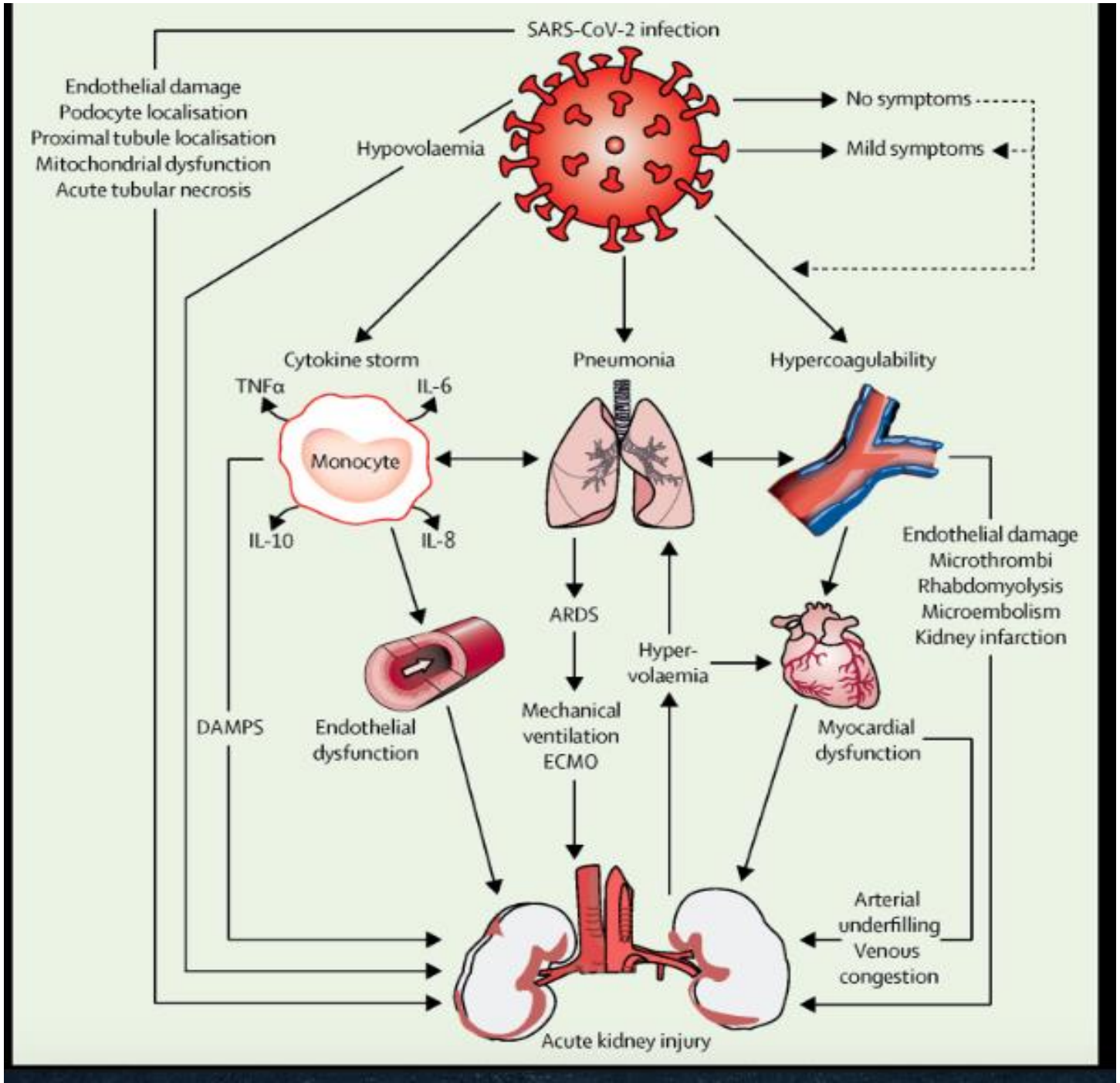
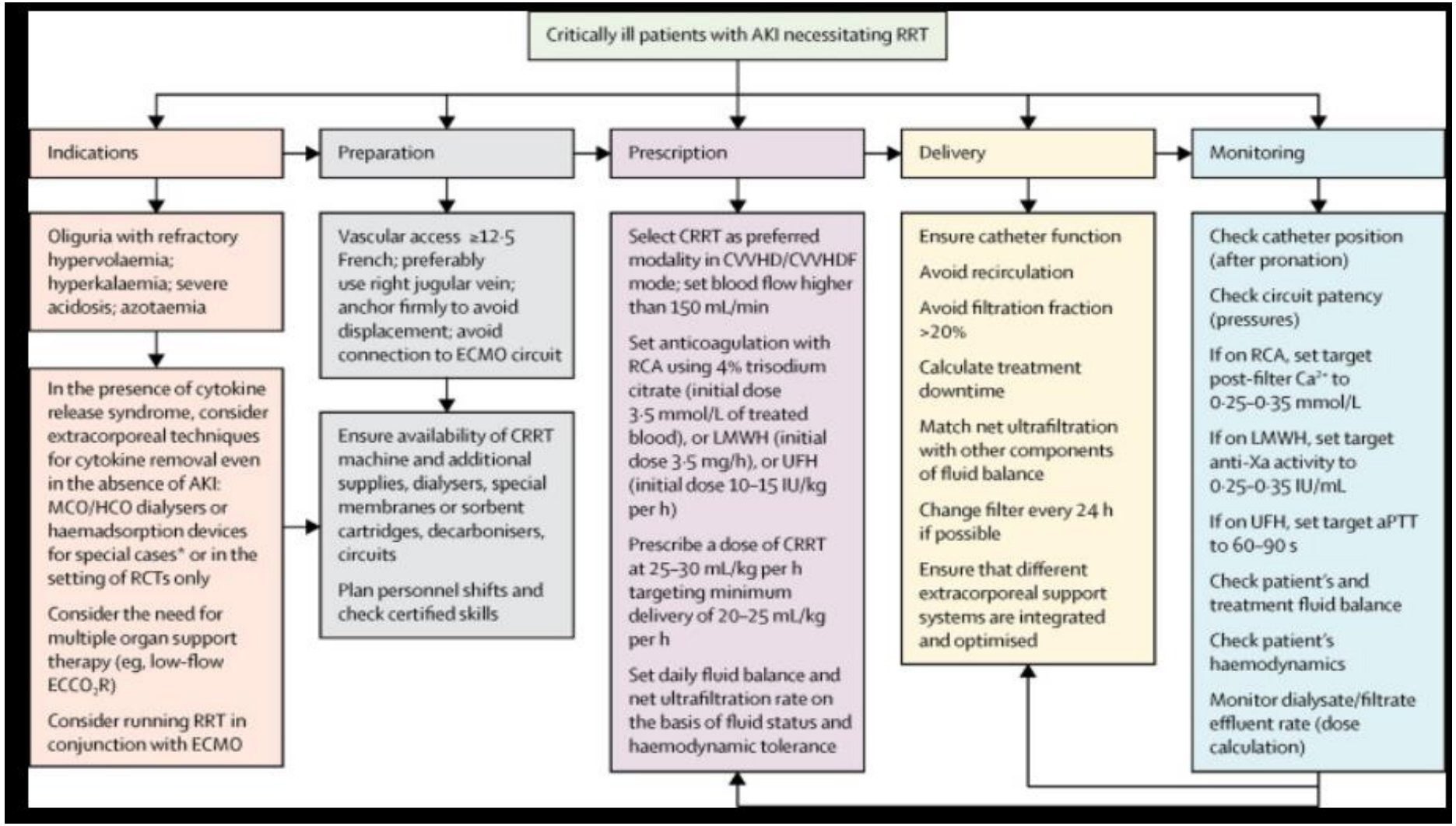
The outbreak of coronavirus disease 2019 (COVID-19) has rapidly evolved into a global pandemic. Most patients with COVID-19 have mild symptoms, but about 5% develop severe symptoms, which can include acute respiratory distress syndrome, septic shock, and multiple organ failure. Kidney involvement is frequent, with clinical presentation ranging from mild proteinuria to progressive acute kidney injury (AKI) necessitating renal replacement therapy (RRT). An understanding of the pathophysiology and mechanisms of kidney damage and AKI in the setting of critical illness and COVID-19 is emerging, although further research is needed to identify patients at risk of AKI and to guide management strategies. As no specific treatment options exist for AKI secondary to COVID-19, intensive care is largely supportive. Current approaches to prevention and management of AKI, and identification of potential indications for use of RRT and sequential extracorporeal therapies, are based mainly on clinical experience, and AKI strategies are adapted empirically to patients with COVID-19. International collaborative and cross-disciplinary research is needed to obtain adequate evidence to support current clinical approaches and to develop new approaches to management.

Introduction

As the global outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is rapidly evolving and expanding, its full spectrum of effects is becoming evident—from mild, self-limiting respiratory tract illness to severe acute respiratory distress syndrome (ARDS), multiple organ failure, and death.[1] Kidney involvement is frequent in COVID-19; >40% of cases have abnormal

Europe and the USA,[3,4] and it is considered a marker of disease severity and a negative prognostic factor for survival.[1,2] Furthermore, the overall burden of AKI in COVID-19 might be underestimated, as creatinine values at admission might not reflect true preadmission baseline kidney function, and previous serum creatinine values might not be readily available.[5] Around 20% of patients admitted to an intensive care unit (ICU) with COVID-19 require renal replacement therapy (RRT) at a median of


SARS-CoV-2 infection
Endothelial damage
Podocyte localisation
Proximal tubule localisation
Mitochondrial dysfunction
Acute tubular necrosis
Hypovolaemia
No symptoms
Mild symptoms
Cytokine storm
Pneumonia
Hypercoagulability
TNFα
IL-6
Monocyte
IL-10
IL-8
Endothelial damage
Microthrombi
Rhabdomyolysis
Microembolism
Kidney infarction
ARDS
Hyper-
volaemia
DAMPS
Endothelial
dysfunction
Mechanical
ventilation
ECMO
Myocardial
dysfunction
Arterial
underfilling
Venous
congestion
Acute kidney injury


Critically ill patients with AKI necessitating RRT
Indications
Preparation
Prescription
Delivery
Monitoring
Oliguria with refractory hypervolaemia; hyperkalaemia; severe acidosis; azotaemia
In the presence of cytokine release syndrome, consider extracorporeal techniques for cytokine removal even in the absence of AKI: MCO/HCO dialysers or haemadsorption devices for special cases* or in the setting of RCTs only
Consider the need for multiple organ support therapy (eg, low-flow $ECCO_2R$)
Consider running RRT in conjunction with ECMO
Vascular access ≥12·5 French; preferably use right jugular vein; anchor firmly to avoid displacement; avoid connection to ECMO circuit
Ensure availability of CRRT machine and additional supplies, dialysers, special membranes or sorbent cartridges, decarbonisers, circuits
Plan personnel shifts and check certified skills
Select CRRT as preferred modality in CVVHD/CVVHDF mode; set blood flow higher than 150 mL/min
Set anticoagulation with RCA using 4% trisodium citrate (initial dose 3·5 mmol/L of treated blood), or LMWH (initial dose 3·5 mg/h), or UFH (initial dose 10–15 IU/kg per h)
Prescribe a dose of CRRT at 25–30 mL/kg per h targeting minimum delivery of 20–25 mL/kg per h
Set daily fluid balance and net ultrafiltration rate on the basis of fluid status and haemodynamic tolerance
Ensure catheter function
Avoid recirculation
Avoid filtration fraction >20%
Calculate treatment downtime
Match net ultrafiltration with other components of fluid balance
Change filter every 24 h if possible
Ensure that different extracorporeal support systems are integrated and optimised
Check catheter position (after pronation)
Check circuit patency (pressures)
If on RCA, set target post-filter Ca^{2+} to 0·25–0·35 mmol/L
If on LMWH, set target anti-Xa activity to 0·25–0·35 IU/mL
If on UFH, set target aPTT to 60–90 s
Check patient's and treatment fluid balance
Check patient's haemodynamics
Monitor dialysate/filtrate effluent rate (dose calculation)