Acute Kidney Injury

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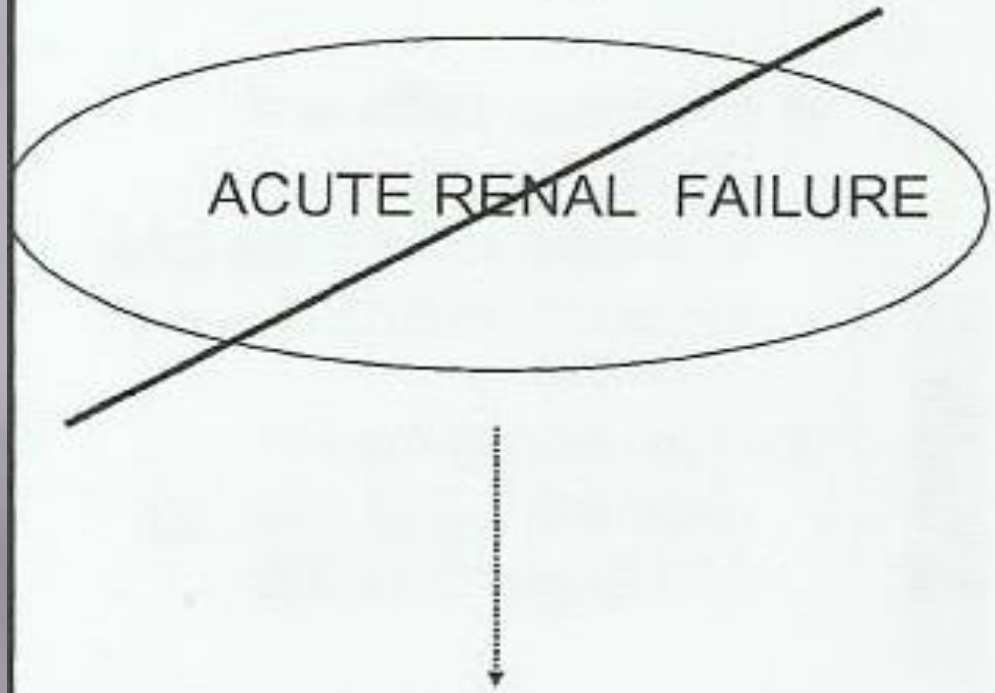
athens-NEPHROLOGY

Evolving terminology



ACUTE KIDNEY INJURY

- Experts from nephrology and intensive care: Acute Kidney Injury Network
- Consensus that term "ARF" needed updating in light of:
  - 'Failure' denotes severe dysfunction, fails to capture spectrum of condition
  - Injury short of failure (i.e., small increase in SCr) is clinically important

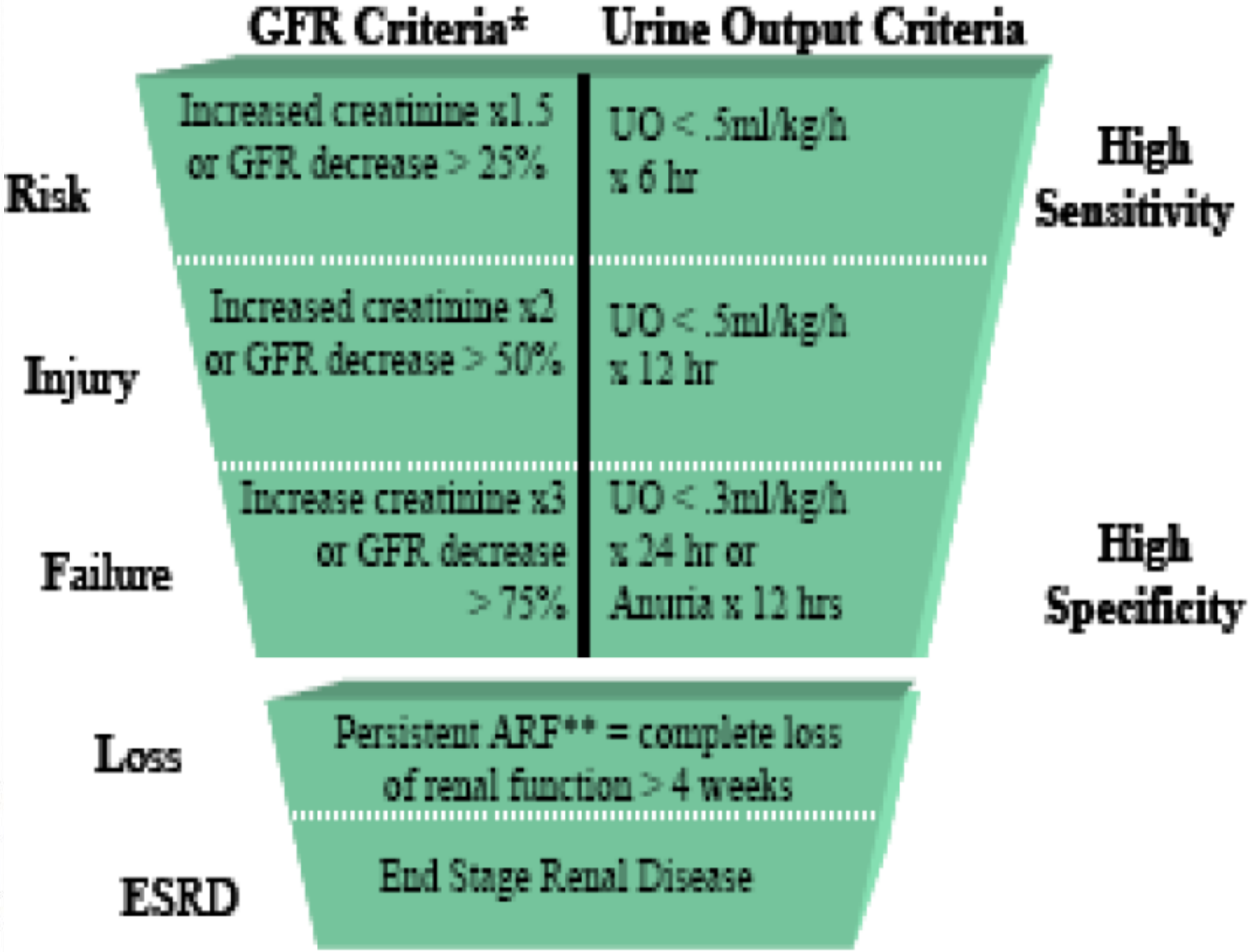
Definition Acute Renal failure (ARF)-Acute Kidney Injury (AKI)

- Inability of kidney to maintain homeostasis leading to a build up of nitrogenous wastes
- Different to renal insufficiency where kidney function is deranged but can still support life
- Exact biochemical/clinical definition not clear - 26 studies - no 2 used the same definition

AKI

- Occurs over hours/days
- Lab definition
  - Increase in baseline creatinine of more than 50%
  - Decrease in creatinine clearance of more than 50%
  - Deterioration in renal function requiring dialysis

RIFLE Criteria for Acute Renal Dysfunction



Acute kidney injury stages

AKI STAGE	Serum creatinine criteria	Urine output criteria
1	Increase in serum creatinine of 26 micromol/litre or more within 48 hours OR 1.5 to 2-fold increase from baseline	Less than 0.5 ml/kg/hour for more than 6 hours*
2	Increase in serum creatinine to more than 2 to 3-fold from baseline	Less than 0.5 ml/kg/hour for more than 12 hours
3	Increase in serum creatinine to more than 3-fold from baseline OR Serum creatinine more than 354 micromol/litre with an acute increase of at least 44 micromol/ litre	Less than 0.3 ml/kg/hour for 24 hours or anuria for 12 hours

* Urine output of less than 0.5 ml/kg/hour more than 8 hours in children and young people

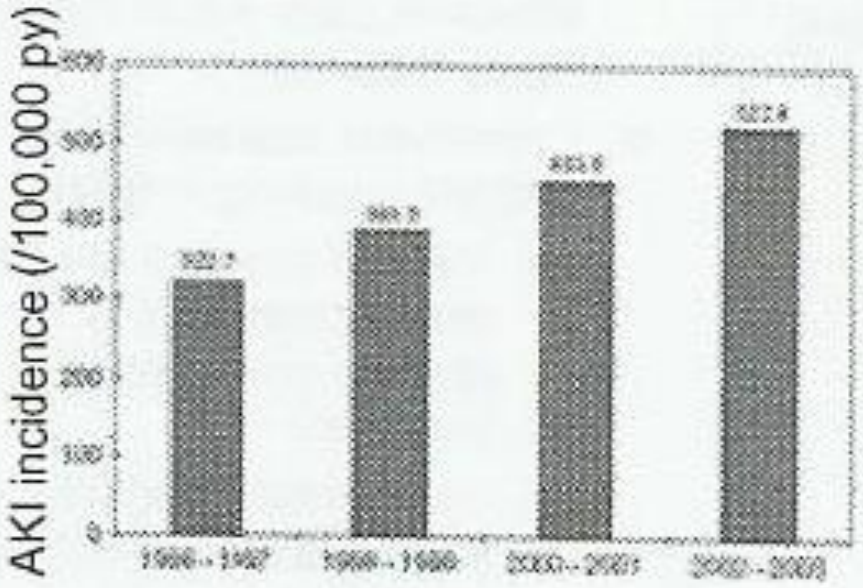
AKI definitions

- Anuria - no urine output or less than 100mls/24 hours.
- Oliguria - <500mls urine output/24 hours or <20mls/hour.
- Polyuria - >2.5L/24 hours.

Incidence of AKI

- Estimates depend entirely on definition, population being studied
  - 5 to 7% of hospital admissions (0.5, 1.0, or 1.5 mg/dL increase in SCr depending on baseline)
  - 1% of admissions from community-acquired AKI
  - Following CABG:
    - 15% of patients have a ≥ 25% increase in SCr
    - 1-2% require renal replacement therapy
  - Sepsis:
    - Doubling of SCr in 9% with SIRS, 51% with shock

Rising incidence of AKI



[1]Hsu *Kidney Int* 2007

- Between 1988 and 2002: Four-fold increase in AKI, six-fold increase in AKI-D (Waikar *JASN* 2006)
- Community-based estimate[1]: 522 AKI, 30 AKI-D per 100,000

Risk factors for AKI

- Best studied in cardiac catheterization and CABG
- Cardiac catheterization:
  - Age, higher SCr, CHF, diabetes
  - contrast volume, intra-aortic balloon pump
- CABG:
  - Age, higher SCr, CHF, diabetes, concomitant valve surgery
  - urgency of operation, bypass time

Clinical features of AKI

- BEST Kidney
  - Septic shock 48%
  - Major surgery 34%
  - Cardiogenic shock 27%
  - Hypovolemia 26%
  - Drug-induced 19%
  - Hepatorenal 6%
  - Obstructive uropathy 3%
  - Other 12%

Uchino *JAMA* 2005

- PICARD
  - ATN (unspecified) 50%
  - Drug-induced 26%
  - Sepsis 19%
  - Cardiac disease 20%
  - Hypotension 20%
  - Pre-renal 20%
  - Liver disease 11%

Mehta *Kidney Int* 2004

Predictors of dialysis in AKI

- PICARD
  - Age
  - Oliguria
  - High BUN
  - Liver failure

Small changes in SCr

- Recent reports suggest that even small increases in SCr increase risk of death
- Among ~10,000 inpatients[1]: increase in SCr of 0.3 or 0.4 mg/dL → 70% higher adjusted odds of death in hospital
- Following CABG[2]: 50% to 99% increase in SCr → 6.6-fold higher adjusted risk of death at 90d

[1]Chertow *JASN* 2005

[2]Brown *Circulation* 2006

Predictors of death in AKI

Results from multicenter observational studies

- BEST Kidney Invest.
  (Uchino JAMA 2005)
  - Overall mortality 60%
  - Age
  - Duration between admission and AKI
  - Mechanical ventilation
  - Vasopressor use
  - Sepsis
  - Cardiogenic shock
  - Hepatorenal syndrome
- PICARD
  (Chertow Kidney Int 2006)
  - Overall mortality 37%, over 60% for AKI-RRT
  - Age
  - Higher BUN
  - Liver failure
  - Sepsis
  - CKD stage IV: ***protective***

Community-acquired AKI

- 1% of hospital admissions
- Differs greatly from hospital-acquired:
  - 70% pre-renal azotemia
  - 17% obstruction
  - 11% intrinsic (mostly drug-induced, only 1 with ATN)

Kaufman *AJKD* 1991

AKI following cardiac surgery

- 1 – 2% AKI requiring RRT
- 15% less severe AKI (25% increase SCr)
- Major causes
  - Pre-renal azotemia (hypovolemia, overdiuresis, cardiac failure)
  - Intrinsic (ATN, atheroemboli, contrast, AIN from perioperative antibiotics)

AKI in pregnancy

- Marked reduction in incidence (industrialized world)
- Causes
  - Early pregnancy: pre-renal azotemia from hyperemesis gradivarum, ATN from septic abortion
  - Severe pre-eclampsia: usually preserved GFR unless severe bleeding, DIC, etc
  - TTP-HUS
    - Mid-pregnancy, peripartum, or postpartum
  - Cortical necrosis: anuria, gross hematuria, flank pain
    - Abruption, placenta previa, fetal death, amniotic fluid embolus
  - Acute fatty liver of pregnancy

Contrast nephropathy

- Incidence
  - Negligible following radiologic procedures in patients with normal SCr
  - 50% in pts with advanced CKD
  - Following PCI
    - ~3% overall (defined as 0.5 mg/dL increase)
    - 25% in patients with SCr > 2.0 mg/dL
    - Clear association with in-hospital and 5-yr mortality
- Risk factors: age, higher SCr, CHF, diabetes, contrast volume, intra-aortic balloon pump

AKI in bone marrow transplant

- Incidence (defined as 50% increase SCr)
  - Myeloablative allo > non-myeloablative allo > myeloablative auto (75% vs 40% vs 20%)
- Common causes in first 3 weeks
  - ATN from sepsis
  - Hepatic veno-occlusive disease
  - Nephrotoxins
  - Other: tumor lysis, thrombotic microangiopathy, CNI toxicity

Reviewed by Parikh *Kidney Int* 2006

AKI in cancer

- Tumor lysis syndrome
  - Most commonly in poorly differentiated lymphoma (e.g., Burkitt's)
  - ALL > AML
  - Also described in other solid tumors
- Multiple myeloma
  - Cast nephropathy
  - Hypercalcemia
  - Hyperuricemia
  - Contrast nephropathy
- Obstruction
  - Prostate, bladder, uterus, cervix
  - Absence of hydronephrosis in retroperitoneal tumors and retroperitoneal fibrosis

Reviewed by Humphreys *JASN* 2005

AKI and NSAIDs

- Hemodynamically mediated
  - Inhibition of prostaglandin synthesis → afferent arteriole vasoconstriction → GFR decline
  - Risk factors: CHF, cirrhosis, volume depletion, underlying CKD, diuretic therapy, age
  - COX-2 inhibitors have similar toxicity
- Acute tubulointerstitial disease
  - Fenoprofen, but all NSAIDs
  - Absence of fever, rash, eosinophilia is common
- Nephrotic syndrome
  - Mimimal change disease >> membranous nephropathy

AKI from other nephrotoxins

- Aminoglycoside antibiotics
  - Nearly 50% of patients treated > 14d; dose related
  - Proximal tubular injury
  - Typically nonoliguric AKI, slow onset
  - Recovery can take weeks, may be incomplete
- Cisplatin
  - Cumulative dose-related
  - Tubulointerstitial pattern without heavy proteinuria
  - 25% decline in GFR in 20-30% of patients
  - Incidence and severity increase with subsequent doses, may be irreversible
  - Nonoliguric; hypomagnesemia common
- Antivirals
  - Acyclovir: intratubular precipitation (U/A: needle shaped crystals)
  - Foscarnet: ATN
  - Tenofovir: ATN

Abdominal compartment syndrome

- Increased intra-abdominal pressure can lead to dysfunction of several organs
  - Cardiac, pulmonary, renal, GI, CNS
  - Abdominal pressure > 25
- Most common settings
  - Volume resuscitation for trauma
  - Post-laparotomy
  - Pancreatitis
  - Peritonitis
- Increased renal venous pressure
- Suspect in: tense abdomen, oliguria, azotemia

Del Giudice et al., J Nephrol Therapeut 2012, 2:6
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Nephrology & Therapeutics

Review Article Open Access

Acute Kidney Injury in the Elderly: Epidemiology, Risk Factors and Outcomes

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Parenchyma: reduced total mass

Glomeruli: decreased epithelial cells, increased mesangial cells, sclerosis

Afferent arterioles: hyalinosis

Glomerular capillaries: atrophy

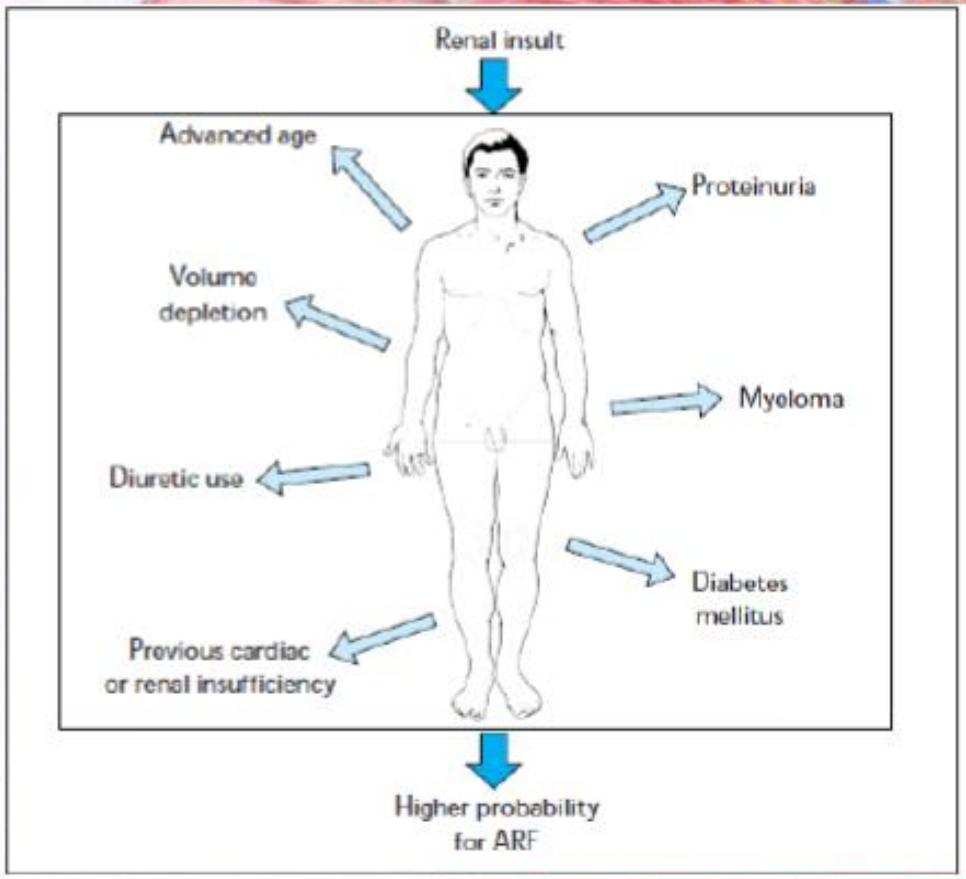
Proximal tubules: decreased number and length

Distal tubules: diverticula and cysts

Interstitium: fibrosis

Arterial vessels: atherosclerosis and constriction

Box 1: Structural changes occurring in aging kidney [10].



Acute Renal Failure: Causes and Prognosis

Fernando Liaño
Julio Pascual

Risk factors in adults having surgery or iodinated contrast agents

Risk factor	Surgery	Iodinated contrast agents
Age	Age 65 years or over	Age 75 years or over
CKD	CKD with eGFR <60	CKD with eGFR <40
Diabetes	Yes	Yes, if also has CKD
Heart failure	Yes	Yes
Hypovolaemia	Yes, especially if acutely unwell	Yes
Other conditions	Liver disease	Renal transplant
Clinical treatments or drugs	a) Emergency surgery, especially if patient has sepsis or hypovolaemia b) Nephrotoxic drugs in the perioperative period c) Intraperitoneal surgery	Increased volumes of contrast agent Intra-arterial route

REVIEW ARTICLE

JIACM 2011; 12(4): 290-6

Acute renal failure in the elderly

SC Dash*, D Bhowmik**

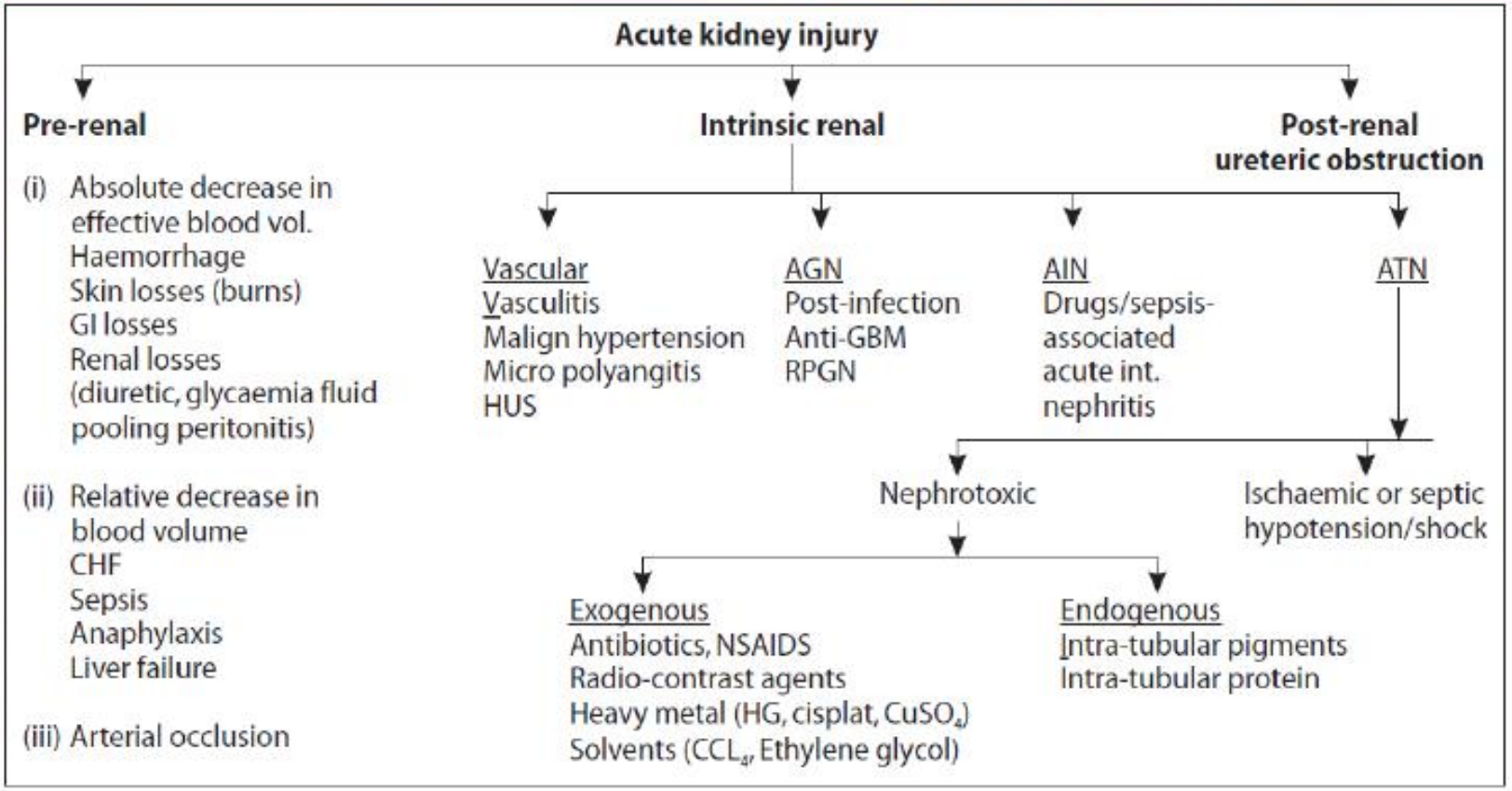
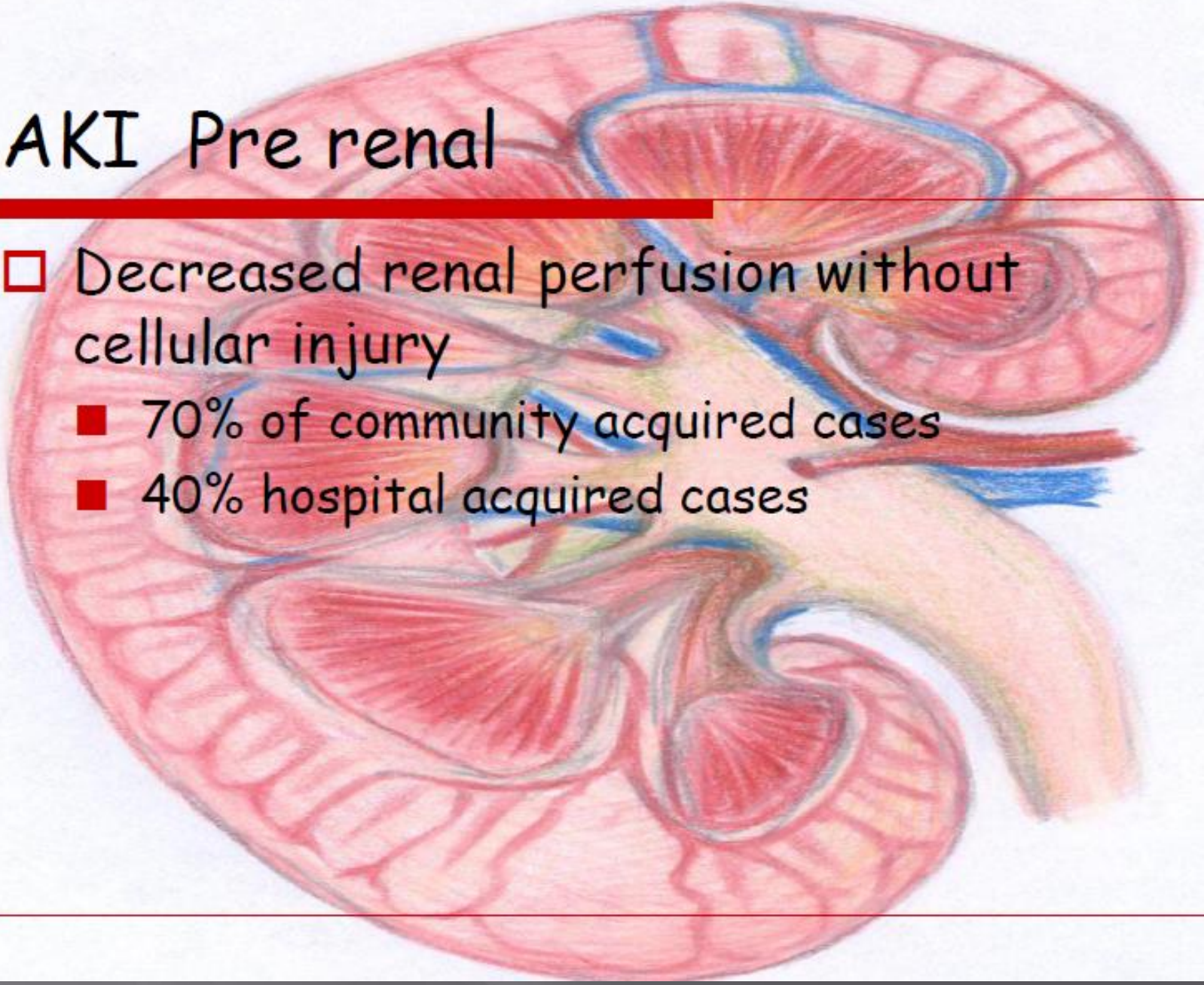


Fig. 1: *Acute kidney injury.*

AKI Pre renal

- Decreased renal perfusion without cellular injury
  - 70% of community acquired cases
  - 40% hospital acquired cases

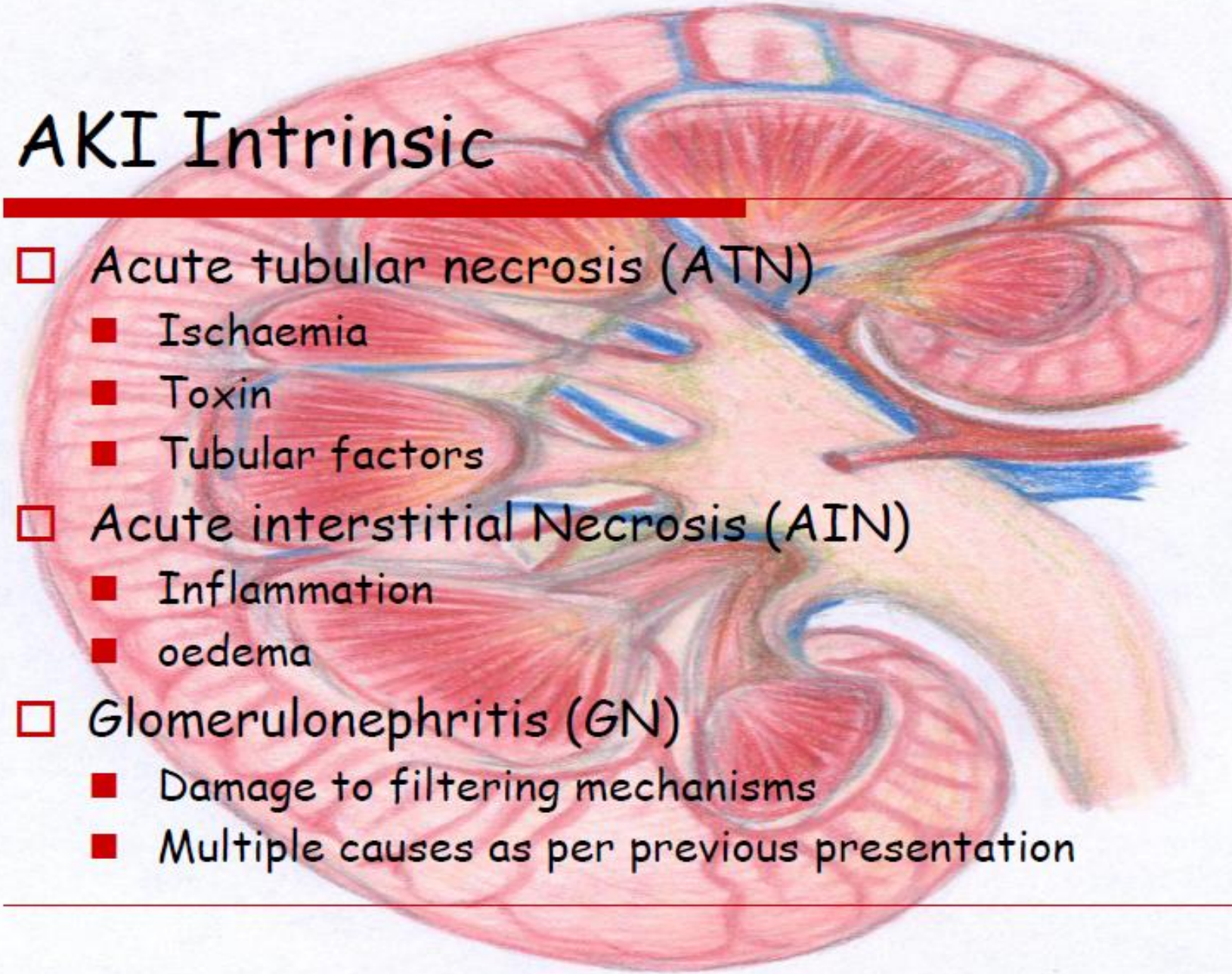


Prerenal

- Often rapidly reversible if we can identify this early
- The elderly at high risk because of their predisposition to hypovolemia and renal atherosclerotic disease
- This is by definition rapidly reversible upon the restoration of renal blood flow and glomerular perfusion pressure
- THE KIDNEYS ARE NORMAL
- This will accompany any disease that involves hypovolemia, low cardiac output, systemic dilation, or selective intrarenal vasoconstriction

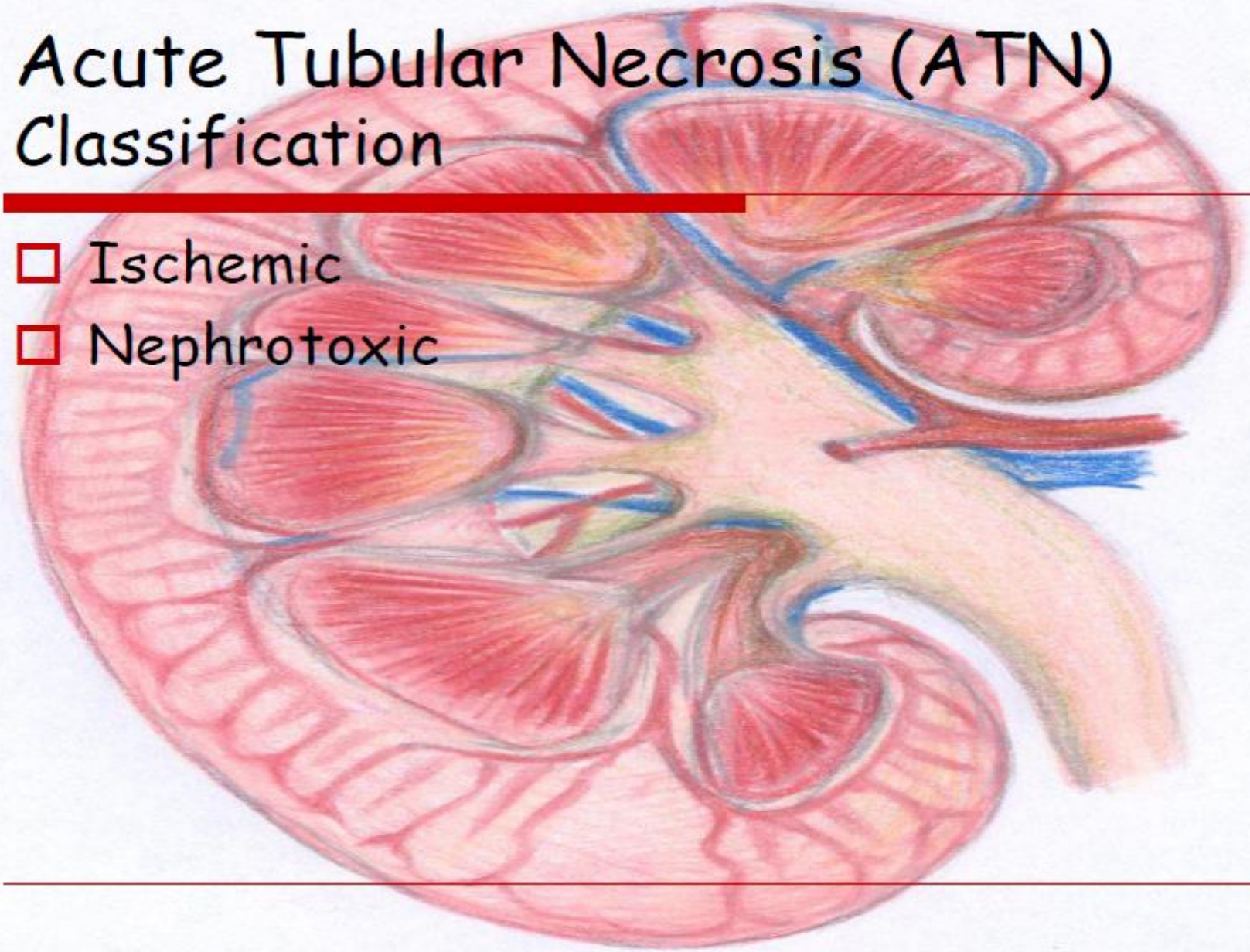
AKI Intrinsic

- Acute tubular necrosis (ATN)
  - Ischaemia
  - Toxin
  - Tubular factors
- Acute interstitial Necrosis (AIN)
  - Inflammation
  - oedema
- Glomerulonephritis (GN)
  - Damage to filtering mechanisms
  - Multiple causes as per previous presentation



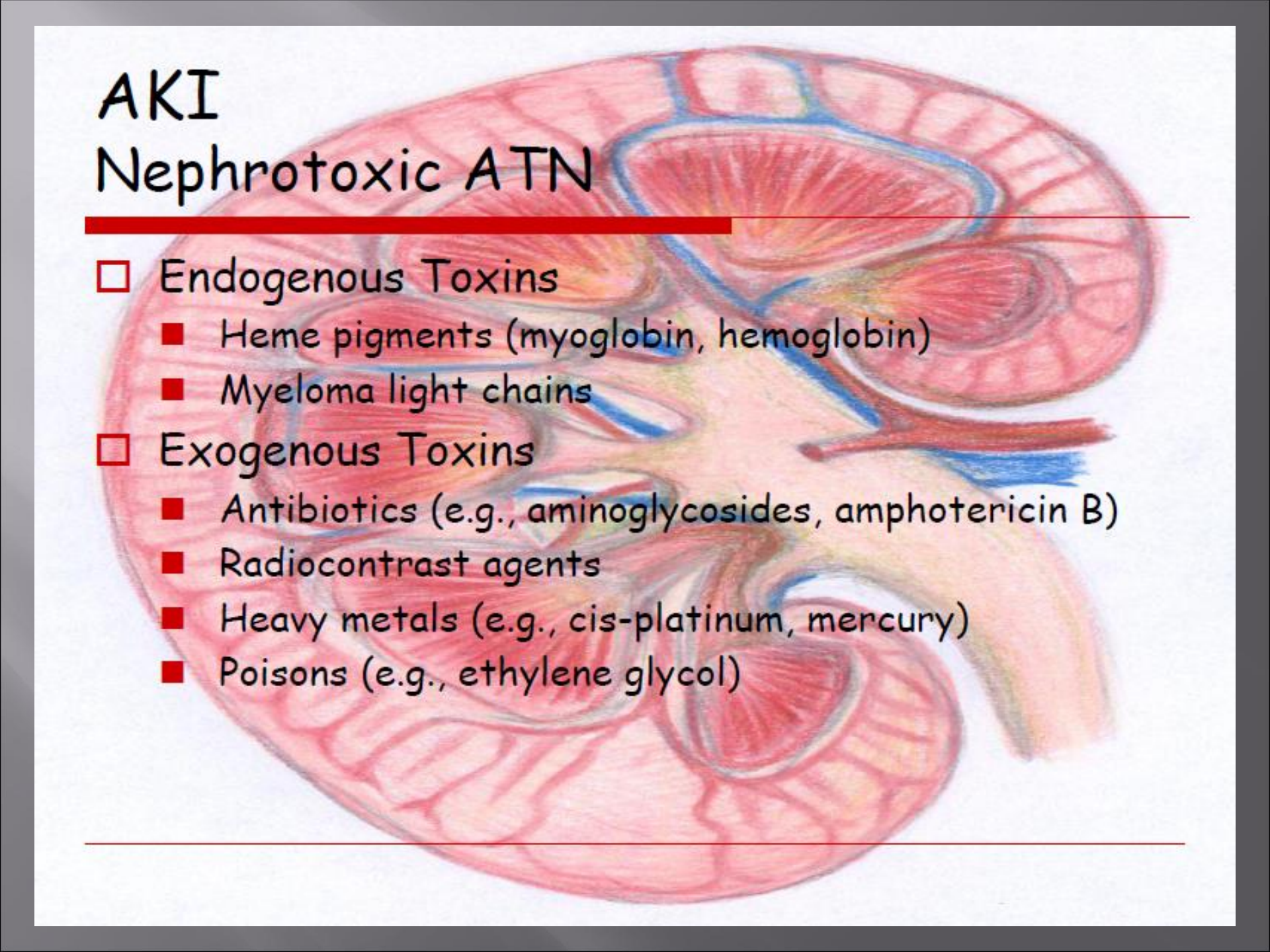
Acute Tubular Necrosis (ATN)
Classification

- Ischemic
- Nephrotoxic

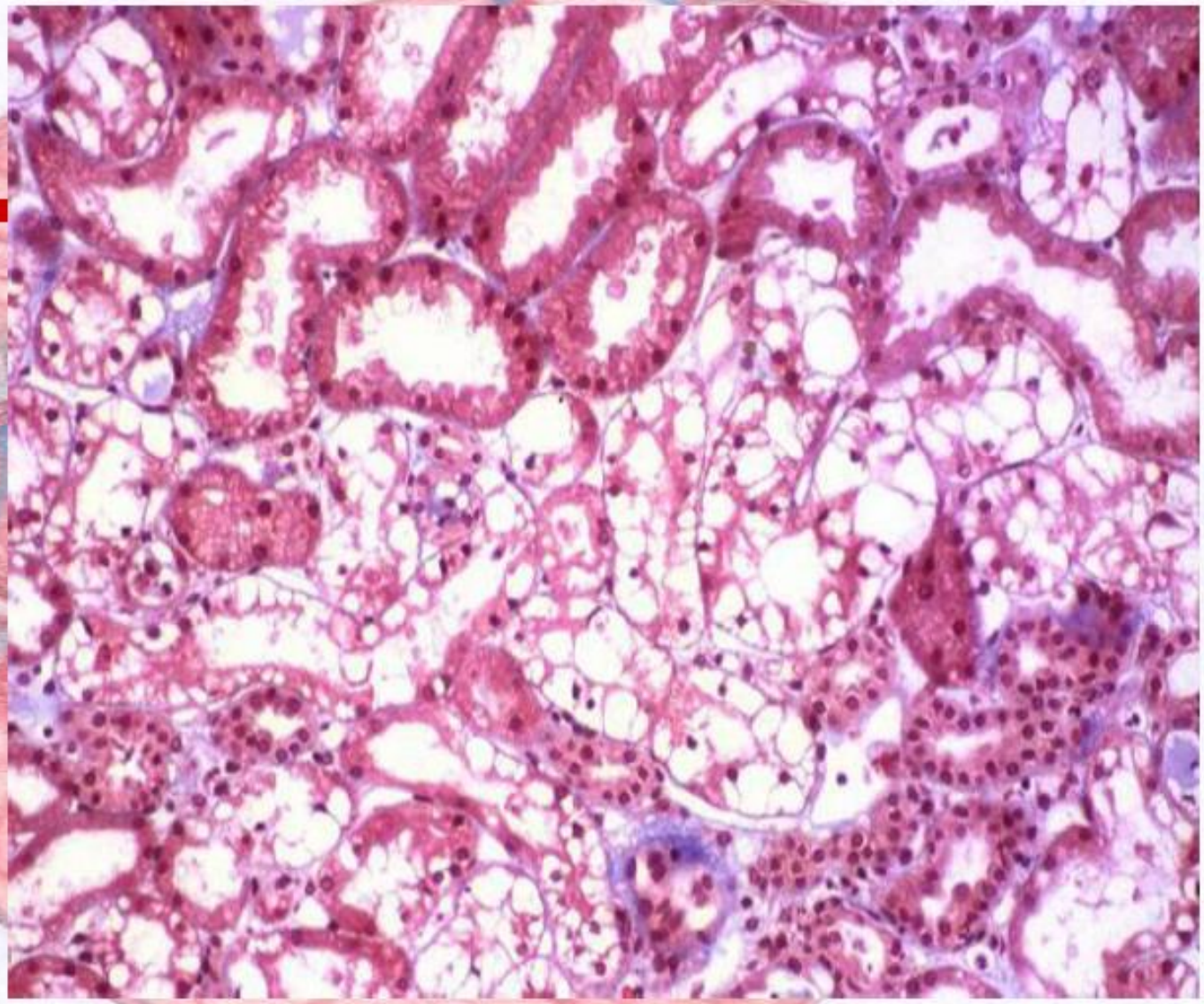


AKI
Nephrotoxic ATN

- Endogenous Toxins
  - Heme pigments (myoglobin, hemoglobin)
  - Myeloma light chains
- Exogenous Toxins
  - Antibiotics (e.g., aminoglycosides, amphotericin B)
  - Radiocontrast agents
  - Heavy metals (e.g., cis-platinum, mercury)
  - Poisons (e.g., ethylene glycol)



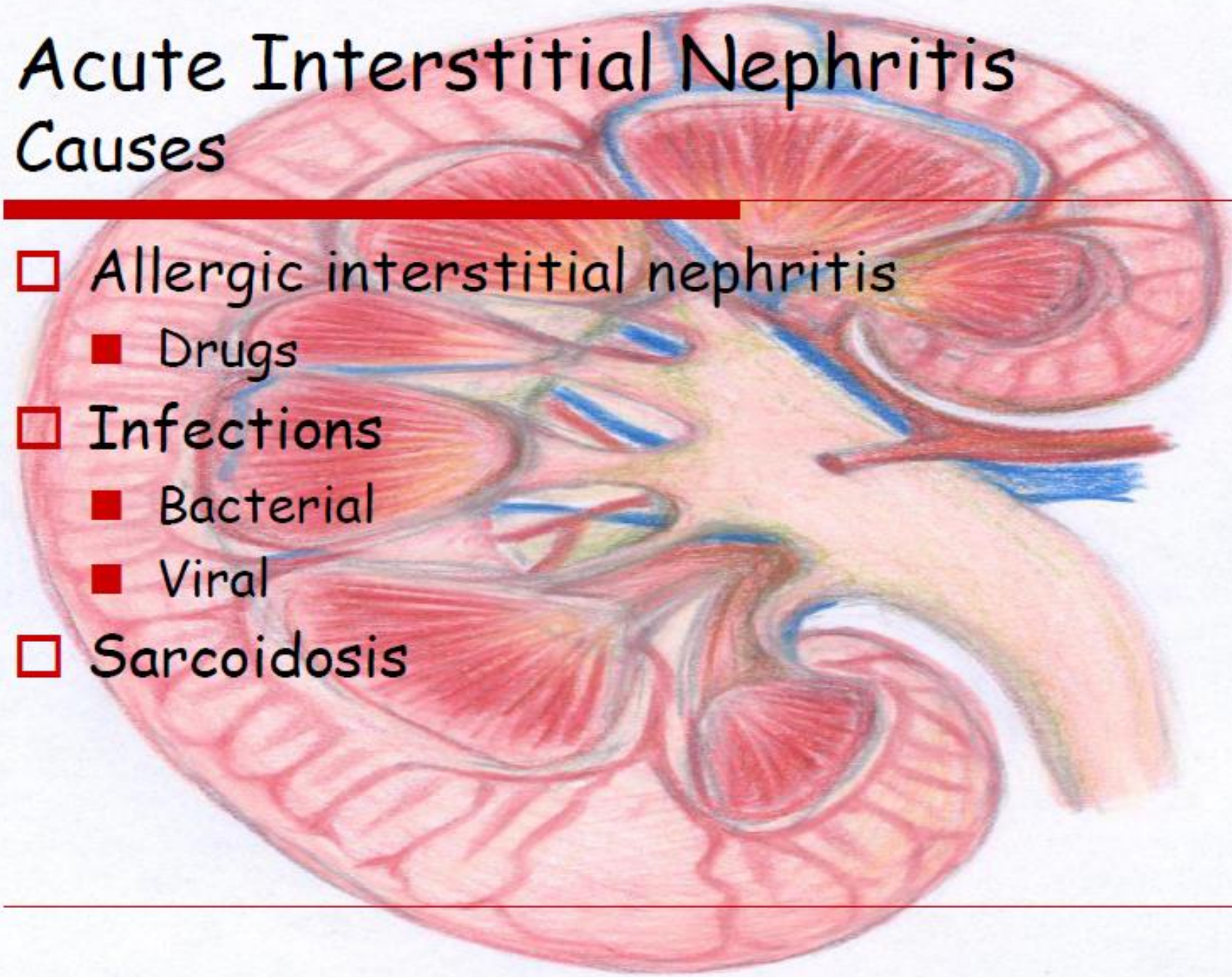
ATN



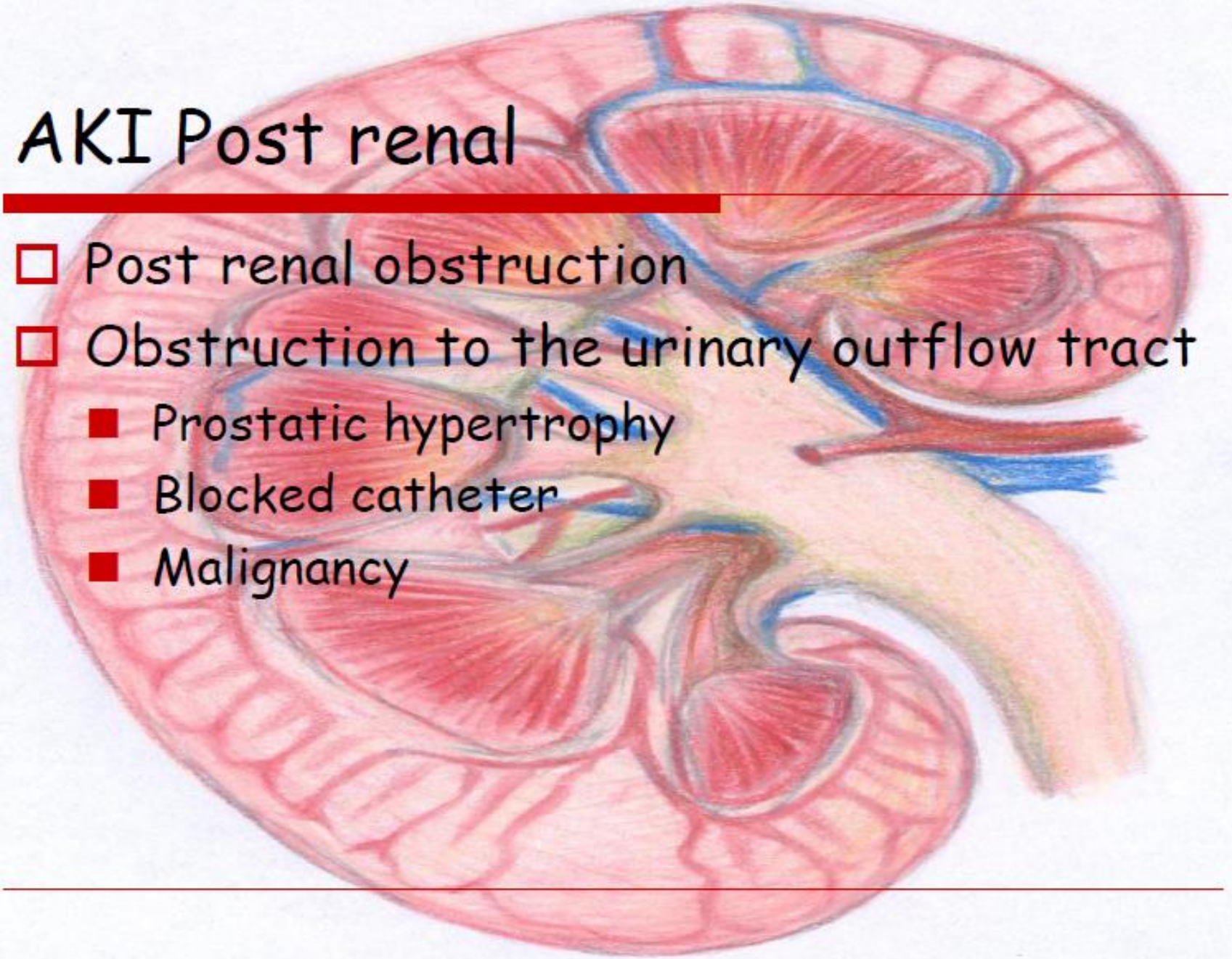
Acute Interstitial Nephritis

Causes

- Allergic interstitial nephritis
  - Drugs
- Infections
  - Bacterial
  - Viral
- Sarcoidosis



AKI Post renal

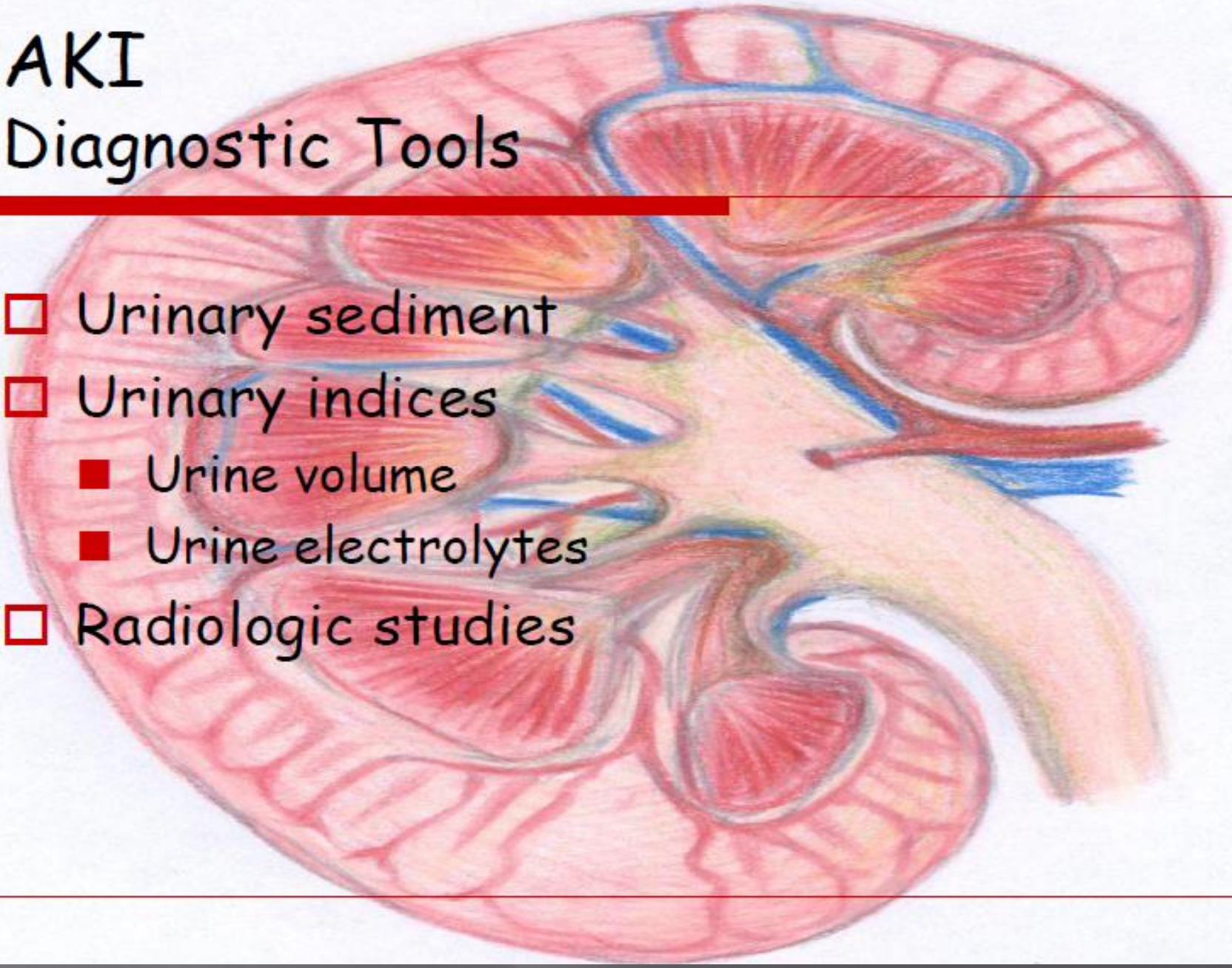


- Post renal obstruction
- Obstruction to the urinary outflow tract
  - Prostatic hypertrophy
  - Blocked catheter
  - Malignancy

AKI Post-renal Causes

- Intra-renal Obstruction
  - Acute uric acid nephropathy
  - Drugs (e.g., acyclovir)
- Extra-renal Obstruction
  - Renal pelvis or ureter (e.g., stones, clots, tumors, papillary necrosis, retroperitoneal fibrosis)
  - Bladder (e.g., BPH, neuropathic bladder)
  - Urethra (e.g., stricture)

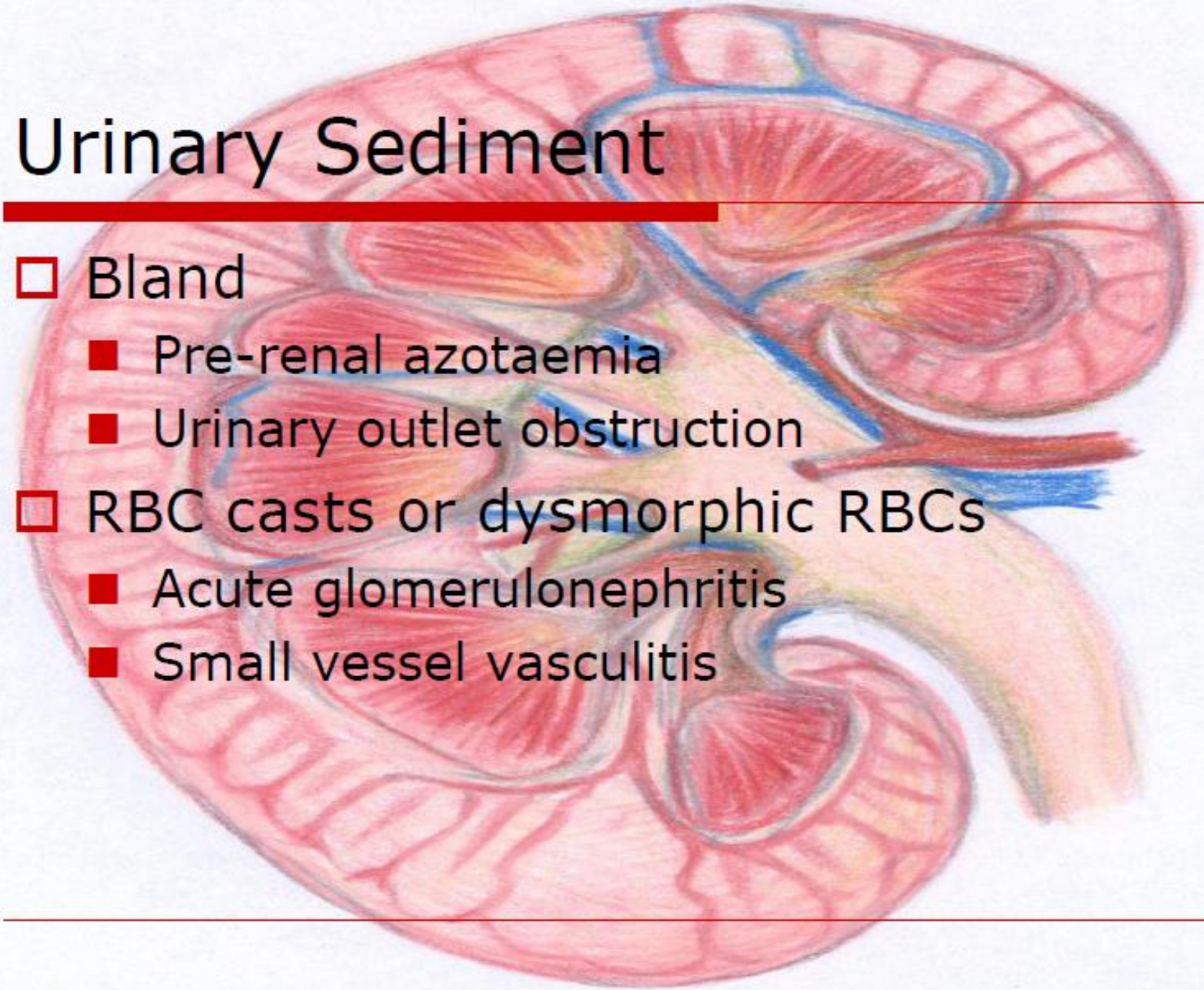
AKI
Diagnostic Tools



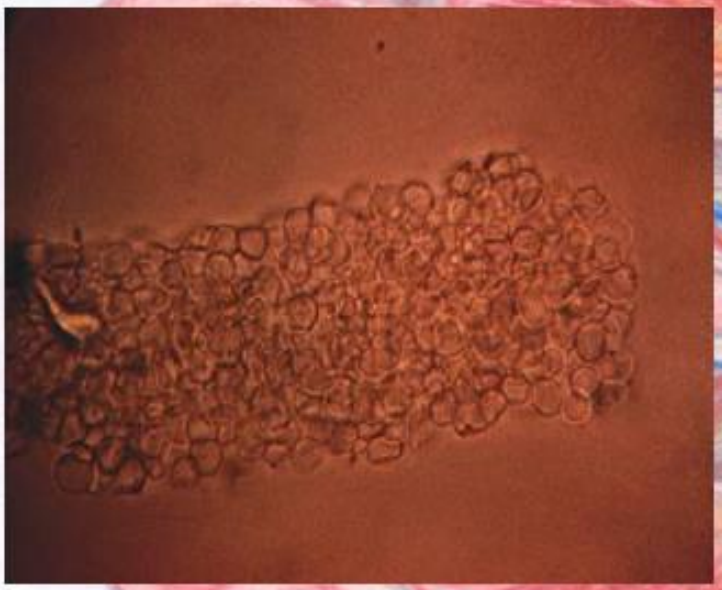
- Urinary sediment
- Urinary indices
  - Urine volume
  - Urine electrolytes
- Radiologic studies

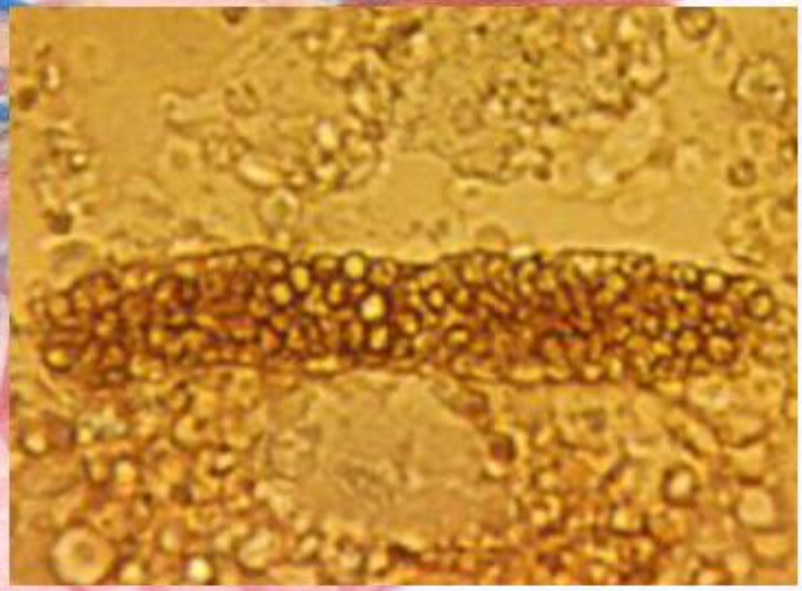
Urinary Sediment

- Bland
  - Pre-renal azotaemia
  - Urinary outlet obstruction
- RBC casts or dysmorphic RBCs
  - Acute glomerulonephritis
  - Small vessel vasculitis

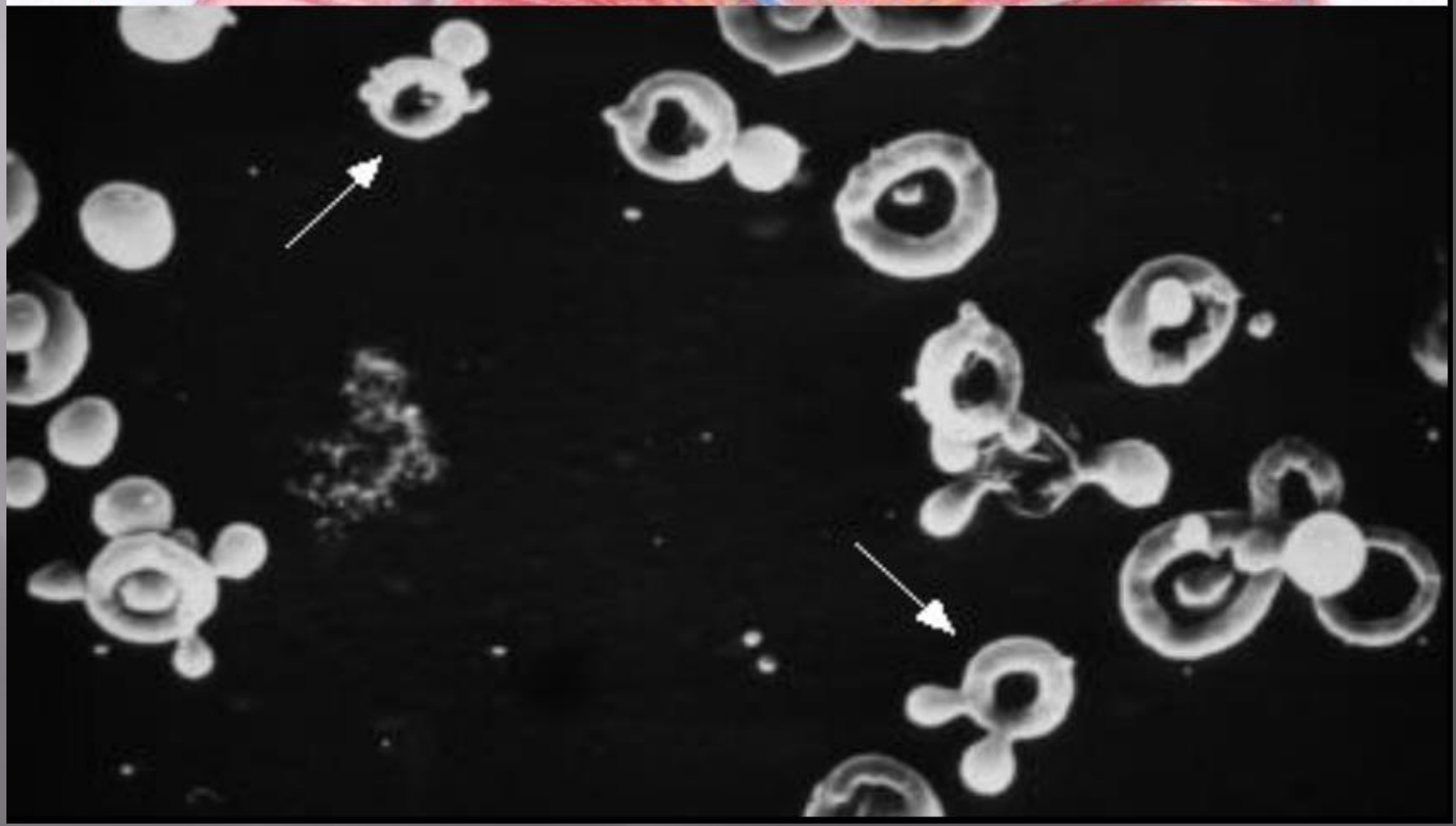


Red Blood Cell Cast

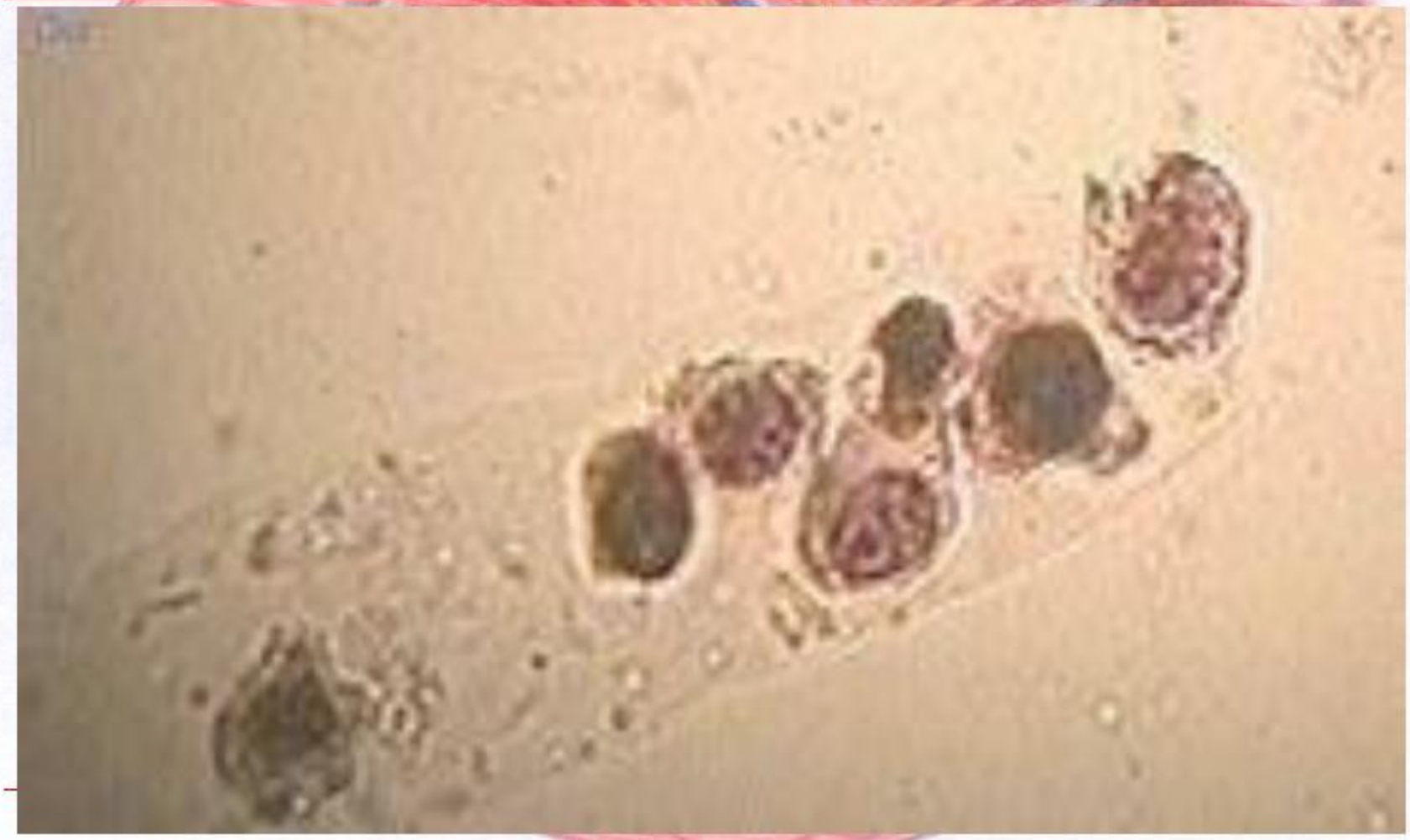




Dysmorphic Red Blood Cells



Renal Tubular Epithelial Cell Cast



Chapter 18: Acute Kidney Injury in the Elderly

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TREATMENT OF THE ELDERLY WITH AKI

In general, the treatment of AKI in the elderly follows the same principles as for the general population. However, the decision to initiate dialytic support in the very elderly with multiple comorbidities and a very poor prognosis may be difficult. This is especially true for those individuals with significant baseline renal impairment where the likelihood of renal recovery may be low. The decision to initiate dialysis in these patients requires a coordinated discussion with family members, consulting physicians and other care providers.

The only organ with entry and exit arteries