ACUTE KIDNEY INJURY (AKI)

Nephrology unit
Mansoura Faculty of Medicine

Definitions:

A rapid deterioration of parenchymal renal functions sufficiently severe to result in uremia.

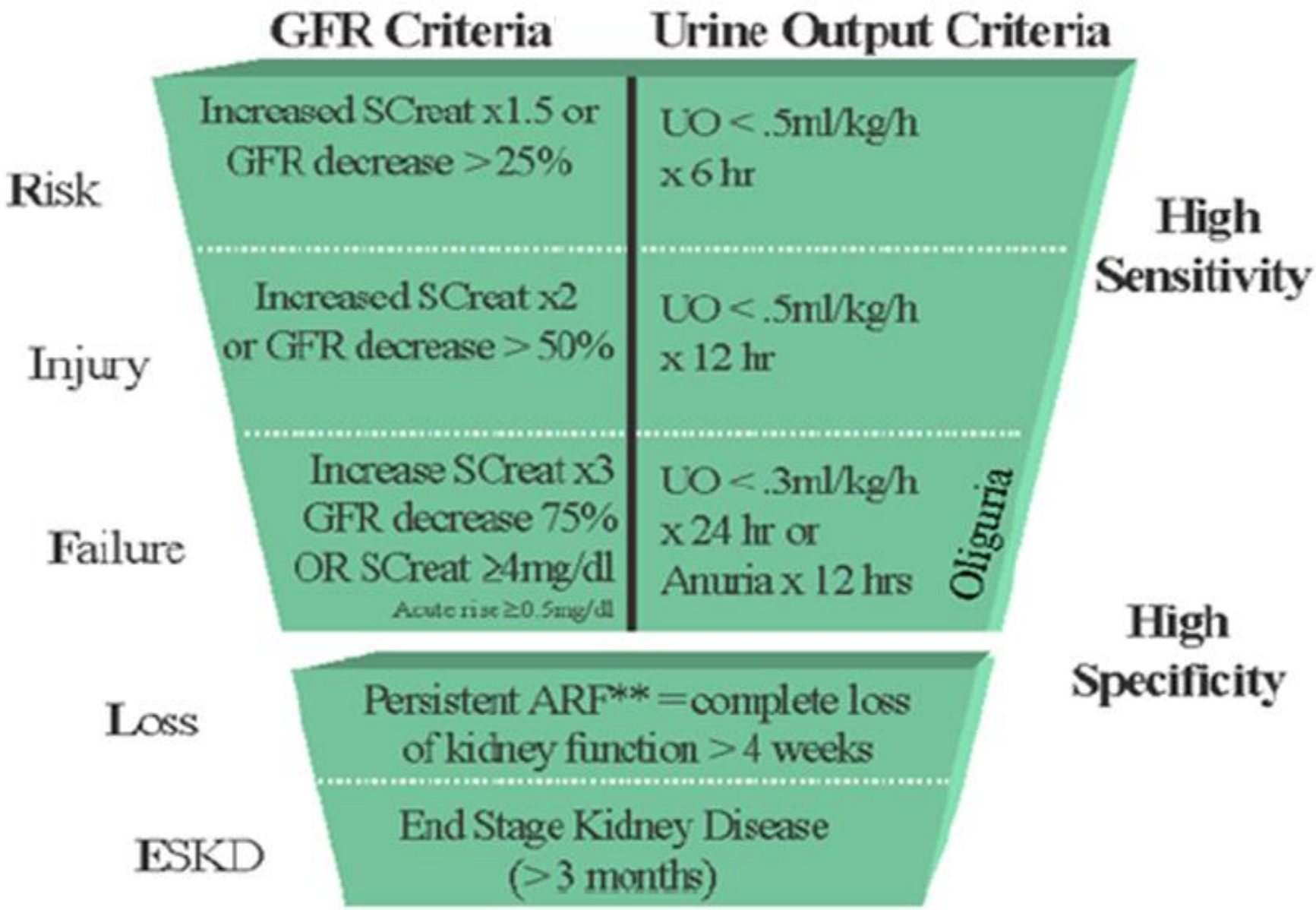
- *Usually but not invariably reversible.*
- *Oliguria is usually, but not invariably a feature.*

Recently the term AKI has replaced the term ARF .

RIFLE Criteria

- The RIFLE criteria consists of three graded levels of injury (Risk, Injury, and Failure)

- Based upon either the magnitude of elevation in serum creatinine or urine output,
- Two outcome measures (Loss and End-stage renal disease
- The RIFLE strata are as follows



Proposed classification scheme for acute renal failure (ARF)

Definition of Acute Kidney Injury (AKI) based on "Acute Kidney Injury Network"

Stage	Increase in Serum Creatinine	Urine Output
1	1.5-2 times baseline **OR** 0.3 mg/dl increase from baseline	<0.5 ml/kg/h for >6 h
2	2-3 times baseline	<0.5 ml/kg/h for >12 h
3	3 times baseline **OR** 0.5 mg/dl increase if baseline>4mg/dl **OR** Any RRT given	<0.3 ml/kg/h for >24 h **OR** Anuria for >12 h

KDIGO (2012)

AKI is defined as any of the following:

- Increase in SCr by X0.3 mg/dl within 48 hours; or
- Increase in SCr to X1.5 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.

KDIGO (2012)

Stage	Serum creatinine (SCr) criteria	Urine output criteria
1	1.5 to 1.9 times baseline OR ≥26 µmol/L (≥3.0 mg/dL) increase	<0.5 ml/kg/hr for 6-12 hrs
2	2 to 2.9 times baseline	<0.5 ml/kg/hr for ≥12 hrs
3	Serum creatinine increase 3.0 times baseline OR Increase in serum creatinine ≥354 µmol/L (≥4.0 mg/dL) OR Initiation for RRT OR In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/hr for ≥24 hrs OR Anuria for ≥12 hrs

*** Must have met initial criteria for definition of AKI**

Reference: *Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney inter., Suppl. 2012; 2: 1–138*

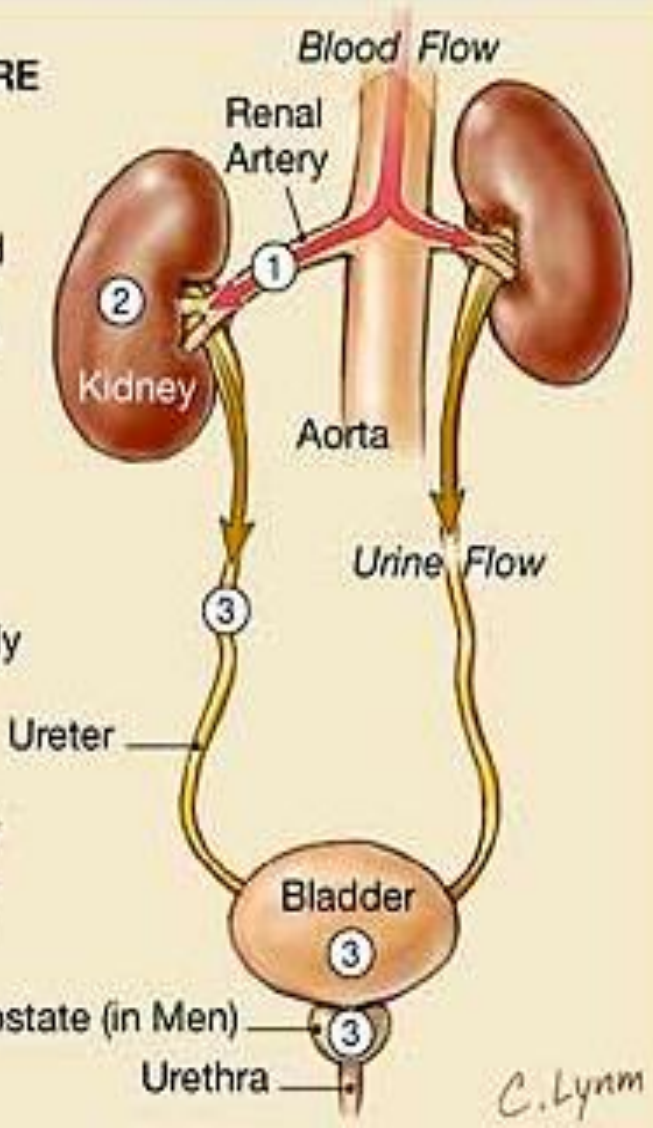
Classification of AKI

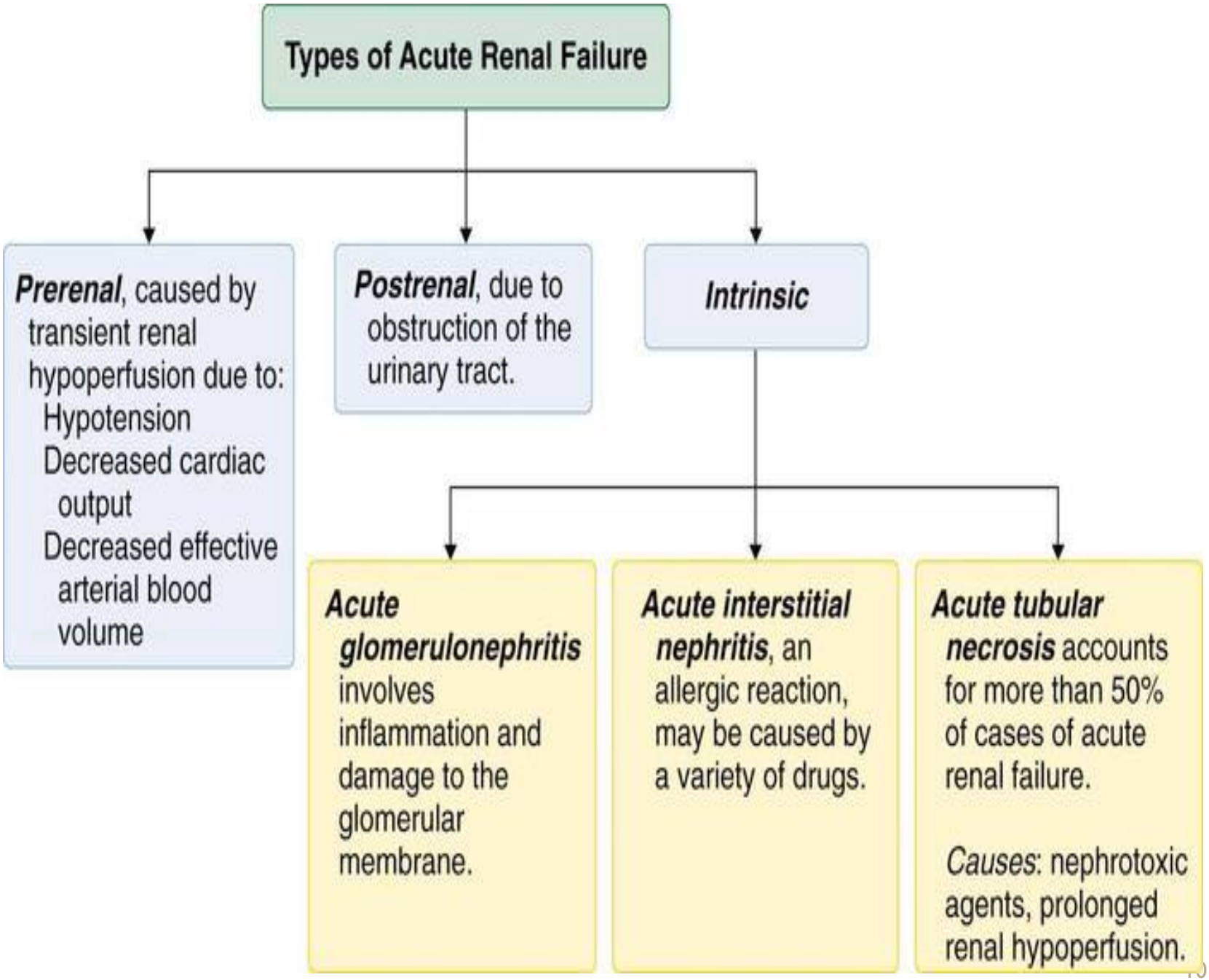
CAUSES OF ACUTE RENAL FAILURE

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




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.

In pre-renal

- Renal tissue is intact
- Kidney biopsy shows normal renal histology.
- Oliguria and high serum creatinine are due to functional impairment.

- Since there is no structural renal damage, early diagnosis and correction of renal hypoperfusion results in immediate diuresis and rapid drop in serum creatinine and blood urea levels.

- If hypoperfusion is severe or neglected, renal compensatory mechanisms will fail and acute tubular necrosis occurs

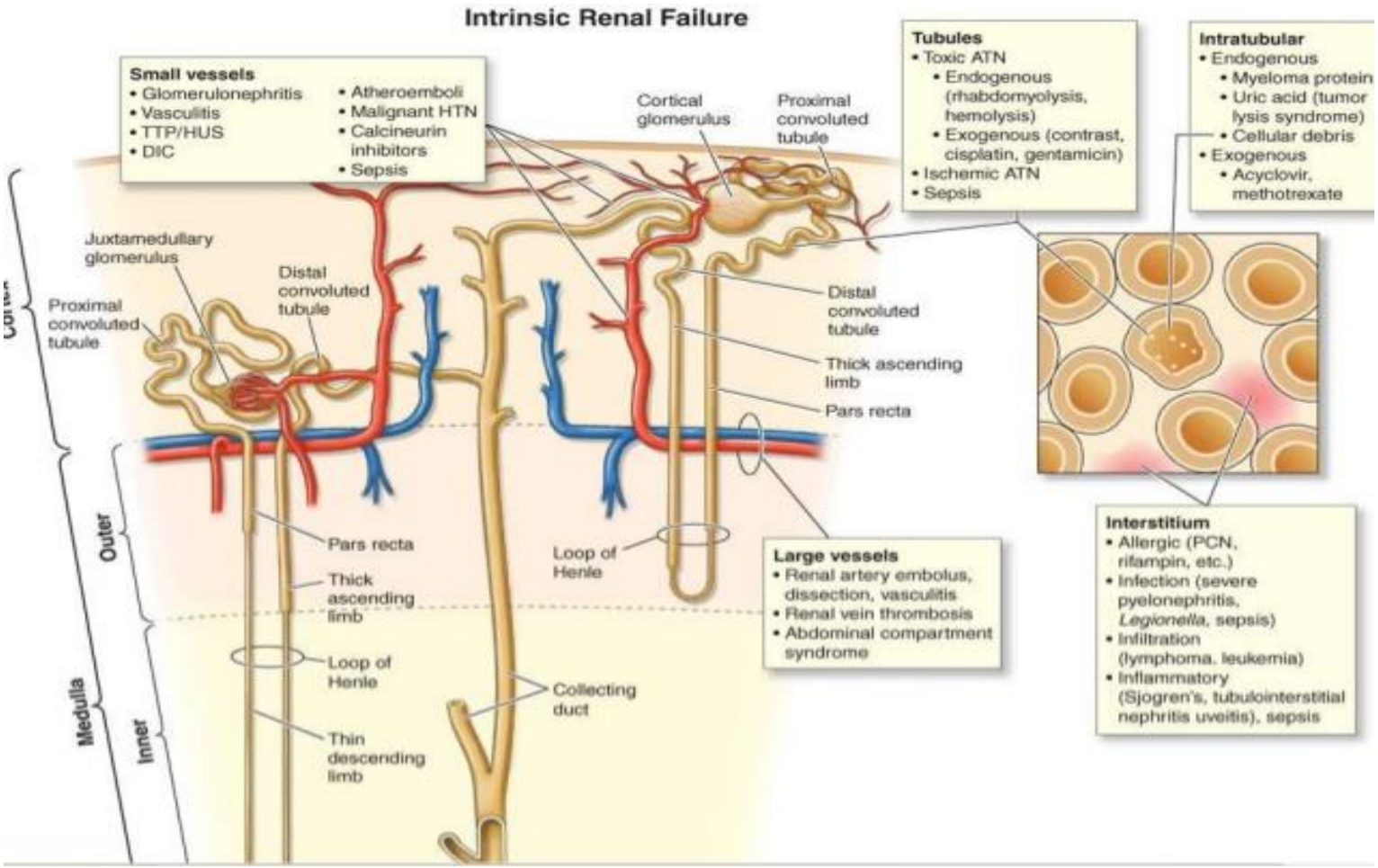
In post-renal

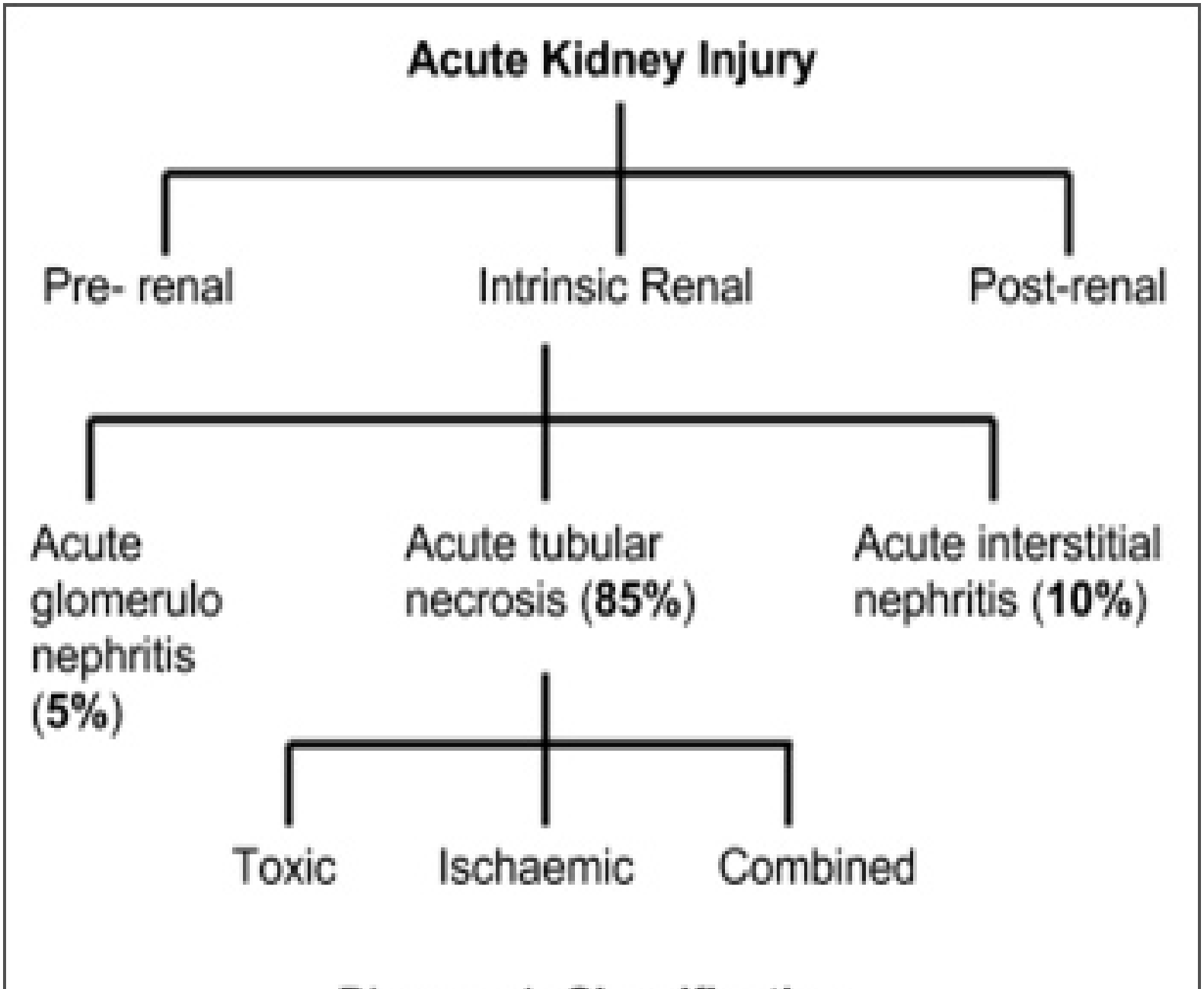
- The obstruction of the urinary tract results in increasing the pressure above the level of the obstruction.

- When this back pressure exceeds that of the filtration pressure in the renal glomeruli, the process of urine formation will stop with progressive accumulation of wastes and increase of serum creatinine and blood urea.

Intrinsic Renal

- This includes:
  - Acute tubular necrosis (ATN)
  - Acute interstitial nephritis
  - Acute glomerulonephritis


Intrinsic Renal Failure
Small vessels
• Glomerulonephritis
• Vasculitis
• TTP/HUS
• DIC
• Atheroemboli
• Malignant HTN
• Calcineurin inhibitors
• Sepsis
Cortical glomerulus
Proximal convoluted tubule
Tubules
• Toxic ATN
• Endogenous (rhabdomyolysis, hemolysis)
• Exogenous (contrast, cisplatin, gentamicin)
• Ischemic ATN
• Sepsis
Intratubular
• Endogenous
• Myeloma protein
• Uric acid (tumor lysis syndrome)
• Cellular debris
• Exogenous
• Acyclovir, methotrexate
Juxtamedullary glomerulus
Proximal convoluted tubule
Distal convoluted tubule
Distal convoluted tubule
Thick ascending limb
Pars recta
Cortex
Outer
Medulla
Inner
Pars recta
Thick ascending limb
Loop of Henle
Thin descending limb
Loop of Henle
Collecting duct
Large vessels
• Renal artery embolus, dissection, vasculitis
• Renal vein thrombosis
• Abdominal compartment syndrome
Interstitium
• Allergic (PCN, rifampin, etc.)
• Infection (severe pyelonephritis, Legionella, sepsis)
• Infiltration (lymphoma, leukemia)
• Inflammatory (Sjogren's, tubulointerstitial nephritis uveitis), sepsis


Acute Kidney Injury
Pre- renal
Intrinsic Renal
Post-renal
Acute glomerulo nephritis (5%)
Acute tubular necrosis (85%)
Acute interstitial nephritis (10%)
Toxic
Ischaemic
Combined

Acute tubular necrosis (ATN)

Acute Tubular Necrosis

ATN can be induced by:

- Renal hypoperfusion (ischemia)
- Exposure to nephrotoxins (exogenous or endogenous toxins)
- A combination of both.

Causes of Ischaemic ATN:

A- Blood Loss

- Haemorrhage (post partum, surgical or gastrointestinal).
- Major trauma

B-Fluid Loss

- Gastrointestinal (vomiting or diarrhoea)
- Renal (aggressive diuresis or polyuria)

C-Third Space

- Haematoma
- Illius
- Peritonitis

D-Severe vasodilatation as in septicemia, rapid edema formation, liver cell failure.

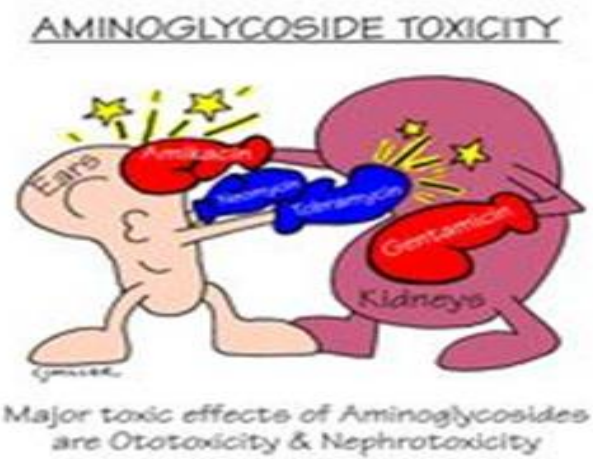
E-Renovascular disease

- Renal artery occlusion by stenosis, embolism or compression.
- Renal vein thrombosis or compression.

Causes of Toxic ATN

(A)Exogenous

Antibiotics:



)hotericin

:lovir

tracin

Anaesthetic a

Contrast Med

Analgesics: Phenacetin

Metals: as Mercury, lead, arsenic, bismuth, cadmium, antimony

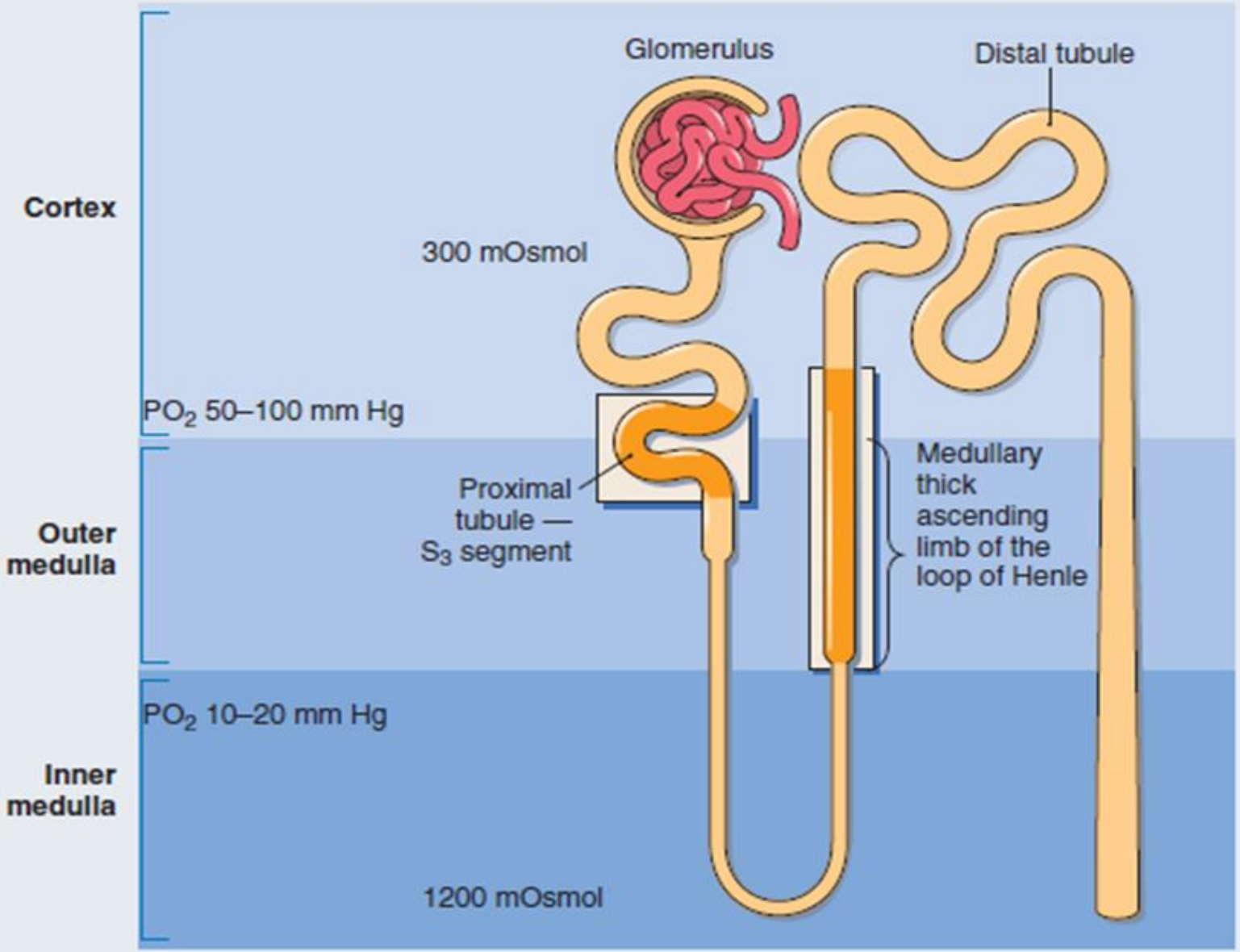
organic solvents: Glycols

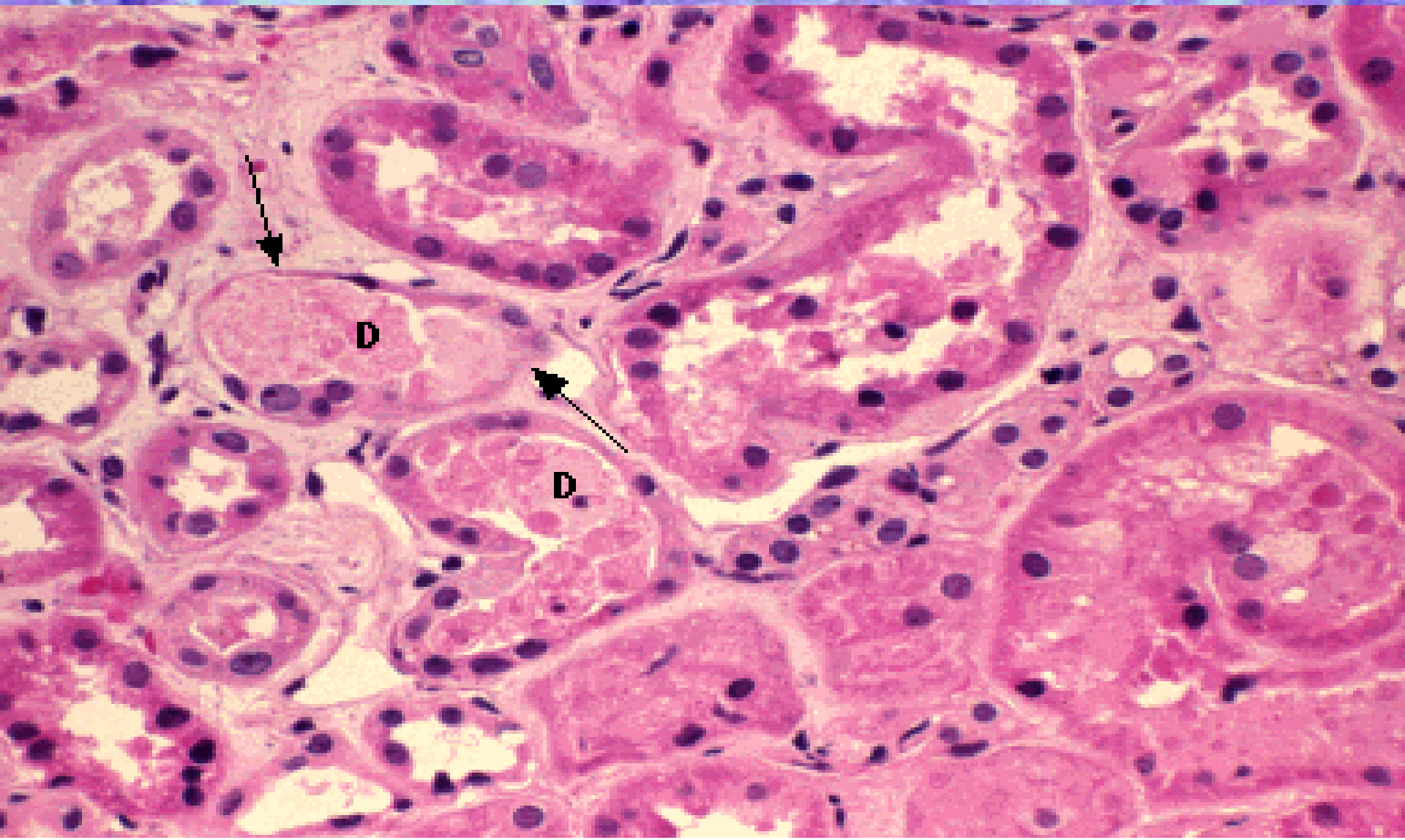
Poisons: snake bite, stings, bacterial toxins.

(B)Endogenous nephrotoxins include

Pigments:	**Crystals:**
Myoglobin	Uric acid
Hemoglobin	Calcium
Methemoglobin	Oxalate

Sites of Tubular Injury in ATN





Acute tubular necrosis Light micrograph in acute tubular necrosis showing focal loss of tubular epithelial cells (arrows) and partial occlusion of tubular lumens by cellular debris (D). Courtesy of Helmut Rennke, MD.

Acute cortical necrosis:

- Is a subset of ATN in which there is a massive necrosis of the tubules and glomeruli of the renal cortex.
- The condition may be focal or diffuse with irreversible damage of the kidneys.
- It is suspected when ATN fails to recover after 4-6 weeks.
- Acute cortical necrosis usually occurs with complicated pregnancy as postpartum hemorrhage and abruptio placenta

Clinical features of AKI

- **Usually, the patient gives history of the etiologic cause such as:**

  - Trauma
  - Shock
  - Hemolysis
  - Drug intake
  - Infection
  - Stone disease
  - Procedure requiring contrast media
  - ICU admission

Careful history is essential

- Exposure to nephrotoxins and drugs
- Anuria may indicate post-renal causes
- Skin rashes may indicate allergic nephritis
- Evidences of vc
- Pelvic and per-r
  of abortion
- Ischemia or trau
  rhabdomyolysis

- **A history of prostatic disease, nephrolithiasis**
- **Recent surgical or radiologic procedures**
- **Past and present use of medications**
- **Family history of renal diseases**

❖ Patient may notice a change in

1. Urine volume and character
2. Oliguria is common, but in 10-50% of cases urine volume will be normal or even higher (Non-oliguric).
3. Absolute anuria is highly suggestive of obstructive AKI (post-renal) or very severe form of ATN (cortical necrosis).

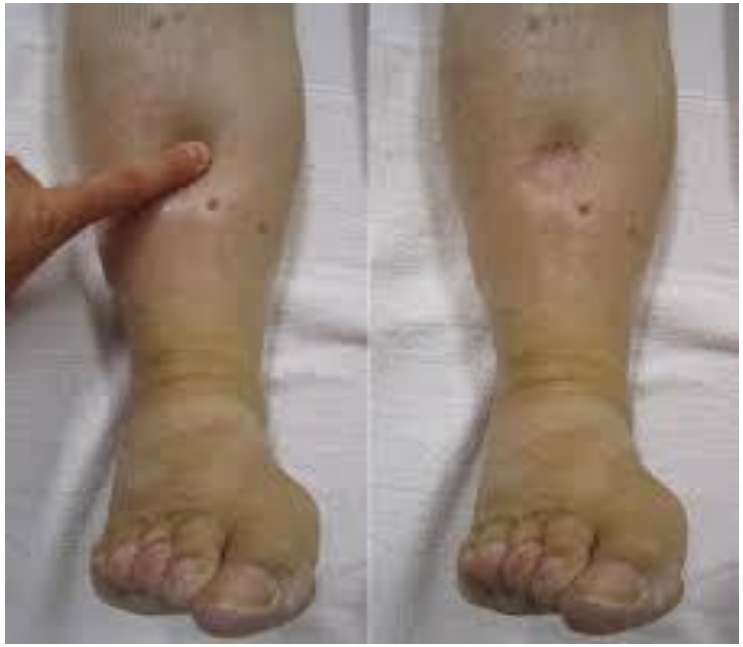
❖ Manifestation of salt and water retention

Edema

Puffiness

Hypertension

Heart failure



Manifestations of uremia

- By time, manifestations of uremia appear as:

  acidotic breathing, dyspnea, nausea, vomiting, headache, muscle twitches and even frank encephalopathy and coma.

- Patient may present as well with complications

Complications of AKI

Cardiovascular

- pulmonary odema
- hypertension
- myocardial infarction
- arrhythmias
- pericardial effusion
- pulmonary embolism

Metabolic

- hyponatremia
- acidosis
- hyperphosphatemia
- hyperkalemia
- hypocalcemia

Neurologic

- coma
- seizures

Gastrointestinal

- gastritis
- gastroduodenal ulcers

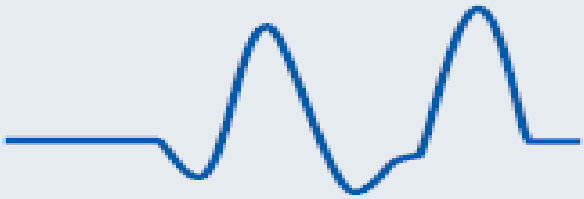
Haematologic

- anaemia
- hemorrhagic diathesis

Infections

- pneumonia
- UTI
- septicemia

ECG Changes in Hyperkalemia

QRS Complex	Approximate Serum Potassium (mmol/l)	ECG Change
	~4	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	Sine wave pattern

Example Of Clinical Cases

Symptoms	Possible Diagnosis
Hypercalcaemia, hyperuricaemia, bone pain, lytic lesions	Multiple myeloma
Recent vascular intervention ± livedo reticularis, hypo-complementaemia	Cholesterol emboli syndrome
Raised serum creatinine, creatine kinase >10,000 U/litre, prolonged severe immobility, crush injuries	Rhabdomyolysis

Investigations of AKI

A- Urinary indices:-

May be helpful in the differentiation between pre-renal failure and acute tubular necrosis.

Diuretics should not be given during the preceding 48 hours for these parameters to be valid.

Guidelines for urinary indices whereby established ARF can be distinguished from renal vasoconstriction with intact tubular function (prerenal azotemia)

Laboratory test	Prerenal azotemia	ARF
Urine osmolality (mOsm/kg)	>500	<400
Urine sodium level (mEq/l)	<20	>40
Urine/plasma creatinine ratio	>40	<20
Fractional excretion of sodium (%)	<1	>2
Fractional excretion of urea (%)	<35	>35
Urinary sediment	Normal; occasional hyaline or fine granular casts	Renal tubular epithelial cells; granular and muddy brown casts

Osm, osmole; Eq, equivalent.

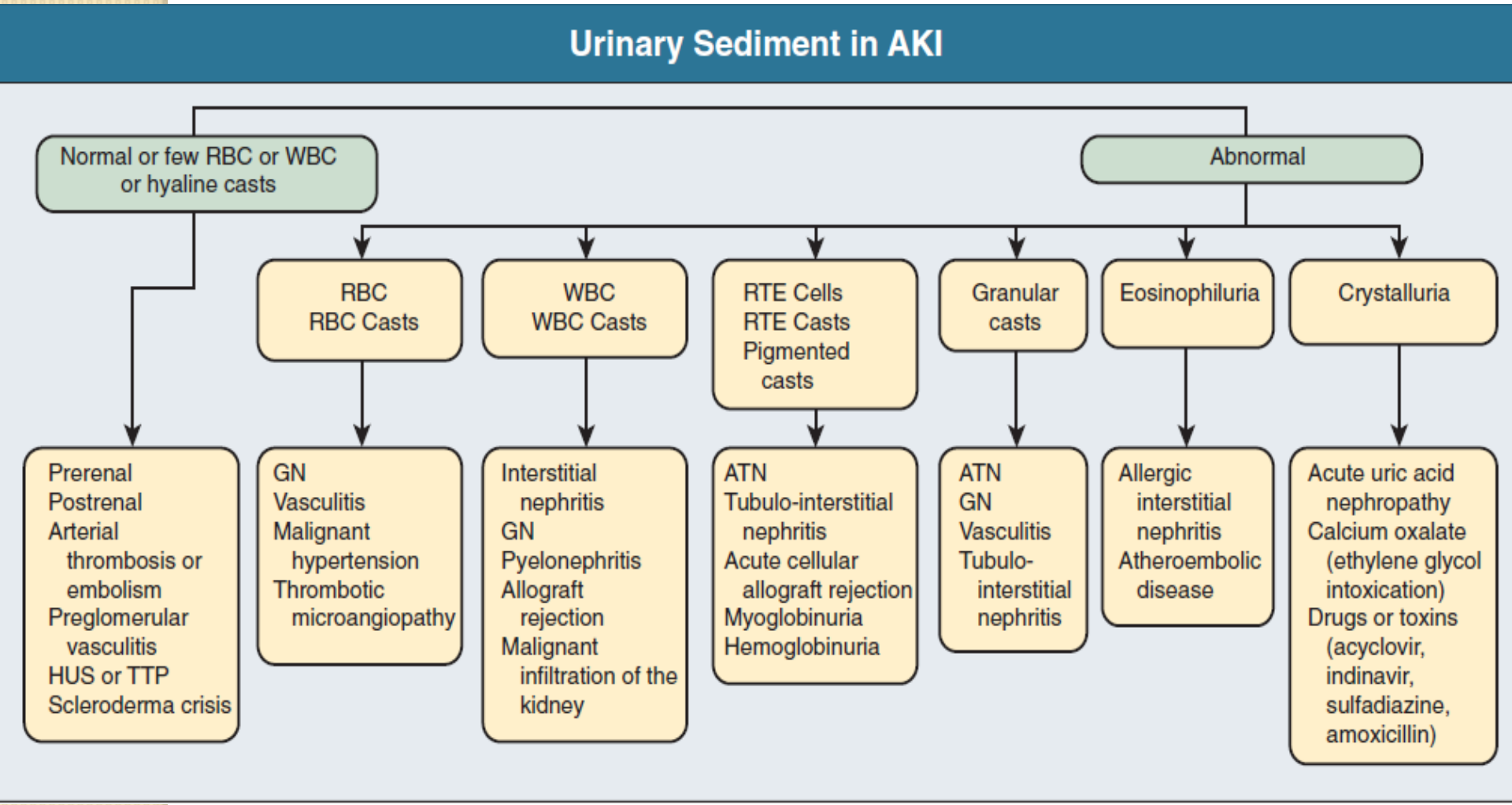
B- Urinary sediment:

Centrifugation of fresh urine sample and examination of the urinary sediment may be helpful in diagnosing different causes of AKI.

In pre-renal failure and in ischaemic ATN urinary sediment is usually free.

Urine sediment in Acute Nephrotic Syndrome and in RPGN is characteristic.

Urine Examination



C- Renal Imaging:

1. Plain film of the abdomen:

This will show kidney parity, size, shape, calcification and stones.

2. Renal Ultrasonography and Echo-Doppler of renal vs:

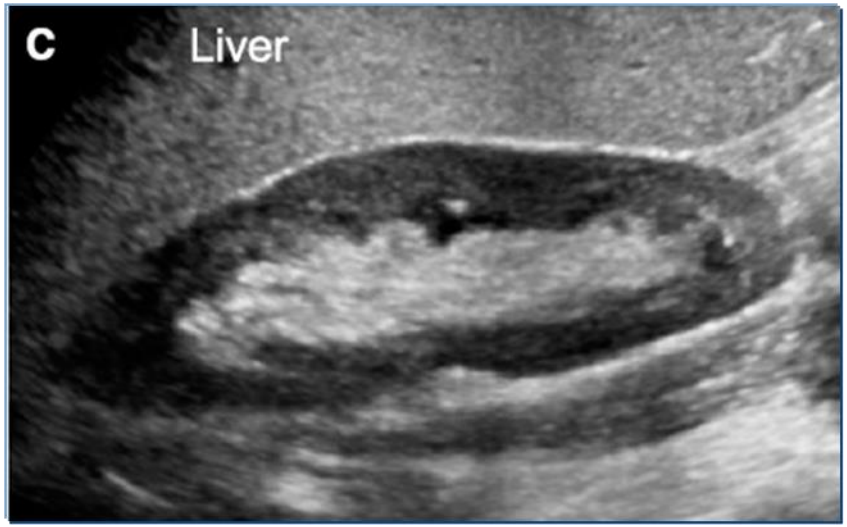
- US safely assesses kidney size, shape and echogenicity.
- Cortical thinning or oedema can sometimes be seen clearly.
- Also, it can exclude obstructive uropathy (back pressure changes).

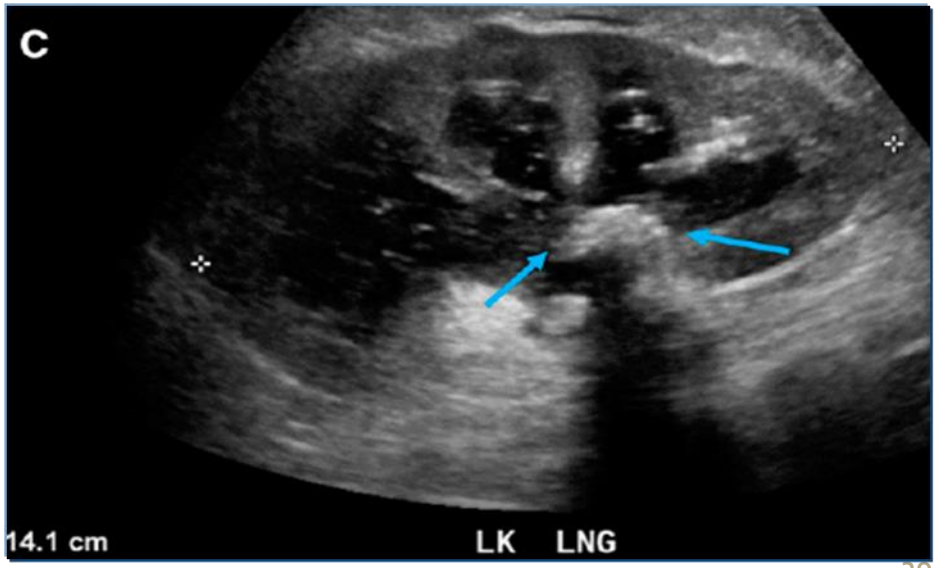
Echo-Doppler of renal vessels can exclude occlusion of the renal arteries and veins.

3. Retrograde and antegrade pyelography:

Provide the most reliable information on the patency of the ureter.

Role of Ultrasound





4. **Angiography:**

Is useful mainly when an acute reversible renovascular event is suspected such as **embolization, thrombosis or involvement in a dissecting aortic aneurysm**. *It carries the risk of exposure to contrast media which could be nephrotoxic*.

5. **C.T. studies:**

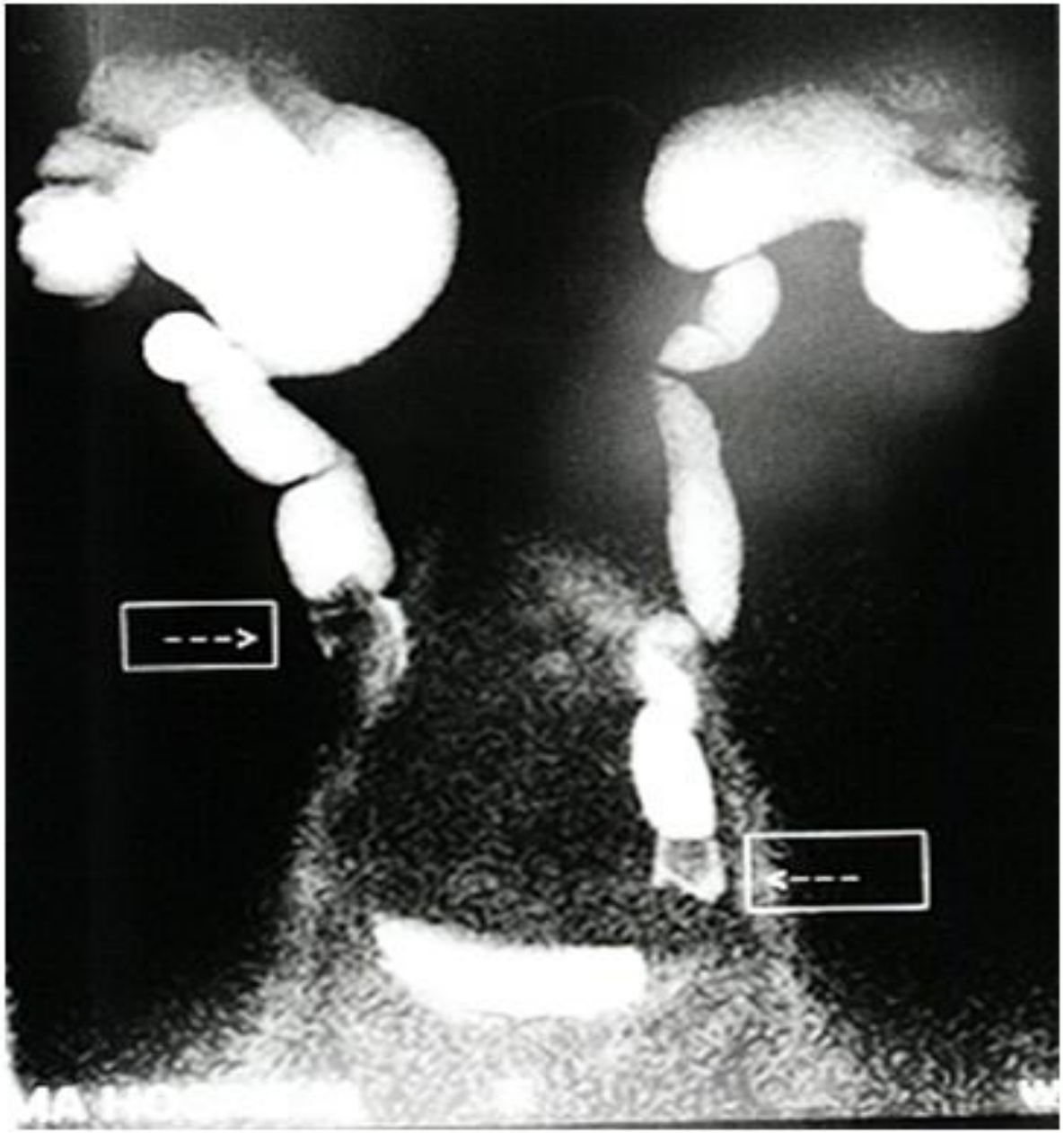
Provide reliable information on kidney parity, size, shape and presence of hydronephrosis.

6. **Magnetic Resonance urography:**

*Recently MRI urography (MRU) without use of contrast media can provide films similar to IVP.

*It is thus of great value to exclude U.T. obstruction without the risk of contrast media nephropathy.

*It is important to know that Gadolinium an MRI contrast is nephrotoxic,.



MR urography shows bilateral hydroureteronephrosis in a patient with 4.8 mg/dl serum creatinine (IVU is not feasible). Note the hypointense ureteric stone bilaterally (arrows).

D. Renal biopsy:

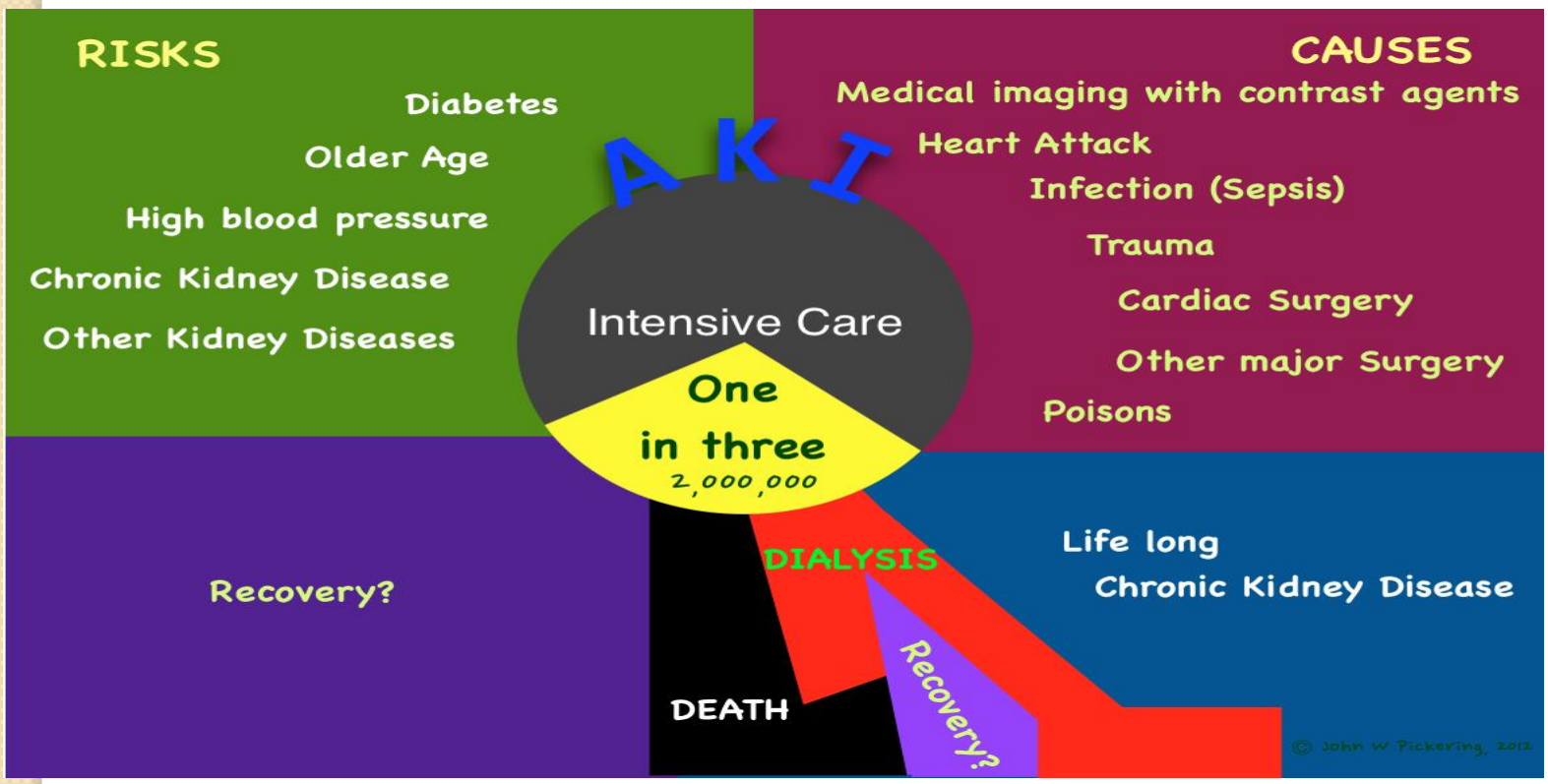
Indications

- Urine: RC cast, WC cast, Proteinuria
- Unexplained
- Systemic disease
- Prolonged course (more than 3 weeks).

TREATMENT OF AKI

A- Treatment of the cause

e.g. any condition causing renal hypoperfusion, exposure to toxic drug or chemical or systemic disease.



B- Conservative measures:

1- fluid balance:

- Careful monitoring of intake/output and body weight is very important to avoid overload and hypovolemia.

  The 1st may lead to pulmonary edema while the 2nd may aggravate renal ischemia.

- Patient should receive fluids =

daily urine output + other sensible losses e.g. vomitus or diarrhea + amount equals the insensible loss which is around 600 c.c. for 60kg body weight patient.

- Fluids could be given orally or (if not possible), it could be given intravenously.

2- Electrolytes and acid-base balance:

- Prevent and treat hyperkalemia.
- Avoid hyponatremia.
- Keep serum bicarbonate above 16 mmol/L.
- Minimize hyperphosphatemia by giving phosphate binders (e.g. Ca Co3 & AL hydroxide) with meals.
- Treat hypocalcaemia.

3- Treatment of hyperkalemia:

- Calcium gluconate I.V.
- Glucose 50% + Insulin
- Na Hco3 I.V.
- K-exchange resins (e.g. resonium)
- Avoid diets and drugs causing hyperkalaemia
- Dialysis

4- Nutritional support:

- With rare exceptions, Na & K restriction is appropriate.
- The place of dietary ptn restriction is controversial:
  - Hope to avoid dialysis → 40gm/day
  - Pt treated with HD → 70gm/day
  - Hypercatabolic pt will need ↑ nitrogen intake

5- Drugs:

- Review all medications.
- Adjust dosage for renal failure.

C-Dialysis

The indications of dialysis in AKI are:

a. Clinical:

- Poor clinical state, nausea, confusion.
- Fluid overload, pulmonary oedema.
- Preoperatively.

b. Biochemical:

- Plasma K+ > 7 mmol/L.
- Plasma bicarbonate < 12 mmol/L
- Arterial pH < 7.15.

Prevention of AKI

- ✓ The timing of intervention to prevent ATN is important. Protective agents must be administered at the time of, or immediately following potential renal insult. This intervention may prevent or at least blunt the severity of ATN.

- ✓ The intervention could be through the following approaches. In different combinations according to the clinical situation:

- Volume expansion by isotonic saline loading.
- Diuretic as furosemide (to change ATN to polyuric-easy manageable type)
- Non dihydropyridine Calcium channel blockers as Verapamil .
- Vasodilating agents as dopamine in renal dose 1-2 ug/kg/min. (are not effective) .

In case of contrast media, the following additional points should be adopted, these are:-

- *Avoid unnecessary contrast procedures.*
- *Avoid multiple contrast exposure within a few days.*
- *Avoid contrast exposure in high risk patient.*
- *Use the smallest dose possible.*
- *Use non-ionic , low viscosity contrast (good evidence).*
- *Hydration by isotonic saline in a dose of 3ml/kg/h. for 12h before and after contrast exposure (has the best evidence).*
- *Acetyl cysteine sachets 600mg/kg tds , 2days before and after exposure (good evidence).*
- *Washing the contrast out immediately after the technique (e.g. coronary angiography) by hemodialysis, is of no value.*

Prognosis of AKI

:

- The mortality of AKI remains high, ranging between 50-80% in surgical and post-traumatic cases.
- It is generally lower in AKI due to drugs and toxins.
- About 75% of deaths occur in the first week of AKI, and 25-50% of these deaths are due to the underlying disease.
- The overall prognosis is better in non-oliguric than in oliguric renal failure.
- The factors influencing patient survival in AKI include the following:
  - Etiology of AKI.
  - Severity of AKI.
  - Number and severity of coexisting illness.
  - Patient's age.
  - Presence of complications

THANK YOU