MED437
KING SAUD UNIVERSITY

PATHOLOGY
TEAM 437

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Revised by

Acute kidney injury(1)

(PATHOLOGY OF THE Renal failure)

" All of us failed to match our dreams of perfection. So I rate us on the basis of our splendid failure to do the impossible"-William Faulkner

Objectives:

- introduction to Acute renal injury

Definition,types,clinical overview , causes , pathological findings

Color Index :-

VERY IMPORTANT. Extra explanation Examples Diseases names: Underlined Definitions

Introduction

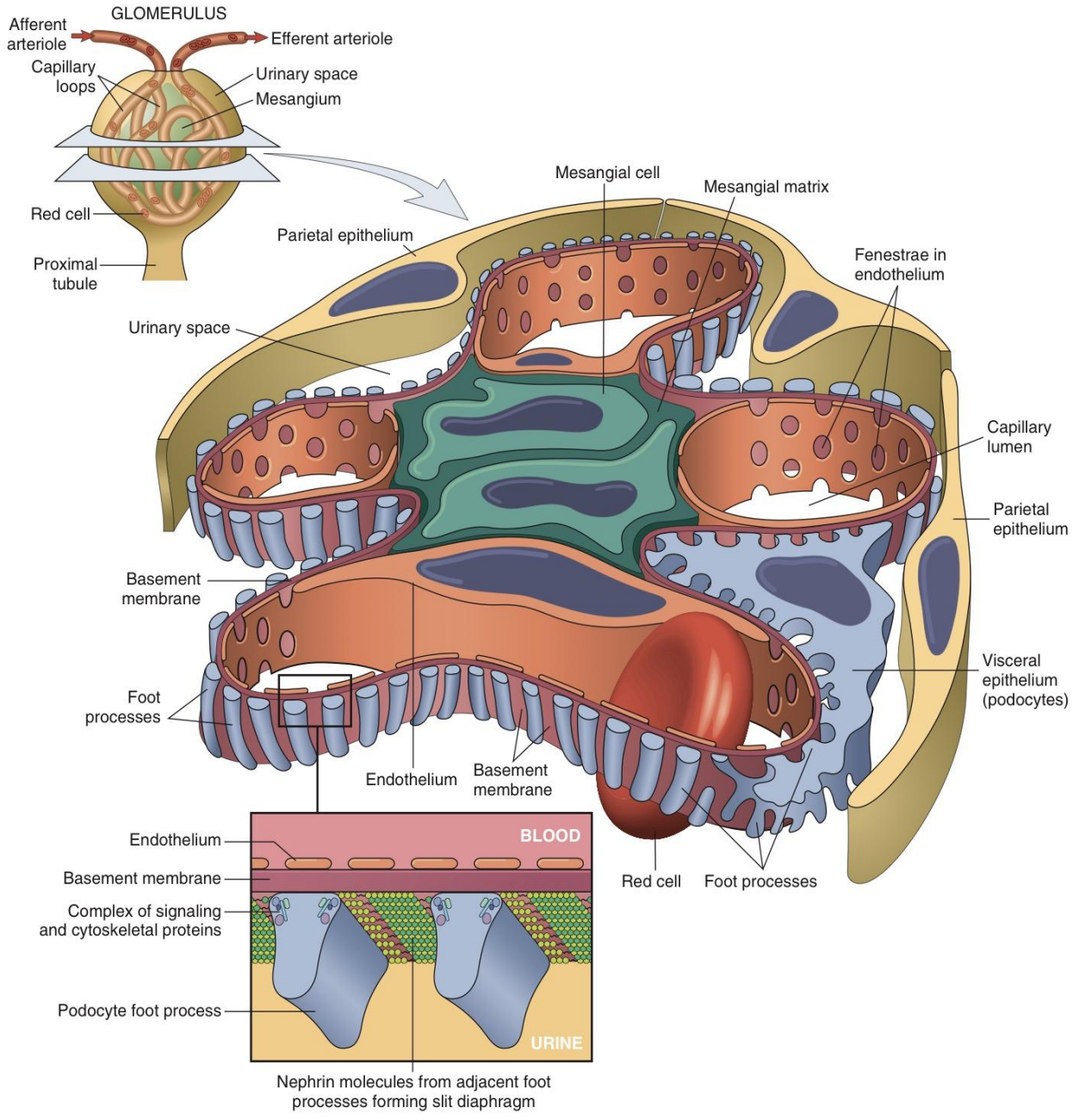


Fig. 14.1 Schematic diagram of a portion of a normal glomerulus.

Background Information

- Creatinine clearance or filtration is dependent on the glomerular filtration rate (GFR).
  - GFR = Glomerular hydrostatic pressure – Bowman's capsule hydrostatic pressure – glomerular oncotic pressure
  - Glomerular pressure is primarily dependent on renal blood flow.
  - In AKI → there is reduction in RBF → leads to decreasing GFR
    (this is the common pathologic pathway for AKI regardless of the cause).

- Uremia is a clinical syndrome associated with fluid, electrolyte, and hormone imbalances and metabolic abnormalities, which develop with deterioration of renal function.
  The term uremia, which literally means urine in the blood. Uremic illness is due largely to the accumulation of organic waste products, that are normally cleared by the kidneys. Uremia develops in chronic kidney disease and also in acute kidney injury.

- Azotemia: is an elevation of blood urea nitrogen (BUN) and serum creatinine levels.
  The reference range for BUN is 8-20 mg/dL, and the normal range for serum creatinine is 0.7-1.4 mg/dL.

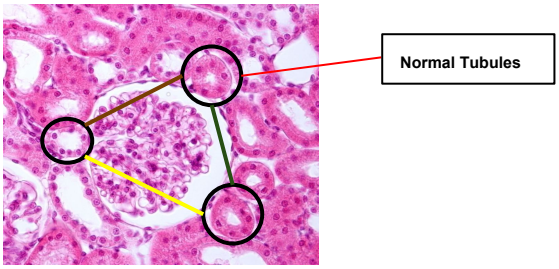
- Uremia: urea= urine in blood.
- Hematuria: urine in blood.

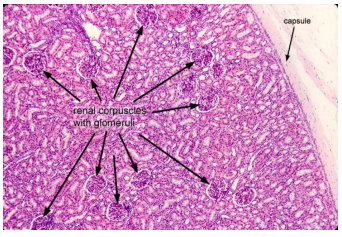
What do you see in this picture? ⟶

1. Normal glomeruli + renal corpuscles.
2. We can see tubules back to back "there is no spaces".
3. In kidney we are assessing four compartments:

1- Glomeruli. 2- Tubules. 3- Interstitium. 4- blood vessel.

- The circles in the black are normal tubules.
- You can see everything clearly here but when you have *acute tubular injury* you will loss all these structures of the tubules, you can't see anything they are all **necrotic**, you will see some remaining parts.





Acute Kidney Injury

Definition

Acute kidney injury (*AKI*) is also called as *acute renal* failure (ARF). **It is an abrupt decrease in renal function resulting in the accumulation of nitrogenous compounds such as urea and creatinine.** It is a syndrome defined by a sudden loss of renal function over several hours to days. Lab results show a **rapid rise in serum creatinine** or **decrease in urine output**.

In AKI/ARF there is:

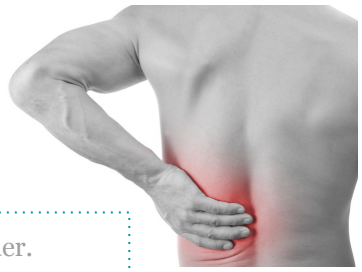
- Accumulation of nitrogenous waste products.
- Increased Serum creatinine.
- Derangement of extracellular fluid balance.
- Acid-base disturbance.
- Electrolyte and mineral disorders.

- Acute kidney failure → treated → it will reversed to its normal state.
- Acute kidney failure → not treated → chronic kidney failure.

Clinical features of acute kidney failure may include:

- **Oliguria**: Decreased urine output (occasionally urine output remains normal)
- Fluid retention, causing **swelling** in your legs, ankles or feet
- Uremic **encephalopathy***, confusion, seizures or coma, **pericarditis**, bleeding in severe cases
- Sometimes acute kidney failure causes **no signs** or symptoms and is detected through lab tests done for another reason.
- **Hypotension**
- **Tachycardia**
- **Nephritic syndrome**
- Nausea, vomiting, **flank pain**
- **Fatigue**

*- Organic brain disorder.



Flank region

ACUTE RENAL FAILURE CLASSIFICATION BY URINE VOLUME

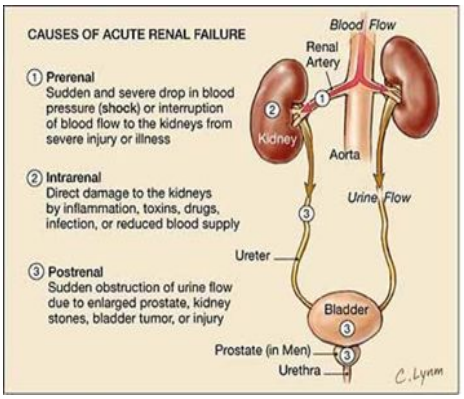
Class *Urine output*

1. **OLIGURIC**: urine output **less than 500cc/24hr.**
2. **NON-OLIGURIC**: urine output **greater than 500cc/24hr**.
3. **ANURIC**: urine output **less than 50cc/24hr**.
4. **Azotemia**: elevated blood urea nitrogen not from an intrinsic renal disease

ETIOLOGY OF ACUTE RENAL FAILURE:

Important to know the cause of each type

AKI (acute kidney injury) can be divided by etiology into:



1. **Pre-renal (55-60%) :** the renal tubular and glomerular functions are normal. Here the **GFR** (glomerular filtration rate) **is decreased due to reduced renal perfusion.**
2. **Renal/ intrarenal/ intrinsic (35-40%)**: is due to **diseases of the kidney itself** (which is associated with release of renal afferent vasoconstrictors)
3. **Post-renal (5%):** due to obstruction in the outflow of urine

-Prerenal ARF the kidney itself is normal but the problem could be anywhere before the kidney which lead to reduced renal perfusion like heart failure or hypovolemic shock ...etc
-Renal ARF the diseases will be in the kidney itself
-Post-renal ARF the kidney itself is normal but the outflow on urine is obstructed due to any reason like stones in the urinary tract or prostatic hyperplasia... etc

➢ Pre-renal ARF (decreased renal blood flow):

- **Most common cause** of ARF
- Results from decreased renal perfusion
- Treatment of the cause restores renal function tubular function intact
- Prolonged pre-renal failure may lead to **acute tubular necrosis** "which is the most common cause of renal ARF"

Table 1. Causes of Acute Renal Failure

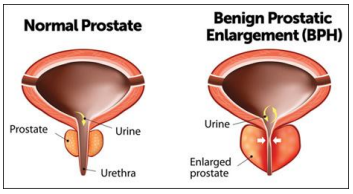
Prerenal
Hypovolemia
Hemorrhage
Fluid loss
Hypoalbuminemia
Third-space losses
Cardiac failure: myocardial dysfunction, valvular dysfunction, cardiac tamponade, pulmonary hypertension
Systemic vasodilatation: sepsis, cirrhosis, anaphylaxis, anesthesia, pharmacologic vasodilation
Afferent arteriolar vasoconstriction: sepsis, hypercalcemia, hepatorenal syndrome, drugs
Efferent arteriolar vasoconstriction: angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers

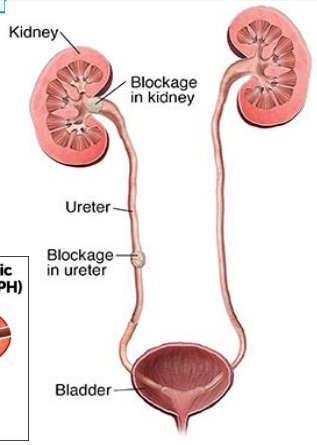
➢ **RENAL ARF:** Renal causes of ARF are divided into:

glomerular	Tubular Acute Tubular Injury/ Necrosis (Ischemic & nephrotoxic)		vascular	interstitial
The destruction of some glomeruli leave less total filtration area, reducing the GFR. **- Acute glomerulonephritis (GN)** --Post infectious GN --Rapid progressive crescentic GN **-Thrombotic microangiopathies** **-Atheroembolic disease**	**Ischemic**: Prolonged ischemia of the nephrons leads to tubular injury and necrosis	**Toxic** I) Endogenous toxins **Pigments**: -Myoglobinuria (Rhabdomyolysis) -Hemoglobinuria II) Exogenous toxins **-Drugs**: --Aminoglycosides (antibiotic) --Amphotericin B --cisplatin **-Radiograph contrast medium -induced:** Toxicity to the nephrons leads to tubular injury and necrosis	Various forms of vasculitis and emboli lead to reduced renal blood flow due to vascular obstruction or destruction, thus lowering the GFR e.g. -Vasculitis -Thromboembolic disease -Malignant hypertension	**Acute Interstitial Nephritis (AIN)** e.g. -drug induced/allergic (NSAIDs) -Autoimmune -Infections (pyelonephritis) -Malignant infiltration

➢ **Post renal ARF:** Any obstruction to the outflow of urine

1. **Anatomical obstruction:**
   - **-In young** = congenital or structural abnormality
   - **-Older male** = prostatic enlargement (prostatic hyperplasia)
   - -Any tumor in the bladder, prostate or urethra
   - -Stones in the urinary tract
2. **Tubular obstruction:**
   - -Crystals (oxalate)in tubules
   - -Casts (myeloma casts nephropathy) in tubules





Acute tubular injury/necrosis

Important

Histology:

Early:

- varies from cell swelling to tubular epithelial necrosis.
- dilated proximal tubules with thinning of tubular wall and loss of brush border.
- hyaline, granular and pigmented cases, particularly in distal and collecting ducts.
- interstitial edema.

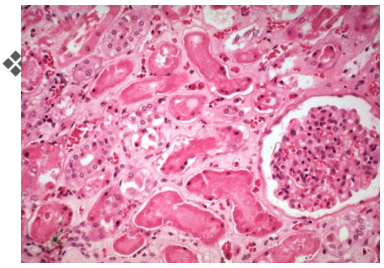
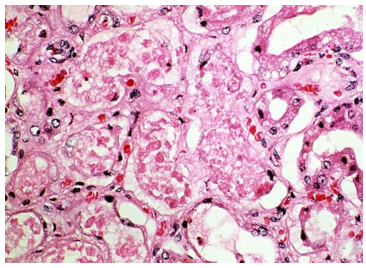
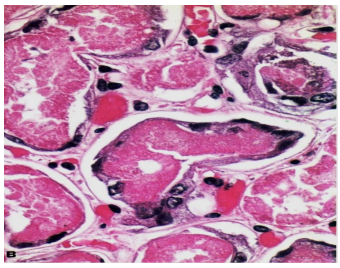
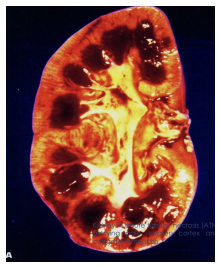
Later:

- epithelial regeneration.

Grossly:

- You can see here part of regeneration of the late stage where tubules become flattened. In regeneration you can see mitosis. Here is all knocked out and you can see the ghost of the cells. You can see there was nucleus here. They will be just resolve and gone.

- You can see grossly all the necrotic tissue and some time regeneration in the periphery .
- Kidney in acute tubular necrosis (ATN) showing pale, swollen cortex and congested medulla.

Treatment of AKI

- Treat underlying etiology(most important thing to do).
- Indications of dialysis:
  1- Metabolic acidosis, hyperkalemia and fluid overload refractory to medical therapy.
  2- Toxins and uremic complications.
- Correction of fluid overload.
- Correction of acidosis.
- Correction of electrolyte imbalance e.g. hyperkalemia.

Summary

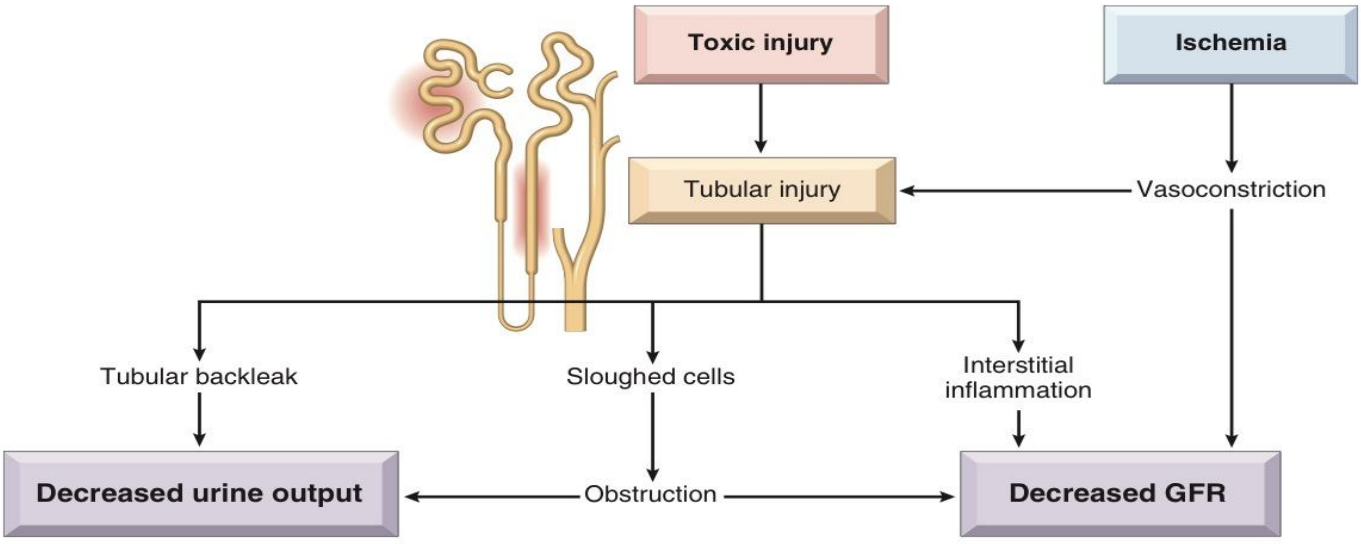


Fig. 14.16 Postulated sequence in ischemic or toxic tubular injury.

SUMMARY

ACUTE TUBULAR INJURY

- ATI is the most common cause of acute kidney injury; its clinical manifestations are electrolyte abnormalities, acidosis, uremia, and signs of fluid overload, often with oliguria.
- ATI results from ischemic or toxic injury to renal tubules, and is associated with intrarenal vasoconstriction resulting in reduced GFR and diminished delivery of oxygen and nutrients to tubular epithelial cells.
- ATI is characterized morphologically by injury or necrosis of segments of the tubules (typically the proximal tubules), proteinaceous casts in distal tubules, and interstitial edema.

Important to know:Toxic injury always affect proximal tubule where the Ischemic have patchy lesions

Summary from pathoma

Acute renal failure (ARF)

BASIC PRINCIPLES

A. Acute, severe decrease in renal function (develops within days)

B. Hallmark is azotemia (increased BUN and creatinine [Cr]), often with oliguria.

C. Divided into prerenal, postrenal, and intrarenal azotemia based on etiology

I-PRERENAL AZOTEMIA :

A. Due to decreased blood flow to kidneys (e.g., cardiac failure); common cause of ARF

B. Decreased blood flow results in J. GFR, azotemia, and oliguria

C. Reabsorption of fluid and BUN ensues , tubular function remains intact.

II-POSTRENAL AZOTEMIA :

A. Due to obstruction of urinary tract downstream from the kidney (e.g., ureters)

B. Decreased outflow results in J. GFR, azotemia, and oliguria.

C. During early stage of obstruction, increased tubular pressure.

D. With long-standing obstruction, tubular damage ensues, resulting in decreased reabsorption of BUN , decreased reabsorption of sodium and inability to concentrate urine .

IV-. ACUTE TUBULAR NECROSIS:

A. Injury and necrosis of tubular epithelial; most common cause of acute renal failure (intrarenal azotemia)

B. Necrotic cells plug tubules; obstruction decreases GFR. 1. Brown, granular casts are seen in the urine. C. Dysfunctional tubular epithelium results in decreased reabsorption of BUN , decreased reabsorption of sodium , and inability to concentrate urine .

D. Etiology may be ischemic or nephrotoxic.

l. Ischemia-Decreased blood supply results in necrosis of tubules.

i. Often preceded by prerenal azotemia

ii. Proximal tubule and medullary segment of the thick ascending limb are particularly susceptible to ischemic damage.

2. Nephrotoxic- Toxic agents result in necrosis of tubules.

i. Proximal tubule is particularly susceptible.

ii. Causes include aminoglycosides (most common), heavy metals (e.g., lead), myoglobinuria (e.g., from crush injury to muscle), ethylene glycol (associated with oxalate crystals in urine), radiocontrast dye, and urate (e.g., tumor lysis syndrome).

E. Clinical features

1. Oliguria with brown, granular casts

2. Elevated BUN and creatinine

3. Hyperkalemia (due to decreased renal excretion) with metabolic acidosis F. Reversible, but often requires supportive dialysis since electrolyte imbalances can be fatal l. Oliguria can persist for 2- 3 weeks before recovery; tubular cells (stable cells) take time to reenter the cell cycle and regenerate

V. ACUTE INTERSTITIAL NEPHRITIS

A. Drug-induced hypersensitivity involving the interstitium and tubules; results in acute renal failure {intrarenal azotemia)

B. Causes include NSAIDs, penicillin, and diuretics.

C. Presents as oliguria, fever, and rash days to weeks after starting a drug; eosinophils may be seen in urine.

D. Resolves with cessation of drug

E. May progress to renal papillary necrosis

VI. RENAL PAPILLARY NECROSIS

A. Necrosis of renal papillae

B. Presents with gross hematuria and flank pain

C. Causes include

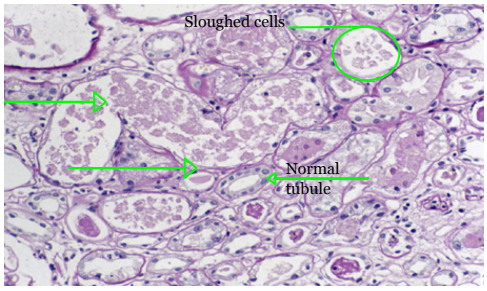
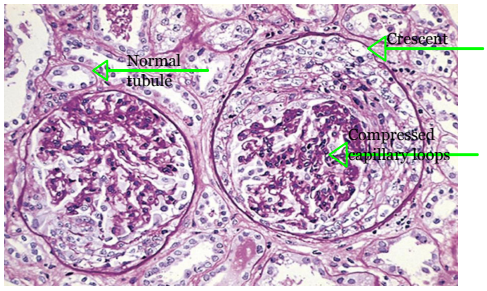
l. Chronic analgesic abuse (e.g., long-term phenacetin or aspirin use)

2. Diabetes mellitus

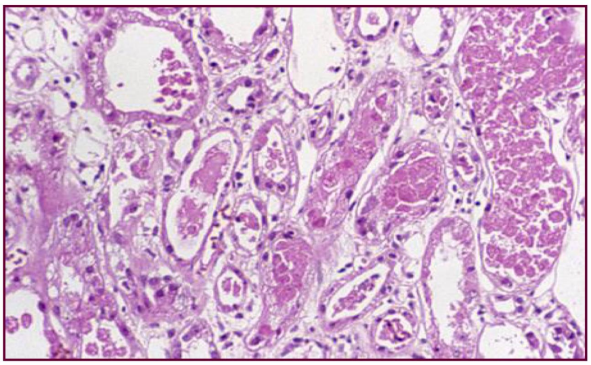
3. Sickle cell trait or disease

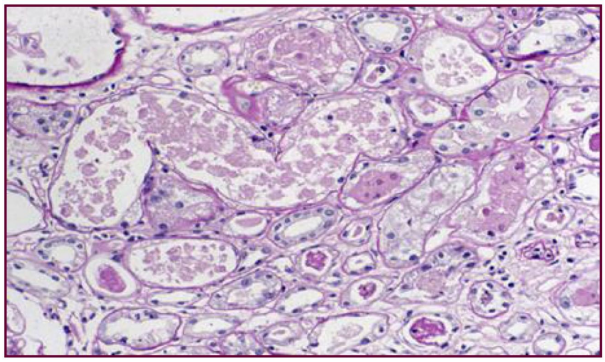
4. Severe acute pyelonephritis

Histopathology Of Acute Kidney Injury

Disease	Acute Tubular Necrosis	Rapidly Progressive Glomerulonephritis (Crescentic GN)
Pictures		
Prominent Features	○ Vacuolated cells. ○ Sloughed, **necrotic cells in tubular lumen**. ○ Some tubules lined by **flat epithelium**. ○ There is no brush boards	○ **Crescents** composed of proliferating epithelial cells. ○ Glomerular injury and crescents with monocytes and macrophages proliferation compressing the glomerulus. ○ Can show mesangial proliferation. ○ It is an emergency.
Notes/ Comparisons	○ The first things that you should look at is brush borders and edema. ○ Basement membrane is **not affected** in RPGN. ○ Acute kidney injury shows **multiple muddy brown granular casts** in urine sediment. ○ If inflammation is in interstitium the main feature will be inflammatory cells. Eosinophils will be prominent. ○ Stains that can be used in acute kidney injury: → H&E → PAS (Periodic acid–Schiff stain) → Silver stain → Trichrome stain	

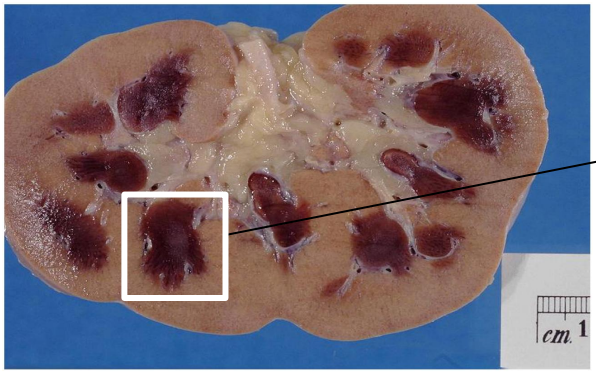
Questions





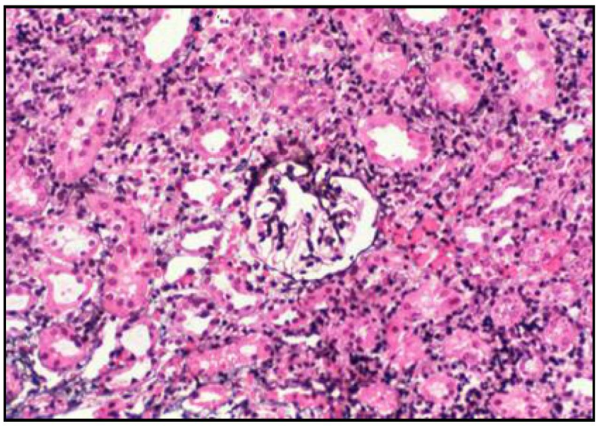
1- a 23 y.o male comes to the hospital for hypotension and fluid retention. A biopsy was taken from his glomerular tubule was shown **flat epithelium** and **necrosis** "**manifest by vacuolated cells and sloughed, necrotic cells in tubular lumina**" what is the most likely diagnosis?

A) acute interstitial nephritis
B) acute tubular necrosis
C) acute kidney injury
D) acute Glomerulonephritis



2- Pathologic kidney specimen showing marked pallor of the cortex, contrasting to the darker areas of surviving medullary tissue. The patient died with.....

A) acute interstitial nephritis
B) acute tubular necrosis
C) acute kidney injury
D) acute Glomerulonephritis

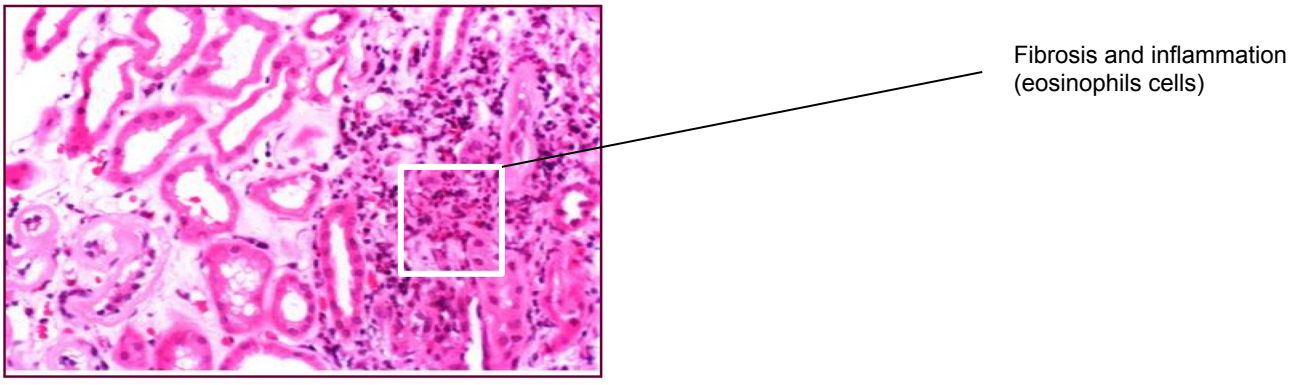


3- a biopsy of 34 y.o female shows **edema** associated with an **interstitial lymphoplasmacytic infiltrat**e. She diagnosed with Acute Interstitial Nephritis, what is the most likely cause?

A) Ischemia
B) acute Glomerulonephritis
C) Thromboemboli
D) Viral infection

4- in this disease the glomeruli are uninvolved, unless there is an associated **minimal change disease-type injury** caused by.....

A) NSAIDs
B) ACE inhibitors
C) CCBs
D) ARBs



5- a histopathologic was taken of female came with tachycardia and Oliguria. It shows **edema** and **fibrosis** also, prominent interstitial **eosinophilic component**, **lymphocytes** and **plasma cells**. The doctor said it caused by **drug-induced hypersensitivity** what is the diagnosis?

A) acute interstitial nephritis
B) acute tubular necrosis
C) acute kidney injury
D) acute Glomerulonephritis

Q6: which stain do we use in order to highlight the basement membrane of the capillaries and the tubular epithelium ?

1 – PAS stain (periodic acid-schiff-diastase stain)
2 – safranin
3 – osmium tetroxide
4 – Bismarck brown

Q7: which of the the following may cause post-renal kidney injury ?

1 – acute interstitial nephritis
2 – renal vein thrombosis
3 – kidney stones
4 – acute tubular necrosis

Q8: in case of acute interstitial nephritis which part of the nephron is uninvolved ?

1 – glomerulus
2 – proximal convoluted tubules
3 – distal convoluted tubules
4 – ascending part of Henle's loop

Q9: which of the following drugs may cause acute interstitial nephritis ?

1 – NSAIDS
2 – Amphotericin B
3 – Aminoglycosides
4 –infliximab

Q10: which type of inflammatory cells is more prominent in case of acute interstitial nephritis ?

1 – macrophages
2 – eosinophils
3 – neutrophils
4 – basophils

Q11: in case of polycystic kidney disease which part of the kidney the cysts can arise from ?

1 – cortex
2 – medulla
3 – renal pelvis
4- renal papilla

Q12-haemorrhage, fluid loss are causes of **:**

A- prerenal AKI

B- post-renal AKI

C- Intrinsic

Q13- Which of the following is the most affected by the toxic drugs ?

A- proximal tubule

B- distal tubule

C- collecting duct

D- Glomerulus

Q14-Outpatient associated with an increased risk of :

A- renal AKI

B- prerenal AKI

C- post-renal AKI

Q15- in one of the following, we don't need to do dialysis In ARF:

A- oliguria: <400cc/24hr

B- Arrhythmia

C- ICU stay

D- neuropathy

Q16-Which of the following one is an endogenous toxins:

A- Myoglobinuria

B- Aminoglycosides t

C- Amphotericin B

D- radiocontrast dye

1- B
2- C
3- D
4- A
5- A
6-1
7-3
8-1
9-1
10-2
11-1
12- A
13- A
14- B
15- D
16- A

17-In acute renal failure lab results show a rapid ..... in serum creatinine or ..... in urine output.
A- increase, increase
B-increase, decrease
C- decrease, increase
D-decrease, decrease

18- a clinical syndrome associated with fluid, electrolyte, hormone imbalance and metabolic abnormalities
A- Anuric
B- Uremia
C- Azotemia
D- Oliguric

19- A condition mostly related to older male considered as a post renal cause of Acute renal failure
A- prostatic hyperplasia
B-Stones
C-Tumor in the bladder
D-congenital abnormality

20-which one of these considered as a Tubular cause of Acute renal failure
A- Acute glomerulonephritis
B- NSAIDS
C- Thromboembolic disease
D- Hemoglobinuria

1- B
2- C
3- D
4- A
5- A
6-1
7-3
8-1
9-1
10-2
11-1
12- A
13- A
14- B
15- D
16- A
17-B
18-B
19-A
20-D

» قُلْ هَلْ يَسْتَوِي ٱلَّذِينَ يَعْلَمُونَ وَٱلَّذِينَ لاَ يَعْلَمُونَ «

سورة الزمر الآية ٩

القادة

فاطمة بالشرف **عبدالله العمر**

الأعضاء

ريناد الغريبي
منيرة المسعد
شوق القحطاني
رزان الزهراني
بتول الرحيمي
فاطمة الديحان
الجوهرة الشنيفي
نورة القاضي
غادة الحيدري
بلقيس الراجحي
غرام جليدان
آلاء الصويغ
ال فهدة السليم
شيرين حمادي
رناد الفرم
نورة الحربي
ميعاد النفيعي
مجد البراك
رهام الحلبي

عبدالجبار اليماني
عبدالله المعيذر
معن شكر
سيف المشاري
عبدالعزيز الجهني
محمد العمر
خالد المطيري
عبدالعزيز العبدالكريم
ماجد الجهني
منصور العبرة
أنس السيف
راكان الغنيم
فايز الدرسوني
خالد العقيلي
بندر الجماز
طارق العلوان
سلطان بن عبيد
تركي الشمري
محمد الأصقه
أحمد الصبي
سعد الفوزان