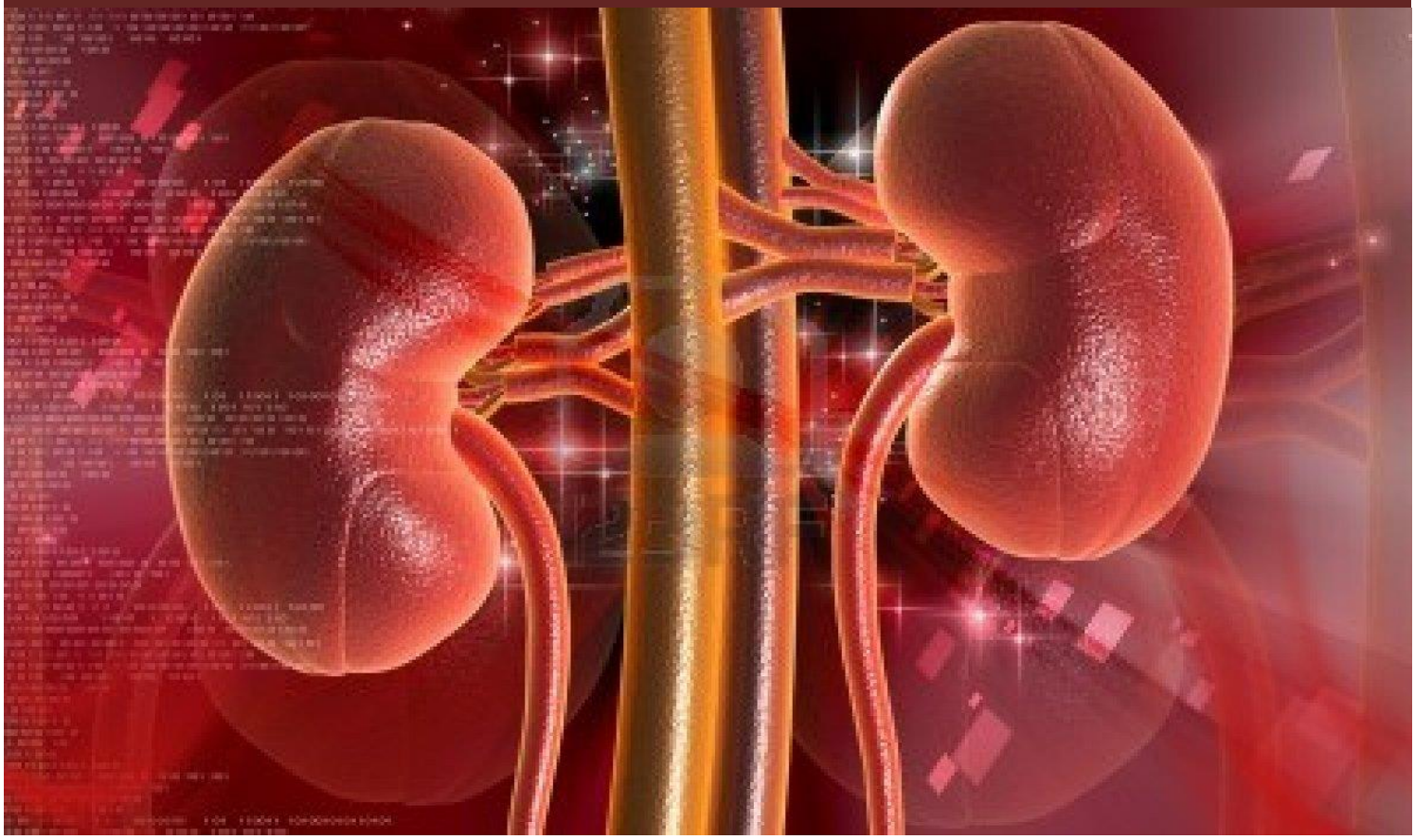

Lecture One

Acute Kidney Injury

432 ***Pathology*** *Team*

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Reviewed By: Dana *Al-Dubaiab &* ***Ammar*** *Al-Yamani*

Renal Block

NOTE: female-side notes are written in purple. Info in the handout not mentioned by Prof. Al-Rikabi are in GREY

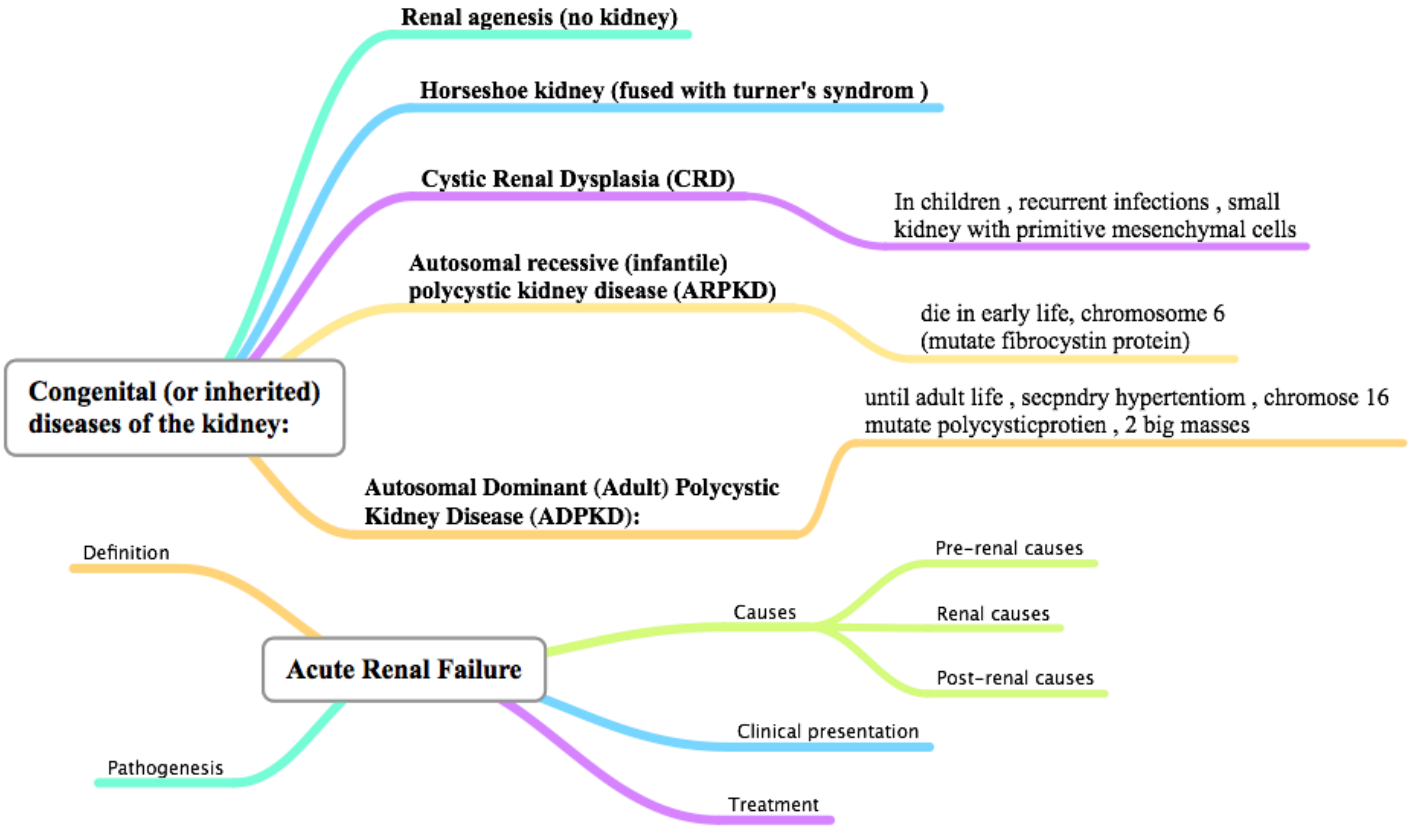
Acute Kidney Injury

Lecture Objectives:

At the end of this lecture the student should be capable of:

- Describe the guidelines of the renal biopsy.
- Recognize the types of acute kidney injury.
- Recognize the clinical manifestations of acute kidney injury.
- Describe the pathological findings in acute kidney injury.

Mind Map:



Congenital (or inherited) diseases of the kidney:

A- Congenital Abnormalities of the kidney:

REMEMBER:

Congenital diseases: are diseases that appear with birth, it is *not necessary that they are inherited.*

Inherited diseases: *are diseases that result* ***from gene mutations or complications****. These diseases pass from the parents to the children and so on.*

1- **Renal agenesis** → Kidneys are absent.

There are two types of agenesis:

A. Unilateral agenesis:

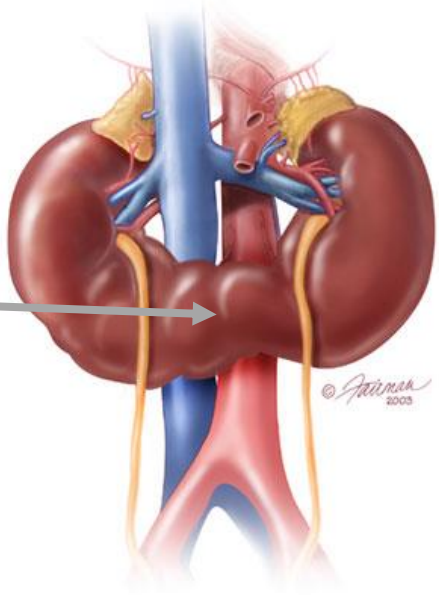
That means he has only one kidney which is compatible with a normal life. It may only be discovered incidentally at autopsy.

B. Bilateral agenesis:

Means the absence of both kidneys. Which usually will leads to death in uterus.

2- **Horseshoe kidney:**

The upper or lower poles (usually) of the kidneys are fused "picture". This type of kidney malformation may be found in fetuses/children who have chromosomal abnormalities such as Turner's syndrome (45x).

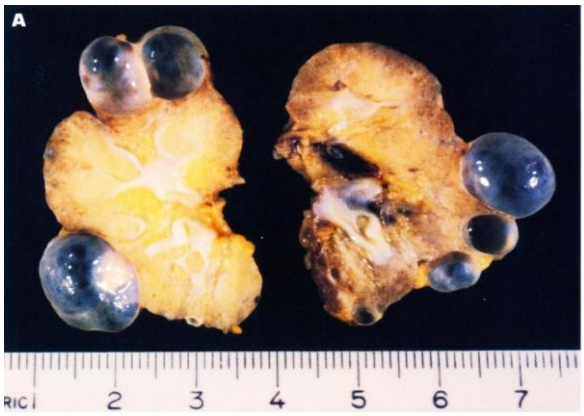


Congenital cystic diseases of the kidney

A- Cystic Renal Dysplasia (CRD)

CRD → Congenital (Children)

Cystic Renal Dysplasia is a congenital disease (not inherited)
It is the commonest cystic renal disease **in children**.



- The kidneys are usually malfunctioned.
- There are various degrees of renal failure
- The patient has recurrent infections.
- The kidneys are small, shrunken and **have cysts** (picture)
- Caused by disorganized renal development.
- Can be unilateral or bilateral.
- Often associated with poorly formed ureter.
- Rarely part of a syndrome.

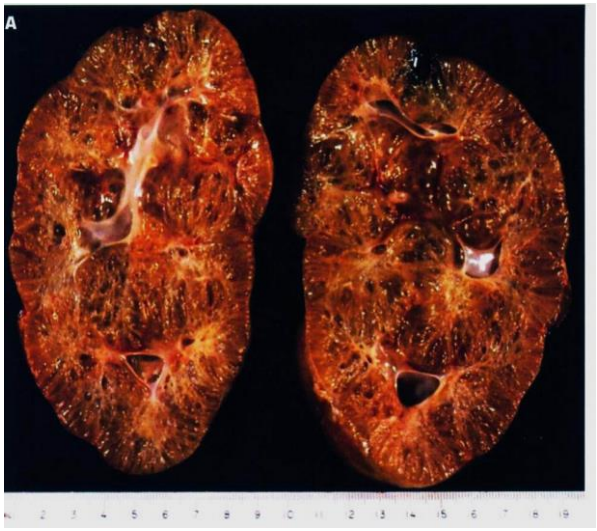
A histopathologic section from this cyst shows primitive mesenchymal cells which are undifferentiated. Also you will find cartilage and sometimes bone.

(Unfortunately we couldn't find an appropriate picture)

REMEMBER: mesenchymal cells = connective tissue cells

B- Autosomal recessive (infantile-childhood) polycystic kidney disease (ARPKD):

The mutated gene (PKHD1) → on chromosome 6



ARPKD is an inherited disease which transforms the kidney into a bag full of cysts having a (spongy like appearance).
the kidney is **full of cysts**.Those cysts occupie the cortex and the medulla. In addition, the kidneys are a little enlarged "Picture".

Pathogenesis:

It is an inherited disease. Patients have a mutated gene in **chromosome 6 which is called (PKHD1).** This gene in normal life encode for a protein called "**fibrocystin protein**"[1]. So, when this protein is impaired due to the mutated gene, you get the disease.

- Rare, 1 case per 20,000 live births.
- Liver also always affected.
- **Large kidneys at birth or early life (may cause death soon after birth due to renal failure).**

"From robbin's basic pathology"

The result from **mutations in a gene *PKHD1,*** coding for a putative membrane receptor protein called ***fibrocystin***[1]***,*** localized to **chromosome 6p**. Fibrocystin[1] may be involved in the function of cilia in tubular epithelial cells.

Complications :

- It is incompatible with long life. That means he may live his childhood normally, but then he will die due to **renal failure**.
- This disease also causes hypertension

[1] Fibrocystin is a large, receptor-like protein that is thought to be involved in the tubulogenesis and/or maintenance of duct-lumen architecture of epithelium.

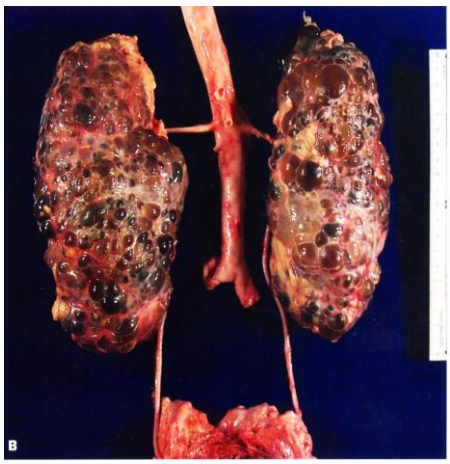
C- Autosomal Dominant (Adult) Polycystic Kidney Disease (ADPKD):

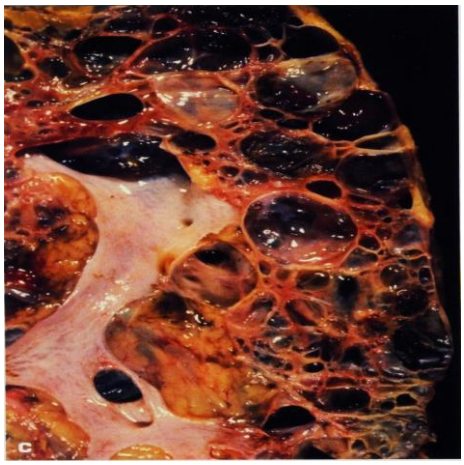
The mutated gene (PKD1) → On Chromosome 16

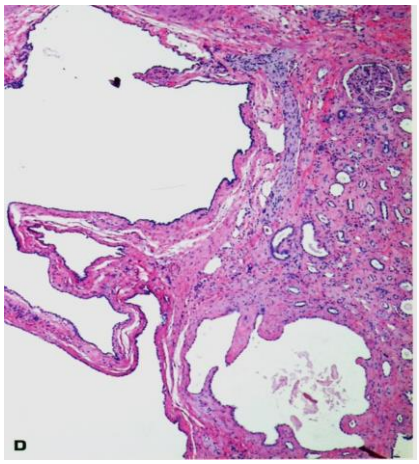
REMEMBER: **ADPKD** is one of the **rare causes of secondary hypertension**

ADPKD is an inherited dominant disease (will be transmitted to all the children). In addition, it is compatible with the patient until he reaches adulthood. They can live until the age of 40 or 50.

- Progressive distention of kidney by enlarging cysts.
- 1-2 cases per 1000 live births
- Usually present in adults.
- About 10% require dialysis/ transplantation
- The gross and histology will show a lot of cysts in the kidney **"picture"**.

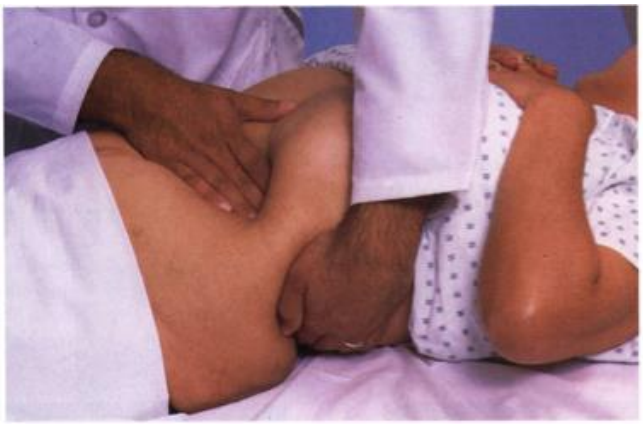






Clinical presentation:

1- **Renal failure**
2- **Hypertension**
3- **Kidneys are very large and readily palpable abdominally as masses extending into the pelvis "Picture".**
4- **Earthy look due to anemia.**
5- **Hematuria**
6- **Azotemia (↑creatinine and urea)**



Pathogenesis:

There is a gene mutated which also called **polycystic kidney disease (PKD) gene**. That encode for **polycystic protein** which has 2 types: **polycystin 1 and polycystin 2**. **("PKD1" 85% of cases is on the chromosome 16**) and (**PKD2** 15% of cases, is on **chromosome 4**) and 10% new mutations.

So, when this protein is impaired due to the mutated gene, you get the disease.

"From robbin's basic pathology"

The *PKD1* gene are present in all renal tubular cells of affected persons, cysts develop in only some tubules. This is most likely due to loss of both alleles of *PKD1.* The *PKD2* gene, implicated in 10% to 15% of cases, resides on chromosome 4 and encodes *polycystin 2*

Complications :

1- **Renal failure**
2- **cysts in liver**
3- **cysts in pancreas**
4- **cysts in spleen**
5- **abnormal coronary arteries**
6- **aneurysms in the cerebral arteries**

The patient may die from one of these complications.

D- Medullary sponge kidney

- Dilated collecting ducts give "spongy" appearance. Cyst in the medulla
- 1 case per 5000 population.
- May present with renal infections in adult life.
- No obvious genetic link.

Summary: "from robbin's"

- **Adult polycystic kidney disease is an autosomal dominant disease caused by mutations in the genes encoding polycystin-1 or -2; it accounts for about 10% of cases of chronic renal failure; kidneys may be very large and contain many cysts.**
- **Autosomal recessive (childhood) polycystic kidney disease is caused by mutations in the gene encoding fibrocystin; it is less common than the adult form and strongly associated with liver abnormalities; kidneys contain numerous small cysts**
- **Nephronophthisis -Medullary cystic disease is being increasingly recognized as a cause of chronic renal failure in children and young adults; it has a complex inheritance, and is associated with mutations in several genes that encode epithelial cell proteins called nephrocystins that may be involved in ciliary function; kidneys are contracted and contain multiple small cysts.**

Acute Renal Failure

A) Acute Renal Failure

Acute Renal Failure is an **acute medical emergency**. The **patient is treated in the ICU**. He has to be intubated and given oxygen and antibiotics. Also, he has to be on dialysis (a machine that replaces the job of the kidney when it can't perform appropriately). Some of these patients are **surgical patients**. The condition is mainly manifested by **acute tubular necrosis** **ATN** **the most common cause of acute renal failure.**

The causes of acute renal failure:

A- Pre-renal causes → Reduce blood volume

- **Massive hemorrhage due to:**
  1- Massive trauma
  2- Major surgical operation
  3- Complicated delivery or obstetric operation.
- **Disseminated intravascular coagulation (DIC).**

B- Renal causes → Problems in the kidney

In the patients who has one of the following:

1- Very severe and fulminant glomerulonephritis. Most important cause
2- Very severe interstitial nephritis caused by drugs or toxins especially those who take **gentamicin** which (a type of antibiotics toxic to renal tubules and causes interstitial nephritis).
3- Direct injury to **the proximal renal tubules** from **exposure to mercury or mercuric compounds** such as: mercuric chloride which is toxic to renal tubules and several other toxic substances.
Ethylene glycol (antifreeze) is extremely toxic when ingested and can result not only in acute tubular necrosis but also in renal oxalosis with massive intratubular oxalate crystal deposition that can be visualized under polarized light.

C – Post renal→caused by obstructive lesions

Which makes an obstruction of the like:

1- Compressing tumor
2- Compressing mass
3- Kidney stones
It is rarely cause the ARF.

Pathogenesis:

The acute condition is most frequently precipitated by **renal ischemia**, which is often caused by **prolonged hypotension or shock**, most often induced by **gram-negative sepsis**, **trauma or hemorrhage**. Another associated condition is **crush injury with myglobinuria**. Myoglobinuria also can be observed after intense exercise , but this is not of clinical consequence

Hemorrhage → Hypoxia → Ischemia → Acute tubular necrosis → Acute renal failure

Clinical presentition:

1- **Oliguria:** it is defined as a urine output that is **less than 400 mL per 24h**.
2- **Anuria:** the nonpassage of urine.
3- **Acid base disturbance:** such as: acidosis, alkalosis
4- **Electrolytes imbalance:** such as: Na+, K+, Ca++...etc.
5- **Raised Creatinine and urea (Azotemia).**
6- **Earthy look and pale**

This condition can also lead to cardiac standstill from hyperkalemia, most often during the initial oliguric phase.

ARF is an injury at the level of tubule and tubular epithelium which are stable cells that can regenerate when needed to. So, the necrotic renal tubular cells are replaced by new cells in **approximately 2 weeks later**, with complete return of renal function to normal if the patient is **maintained on dialysis**

The treatment:

The treatment is **Dialysis**.

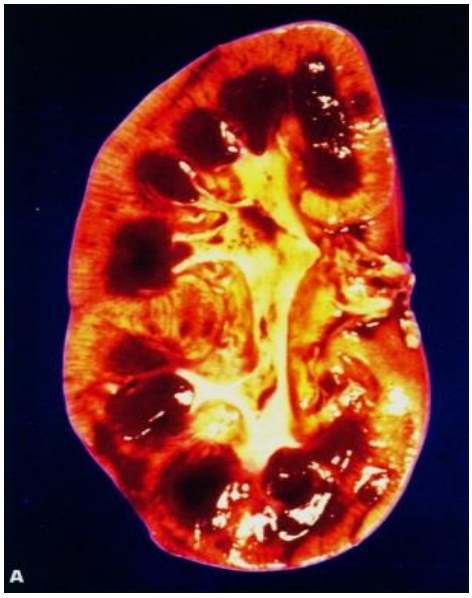
There are **two types of dialysis**:

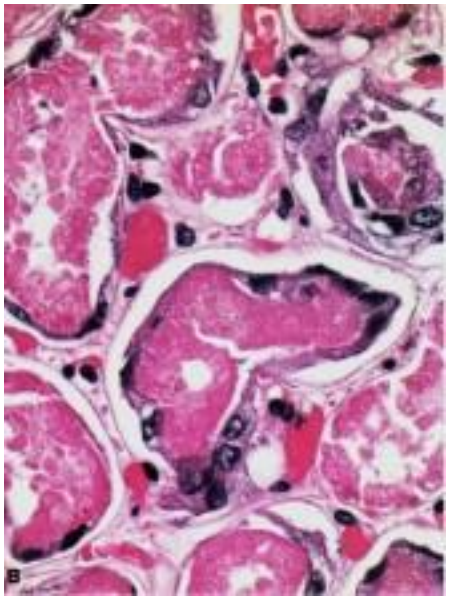
1- **Peritoneal dialysis**: This uses the patient's peritoneum in this process.
2- **Hemodialysis**: remove of waste products such as creatinine and urea from the blood.

After 1 week, the patient starts to recover.

Gross and histopathology:

GROSS: The kidney shows the cortex Precongested and sometimes areas of hemorrhages "picture A".





A microscopic section shows the tubules and especially the proximal tubule and the ascending Thick limb, necrotized, absence of the nuclei or apoptotic nuclei, loss of cell borders and the presence of cellular casts inside the tubule "picture B"

Summary: "from robbin's"

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

MCQ'S from 431 team's work

1- Which one of the following is the most common cause of acute renal failure:

A. Autosomal recessive polycystic kidney disease

B. Acute tubular necrosis

C. Autosomal dominant polycystic kidney disease

D. Cystic renal dysplasia

2- Ischemic acute tubular necrosis occurs most commonly in association with:

A. Septic shock

B. Ruptured aneurysm

C. Carcinoma of prostate

D. Hydronephrosis and pyelonephritis

E. Malignant hypertension

3- Which one of the following is the commonest cystic renal disease in children:

A. Autosomal recessive polycystic kidney disease

B. Acute tubular necrosis

C. Autosomal dominant polycystic kidney disease

D. Cystic renal dysplasia

4- Which one of the following is the mutation gen in Autosomal recessive polycystic kidney disease:

A. Chromosome 8

B. Chromosome 6

C. Chromosome 7

D. Chromosome 11

Answers

1	**B**
2	**A**
3	**D**
4	**B**

Questions from Pathology recall book

1) **What is the most common cause of acute renal failure?**
   - Acute tubular necrosis

2) **What is the most common cause of acute tubular necrosis?**
   - Ischemia **(Toxins are second most common cause)**

3) **Name 4 causes of renal ischemia.**
   - Hypotension
   - Shock due to Gram negative sepsis
   - Trauma
   - Hemorrhage

4) **What is the prognosis in acute tubular necrosis?**
   - Most cases are reversible with complete recovery.

اللهم إني استودعتك ما قرأت و ما حفظت و ما تعلمت فرده عليّ عند حاجتي اليه انك على كل شيء قدير

432 Pathology Team

*Good Luck ^_^*