النادي الطبي

GENITOURINARY SYSTEM

SUBJECT : Pathology

LEC NO. : 5

DONE BY :

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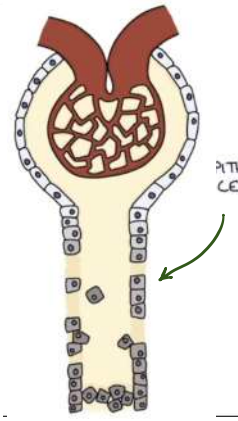
وقل رب زدني علماً

GENITOURINARY SYSTEM

اقرأوا هاي الصفحة
كمقدمة **مهمة جدا**
لتفهمو الموضوع بسرعة



ACUTE TUBULAR NECROSIS
- Sudden
- DAMAGE & DEATH
- RENAL TUBULES

EPITHELIAL CELLS

→ MOST COMMON CAUSE OF ACUTE KIDNEY INJURY

→ DUE TO ISCHAEMIA OR TOXINS — as severe hypotension, shock, or decreased blood flow to the kidneys

→ REVERSIBLE

→ 7-21 DAYS FOR RECOVERY

The necrosis of tubular cells leads to disruption of kidney function, impairing the kidneys' ability to regulate fluid and electrolyte balance, filtration , excrete waste products, and maintain acid-base balance. As a result, individuals with acute tubular necrosis may experience symptoms such as (oliguria), electrolyte imbalances (such as hyperkalemia or metabolic acidosis), fluid retention, and uremia (accumulation of waste products in the blood).

* → MUDDY BROWN CASTS

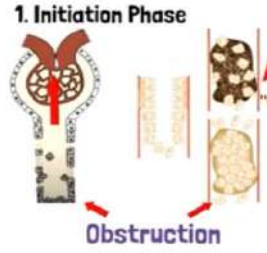
↳ PATHOGNOMONIC FOR ATN

WBCs casts ----> Acute pyelonephritis
RBCs casts ---->nephritis
' Hyaline casts ---> nephrotic syndrome

تزكروا انه

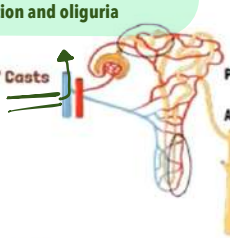
Detachment in Epithelial cells
Shedding the cells off
Casts
Accumulation in the lumen of the tubules causing obstruction and oliguria

1. Initiation Phase



"Granular Muddy Brown " Casts

GFR ↓



Proximal Convoluted Tubule

Ascending loop of Henle

Obstruction

NO production (vasodilator) ↓

GFR ↓

Free Radical Formation

Toxic effects ↑

2.Maintenence Phase

very low

GFR ↓↓

Oliguria

Uremia

1-3 weeks

3.Recovery Phase Reversible زي ما حكينا انها

Regeneration of tubular epithelial cells

Polyuric/Diuresis

BUN and serum creatinine ↓

بس المشكله بهاي المرحلة الخلايا بتكون لسه غير ناضجة فبتكون غير قادرة على الامتصاص او تركيز

ACUTE TUBULAR NECROSIS (ATN)

- characterized morphologically by damaged tubular epithelial cells and clinically by acute suppression of renal function with oliguria(urine flow of <400 mL/day)..
- It is the most common cause of acute renal failure (ARF).
- Other causes of ARF are:
- (1)Severe G diseases, manifesting as RPGN,
- (2) Acute papillary necrosis associated with acute PN,
- (3) Acute drug-induced interstitial nephritis (Paracetamol)
- (4) Diffuse cortical necrosis.
- (5) Diffuse renalvascular diseases, e.g., microscopic polyangiitis & thrombotic microangiopathies.

بينما ال chronic كان سببه مثلاً
chronic glomerular nephritis
chronic pyelonephritis or benign hypertension

ACUTE TUBULAR NECROSIS (ATN)

ازا ما تعالجت بشكل صحيح ممكن تتحول ل irreversible changes

- is a reversible condition if treated properly and quickly.
- Clinical manifestations:
- electrolyte abnormalities, acidosis, uremia, signs of fluid overload, often oliguria.
- Proximal tubular epithelial cells are particularly sensitive to hypoxemia and toxins.
- ATN is quite frequent disorder that can arise in many clinical settings, in one of 2 patterns:
- (1st) Ischemic ATN cause by shock, in which a period of hypotension & shock is common in most of these settings (ranging from severe trauma to acute pancreatitis to septicemia) . A similar picture can be produce by mismatched blood transfusions, hemolytic crises, & myoglobinuria.
- (2nd)Nephrotoxic ATN , is caused by a variety of poisons, including heavy metals(e.g., mercury); organic solvents(e.g., CCl4); & drugs such as gentamicin& other antibiotics, & radiographic contrast agents e.g., those used for angiogram.

why!! In ATN, the necrosis and dysfunction of tubular cells impair their ability to excrete hydrogen ions (H^+) and reabsorb bicarbonate ions (HCO_3^-), leading to decreased acid excretion and metabolic acidosis

من هون بدي نكون عارفين معلومه مهمة جدا جدا و رح تتكرر تحت انه ، PCT اكتر اشي بتأثر بال toxic ATN كونه بوصله السموم قبل ال DCT و بكون بتراكيز اعلى و بالتالي ضرر اكبر لكن ال DCT اكتر مكان بتأثر بال ischemic ATN لانه اتجاه انتقال الدم من PCT الى DCT

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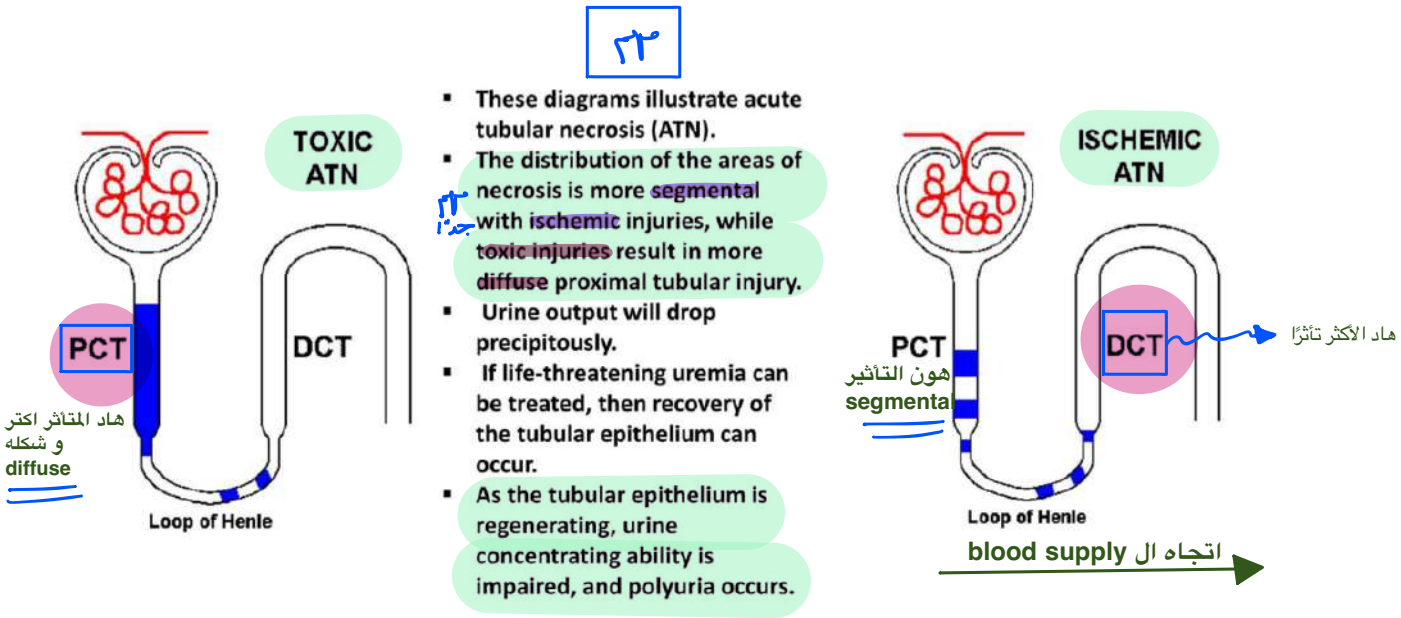
PATHOGENESIS OF ATN

- Tubular epithelial cells are vulnerable to **toxins**& very sensitive to **anoxia**. **Therefore**, the 2 major factors in the pathogenesis of both ischemic & nephrotoxic ATN are:
- **(1) tubular injury.**
- (2) persistent & severe **ischemia** caused by **intrarenal** vasoconstriction, resulting in both: (a) decrease **G** plasma flow, resulting in decrease **GFR**& (b) decrease **O2** delivery to the functionally important tubules in the outer medulla .

بسبب **hypoperfusion** ف بصير في **VC** (شغلنا نظام **renin angiotensin**)لنحاول نرفع الضغط و كمان بصير القلب يضخ اكتر لانه بفكر انه ما عم يوصل دم للكليه بسبب مشكله بالقلب لكن هو المشكله مش بالقلب ، المشكله بأنابيب الكليه و بنتهي المطاف بالاصابة بالضغط



- These diagrams illustrate acute tubular necrosis (ATN).
- The distribution of the areas of necrosis is more segmental with ischemic injuries, while toxic injuries result in more diffuse proximal tubular injury.
- Urine output will drop precipitously.
- If life-threatening uremia can be treated, then recovery of the tubular epithelium can occur.
- As the tubular epithelium is regenerating, urine concentrating ability is impaired, and polyuria occurs.

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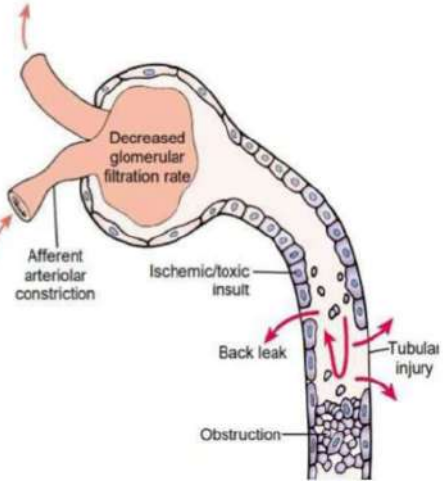
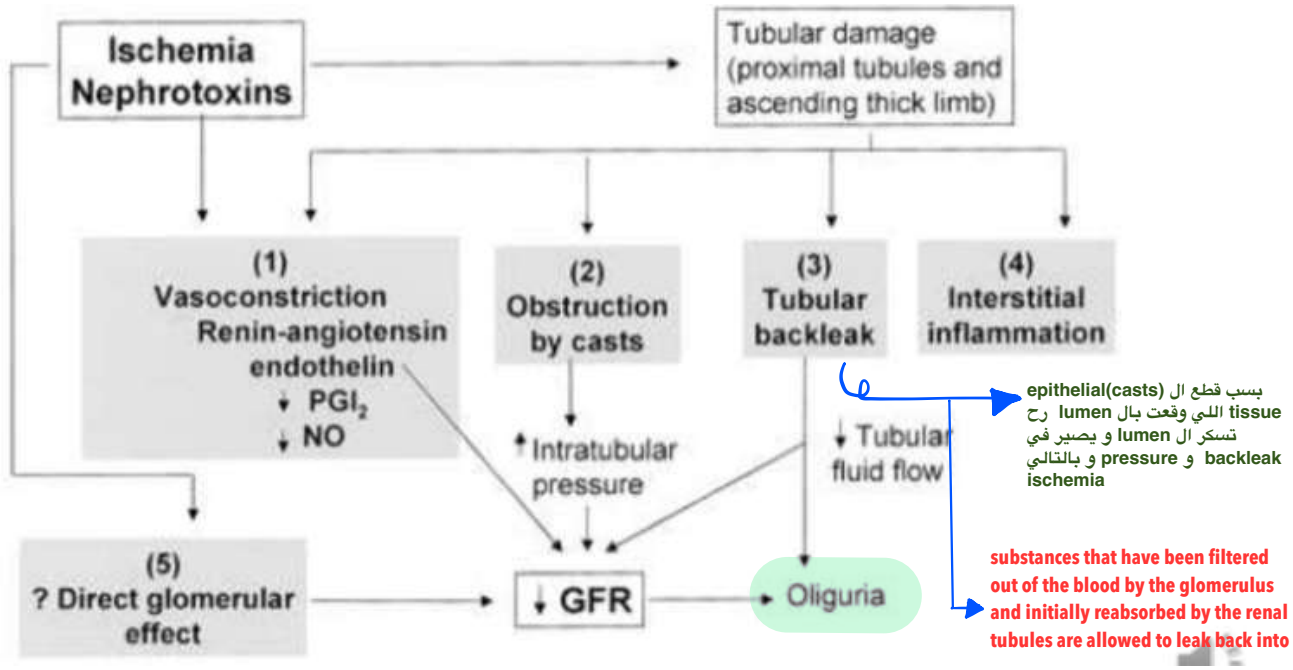
- Pathogenesis of acute tubular necrosis.
- Sloughing and necrosis of tubular epithelial cells leading to obstruction and increased intraluminal pressure, which reduces globular filtration.



ازا متل ما لاحظنا بالبدايه كان في oligurea و بعدها بمرحله ال recovery صار في polyuria و قل تركيز البول



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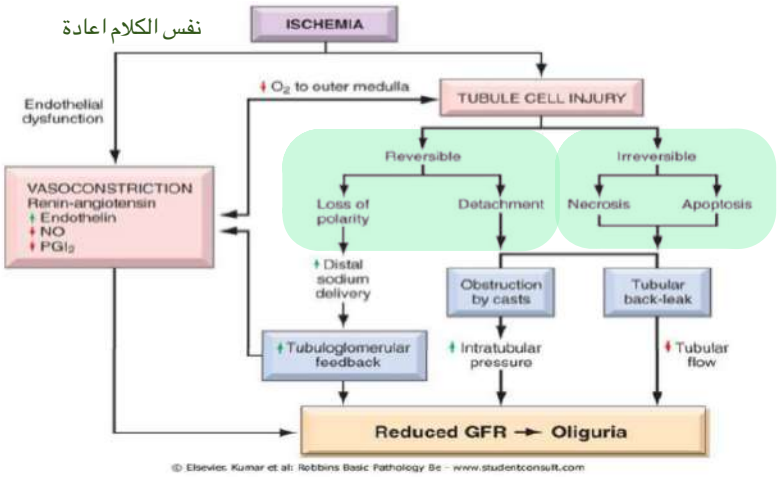

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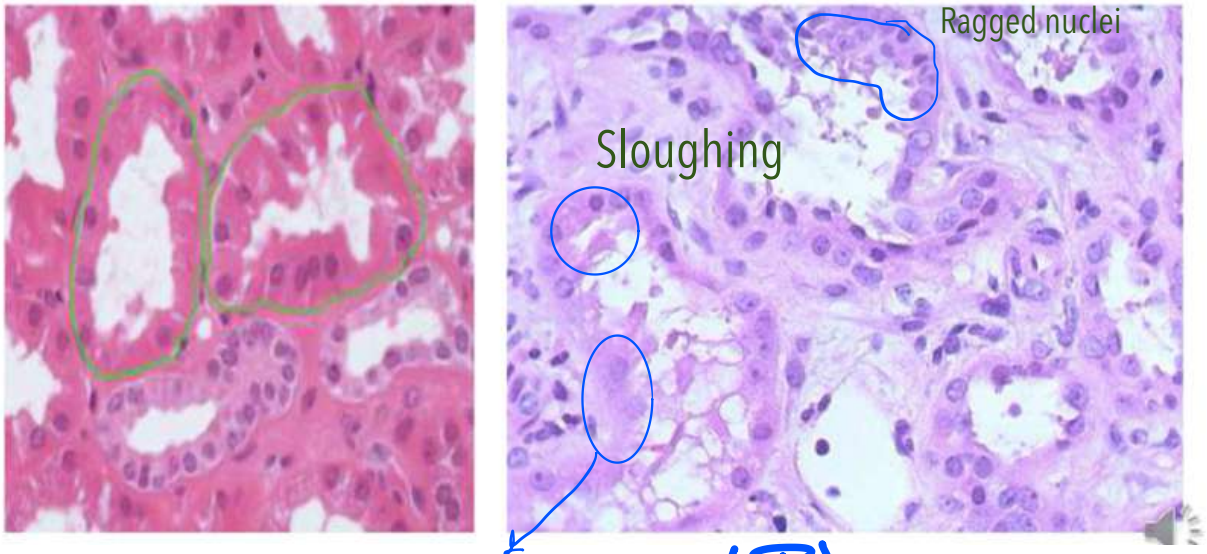
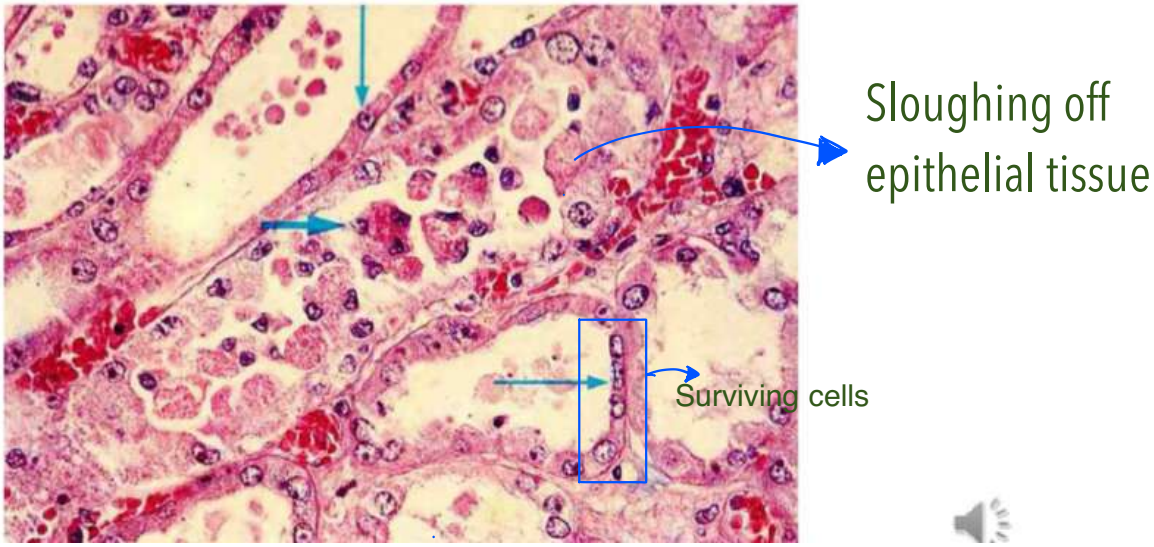
The epithelium of the tubules seen here is ragged from undergoing necrosis with acute tubular necrosis (ATN) from ischemia. In this case, heart failure with hypotension precipitated the ATN. This is one form of acutee kidney injury (AKI) with an abrupt or rapid decline in renal function. (A) left one IS NORMAL TUBULES , (B) right one is Acute tubular necrosis



Acute Tubular Necrosis: kidney. Patient died from RF, 7 days following pericardiectomy for constrictive pericarditis (1) Most of the collecting tubules epithelial cells are **died&** the necrotic cells are sloughed into the lumen (**thicken** arrow). (2) The **surviving** cells attempts at **repair&** already the tubules are lined by flat epithelium (**thin** arrow).



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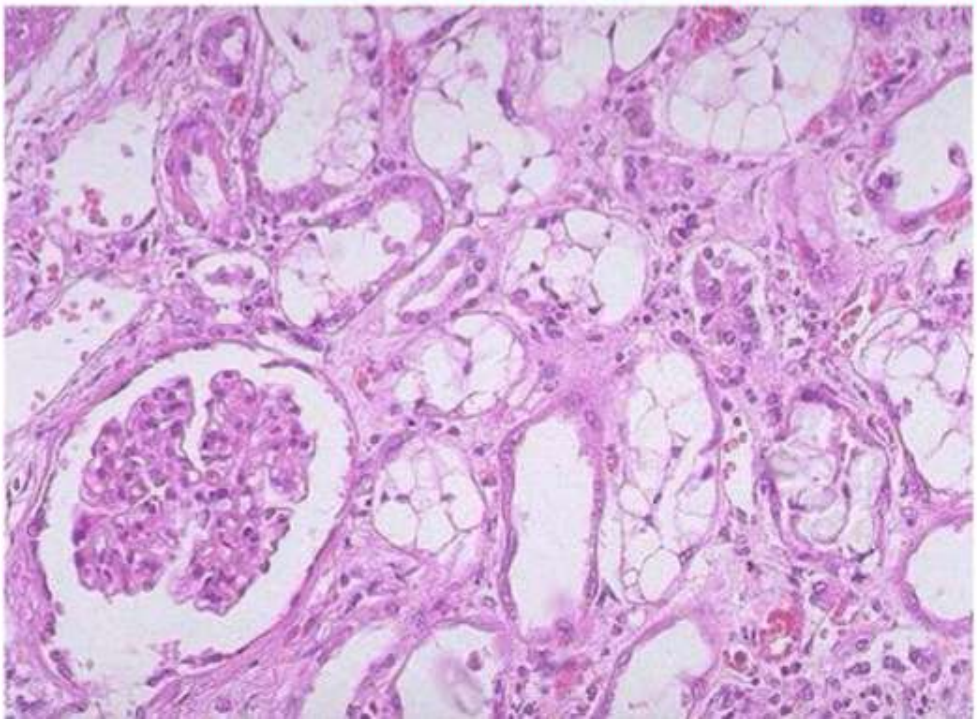
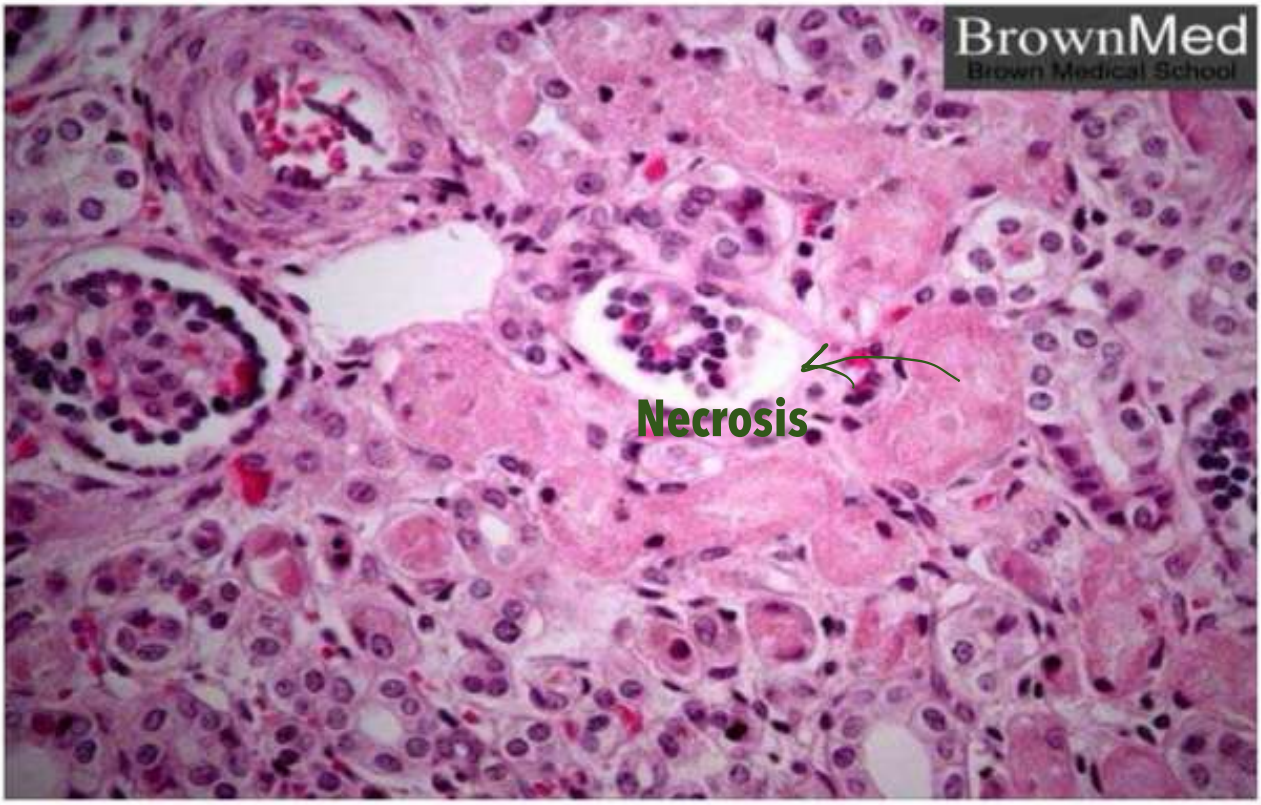
ATN MORPHOLOGY

- **Renal biopsy shows:**
- 1. Blebbing; vacuolization; **necrosis & detachment** of tubular cells from their underlying BM & their **sloughing** in the lumen
- 2. **Proteinaceous casts** in the distal tubules & collecting ducts is a **striking** additional finding. They consist of **Tamm-Horsfall protein (secreted normally by tubular epithelium)** along with hemoglobin & other plasma proteins.
- 3. When **crush injuries** have produced ATN, the casts are composed of **myoglobin**

The tubular vacuolization and tubular dilation here is a result of the toxic effect of ethylene glycol poisoning. This is representative of acute tubular necrosis (ATN), which has many causes. ATN resulting from toxins usually has diffuse tubular involvement, whereas ATN resulting from ischemia (as in profound hypotension from cardiac failure) has patchy tubular involvement.



Note necrosis and sloughing of epithelial cells of the proximal convoluted tubules. The glomeruli and distal convoluted tubules are preserved.



ATI-MANAGEMENT

موكتير بهم الدكتورة

- repair and tubular regeneration → gradual clinical improvement
- With supportive care, patients who survive have a good chance of recovering renal function
- those with preexisting chronic kidney disease, complete recovery is less frequent

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DISEASES INVOLVING BLOOD VESSELS

- All kidney diseases involve the renal BV **secondarily**.
- Systemic vascular diseases, e.g., **arteritis**, also involve renal BV, & often the effects on the kidney are clinically important.
- The kidney is intimately involved in the pathogenesis of both essential & secondary **hypertension(H)**

renal blood vessels عاده الامراض اللي بتصيب
not Limited to the kidney يعني systimatice disease بتكون نتيجه
arthritis , vasculitis , hypertension or diabetes متل

BENIGN NEPHROSCLEROSIS (HYALINE ARTERIOLOSCLEROSIS)

- Term used for the renal changes in benign Hypertention.
- Some degree of benign nephrosclerosis, albeit mild, is present at autopsy in many persons older than 60 years of age.
- But the frequency & severity of the lesions are increase at any age when H or DM are present.
- It is associated with **aging, hypertension, diabetes mellitus and may be seen in response to certain drugs (calcineurin inhibitors).**
- **In malignant hypertension, the vascular damage is acute, and renin release is a very important part of the pressure increase. In benign, essential hypertension, vascular damage is chronic, and its most important pressure-raising influence is sodium retention.**

Nephrosclerosis is Narrowing in the vessels supplying Nephrons as a result of chronic/sudden hypertension

Benign nephrosclerosis refers to non-progressive, chronic changes in the small blood vessels (arterioles) of the kidneys, often seen in individuals with long-standing hypertension. These changes include thickening of the arteriolar walls, hyaline deposition .
Benign nephrosclerosis is typically associated with benign hypertension rather than malignant

if the hypoperfusion persist low it will affect the kidneys causing fibrosis

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PATHOGENESIS OF BENIGN NEPHROSCLEROSIS (HYALINE ARTERIOLOSCLEROSIS)

- Many renal diseases cause HTN, which in turn is associated with benign nephrosclerosis.

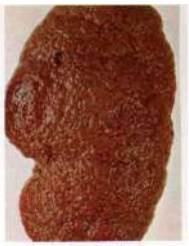
Morphology

Chronic glomerulonephritis and chronic Pyelonephritis كان يعمله كمان ال

- Grossly, both kidneys are symmetrically atrophic each weighing 110 to 130 gm (Normal 300 gm), with a diffusely fine granular surface that resembles grain leather .
- H, there is hyaline arteriolosclerosis, with subendothelial homogeneous, pink hyaline thickening causes narrowing of the BV lumen, resulting in marked decrease blood flow & ischemia through the affected BVs.

بالتالي interstitial fibrosis and the tubular atrophy

- All structures of the kidney show ischemic atrophy.



Benign Nephrosclerosis (Hyaline arteriolosclerosis).
★Diffusely fine granular Kidney surface that resembles **grain leather.**
★**Both kidneys** were equally affected ★together weighed 200 grams.

Because the blood supply to tissue is inadequate

بصير مش سهل نشيل ال cortex بسبب ال sclerosis

hyaline sclerosis

Benign nephrosclerosis. HP view of two arterioles with hyaline deposition, resulting in marked thickening of the walls, & narrowing of the lumen

Narrowing in tubules

MORPHOLOGY OF BENIGN NEPHROSCLEROSIS, ALONE, RARELY CAUSES SEVERE RENAL DAMAGE. A MILD PROTEINURIA IS A FREQUENT PRESENT

Both kidneys are involved cuz it's systematic

- In advanced cases: the G tufts may become globally sclerosed, with diffuse tubular atrophy & interstitial fibrosis.

as Compensatory mechanism

- The larger interlobar & arcuate arteries show (fibroelastic hyperplasia) i.e.,reduplication of internal elastic lamina + fibrous thickening of the media & the sub intima.
- Benign Nephrosclerosis, alone, rarely causes severe renal damage. A mild proteinuria is a frequent present

Malignant HTN

* Diastolic BP > 120 mmHg (على عدة مرات طبعا)

* It could be primmary

OR Secondary → Renal (Niphritic syndrome)
→ other Causes

* Malignant HTN =
↑ pressure + Organ damage

MALIGNANT H & MALIGNANT NEPHROSCLEROSIS

- Malignant **H** is **far less common** in the US **than benign H** & occurs in only about 5% of persons with elevated BP.
- It may arise **de novo**(i.e., from the start, without preexisting **H**), or it may appear suddenly in a person who had mild H .

تذكروا

In malignant hypertension, the vascular damage is acute, and renin release is a very important part of the pressure increase. In benign, essential hypertension, vascular damage is chronic, and its most important pressure-raising influence is sodium retention.

PATHOGENESIS OF MALIGNANT H & MALIGNANT NEPHROSCLEROSIS

- The **basis for this turn in hypertensives** is unclear, but the following scenario is suggested:
- Long-standing benign **H** eventually → injure the arteriolar walls, resulting in (a) **EC injury,** (b) ↑ **permeability** of the small BVs to fibrinogen & other plasma proteins, (c) **platelet deposition.** (Endothelial Cell)
- These 3 changes constitute the... → **Fibrinoid necrosis** of arterioles & small arteries & intravascular thrombosis.
  First Hallmark in malignant hypertension
- Mitogenic factors from platelets (e.g., PDGF) & plasma cause intimal SMCs hyperplasia of BVs, resulting in the...
- → Hyperplastic arteriolosclerosis(onion-skin lesion), with further narrowing of the luminae , **typical of malignant H** & of morphologically similar thrombotic microangiopathies.

- The kidneys become markedly ischemic & the severe ischemia of the renal afferent arterioles... stimulates the renin-angiotensin system (persons with malignant H have **markedly elevated levels of plasma renin**).
- This then **sets up a vicious cycle O,** in which, angiotensin II causes intrarenal vasoconstriction & the resulting renal ischemia increase renin secretion.
- Aldosterone levels are also elevated& salt retention undoubtedly contributes to the elevation of BP.
- The consequences of the markedly elevated BP on the BVs throughout the body are known as malignant arteriolosclerosis& the renal disorder is referred to as malignant nephrosclerosis.

تجميع للنقاط

1. Vascular damage (mainly because hypertension)
2. The underlying collagen is now exposed
3. Platlet aggregation that activate some receptors to make fibrinogen attach causing **fibrinoid necrosis**
4. Ending with hyperplastic arteriosclerosis **
5. Narrowing of the lumen sooo **ischemia**
6. Activation of RAS
7. Further increase in BP

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MORPHOLOGY OF MALIGNANT H & MALIGNANT NEPHROSCLEROSIS

- Grossly:
  benign Nephrosclerosis or diabetes على عكس ال
  atrophy هون ما في
- the kidneys in malignant H may be normal in size or slightly shrunken.
- Multiple small, pinpoint petechial hemorrhages appear on the cortical surface, from rupture of arterioles or G capillaries, giving the kidney **flea- bitten appearance.**
- Microscopicaly :, there are
- (I) **fibrinoid necrosis of the arterioles** , with homogeneous, granular eosinophilic fibrin deposits. **Necrosis** may also involve **G** with microthrombi within the **G** as well as necrotic arterioles.
- **(II) Hyperplastic arteriolosclerosis** in the interlobular arteries & larger arterioles, in which **concentric** proliferation of intimal SMCs producing an **onion-skin appearance, resulting** in marked narrowing, or obliteration, of arterioles & small arteries.
- Similar lesions are seen in persons with acute thrombotic microangiopathies.

CLINICAL MANIFESTATIONS OF MALIGNANT H & MALIGNANT NEPHROSCLEROSIS

Edema around optic nerve

- **malignant H characterize by** ↑ diastolic BP (>120 mm Hg), papilledema, encephalopathy, RF & cardiovascular abnormalities, Most often, the early symptoms are related to ↑intracranial pressure& include headache, nausea, vomiting, & visual impairment.
- Without treatment, malignant H is **fatal**, with 90% of deaths caused by **uremia** & 10% by **cerebral hemorrhage or cardiac failure.**

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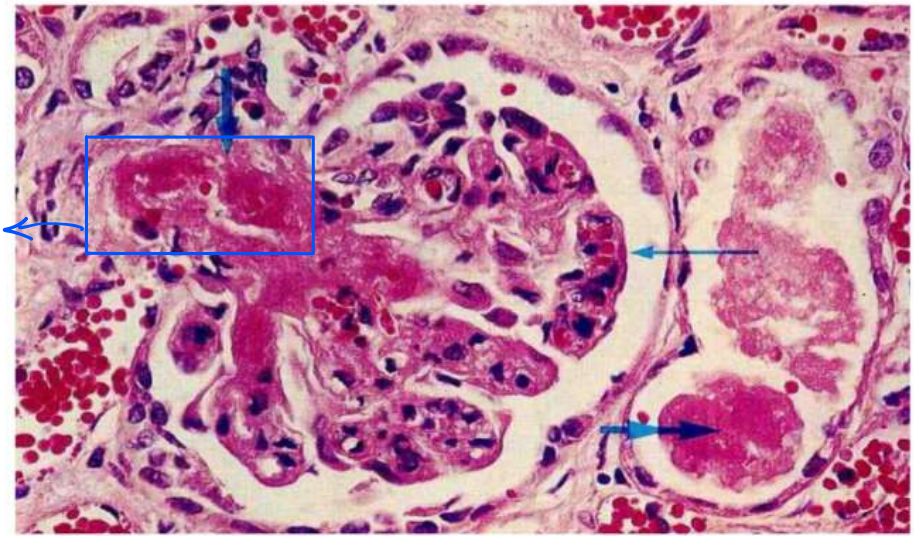
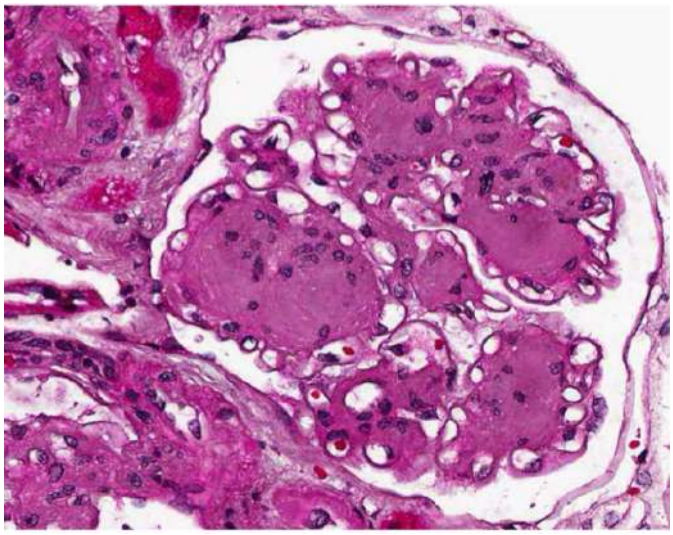
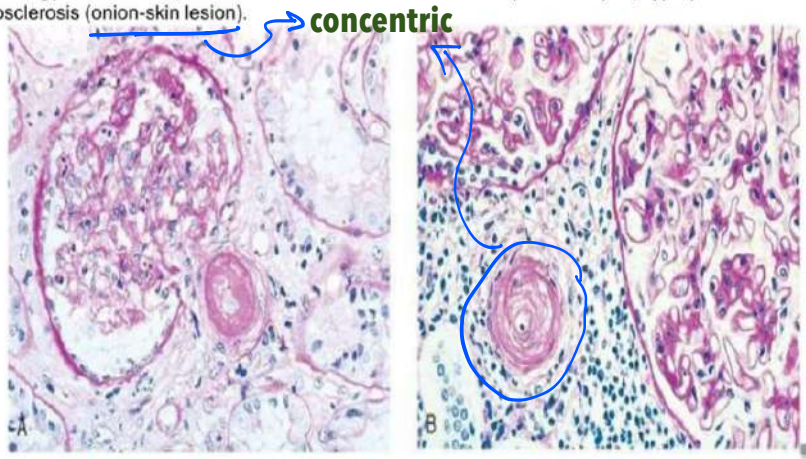
Malignant hypertension: Kidney. ★The afferent arteriole (**thick** arrow) & the adjacent part of the glomerular tuft show **fibrinoid necrosis**, with deposition of homogeneous, granular eosinophilic fibrin. ★Dense protein cast is seen in the tubule (**double** arrow).





Malignant hypertension. A, Fibrinoid necrosis of afferent arteriole (PAS stain). **B,**Hyperplastic arteriolosclerosis (onion-skin lesion).



40. A 48-year-old man is hospitalized after a motor vehicle accident. He is hypotensive and is given several units of packed RBCs by transfusion. He is kept in the intensive care unit for monitoring. On the patient's second day in the hospital, his blood urea nitrogen (BUN) and creatinine levels begin to rise and he develops pitting edema to his knees. His BUN:creatinine ratio is 12:1. A subsequent urinalysis shows numerous muddy brown epithelial and granular casts. Which of the following is another common cause of this man's condition?

(A) Ascending urinary tract infection
(B) Crush injury
(C) Diabetes mellitus
(D) Nonsteroidal anti-inflammatory drug toxicity
(E) Septic shock

49. A 63-year-old man is seen by his doctor after measuring his blood pressure at home and finding it to be 168/100 mm Hg. The patient is concerned because he has had high blood pressure for the past 12 months that has not improved with dietary changes, exercise, or medication. A physical examination is unremarkable except for a thrill heard when auscultating the abdomen just to the left of the midline. What is the most likely cause of the patient's hypertension?

(A) Decreased levels of ADH
(B) Decreased levels of angiotensin II
(C) Elevated levels of aldosterone
(D) Excessive production of cortisol
(E) Increased levels of angiotensin-converting enzyme