النادي الطبي

GENITOURINARY SYSTEM

SUBJECT : Pathology of GUS

LEC NO. : Six

DONE BY : Mo. Alajou

وَقُل رَّبِّ زِدْنِي عِلْمًا

GENITOURINARY SYSTEM

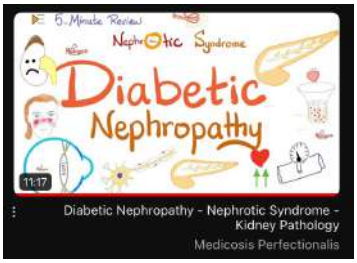
السلام عليكم انا محمد عمري ٢١ سنة و اليوم بدي افرغ محاضرة الباثو ٦

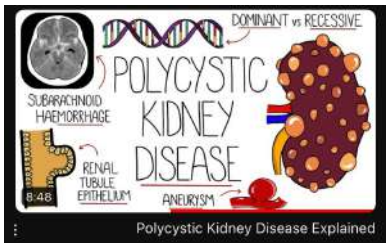
و تحية لعبد الرحمن علاونة
I love you

طيب اول اشي اللون الازرق هذا كلام خرجي و اللون الاحمر هذا ملاحظات
ارشادية جدعنة مني و اللون هاظا مش عارف شو هو المهم هذا كلام الدوك

طيب ابو حميد شو استخدمت مصادر خارجية للتفريغ (ثواني هذا لون خط الدكتورة خليني اغيره) اه جيت ، والله يا أيها القارئ العزيز استخدمت المصادر يلي حاطها ادناه و للأمانة مصادر مرتبة بتقدروا تلموا فيها المحاضرة ، و المحاضرة زنخة للأمانة لولا اني بحب دكتورة غادة كان أوتتها

و قبل لا انسى ، بوجه التحية لكل الكادر القائم على تنظيم ايفنت شيك عحالك ٧ ، على راسهم نائب الرئيس الدكتورة جهينة طه نايف طه و اصدقئي الاعزاء بهاء عبيدات و براء العتيبي (ما نظموا بس بحييهم لإنهم أعزاء)





لا تنسوا أهل غزة من دعاؤكم ، ،
بسم الله نبدأ . .

وقل رب زدني علماً

تحية لكل حد بشوف هذا التفريغ بالمستقبل

GENITOURINARY SYSTEM

Diabetic nephropathy

Diabetic nephropathy is a subtype of nephrotic syndrome .
There are many systemic diseases that can lead to nephrotic syndrome. One of them is diabetes. Another one is lupus. The third one is Emily doses.

في المحاضرات يلي قبل كنا ندرس عن امراض بتعمل primary glomerulopathy اما اليوم رح ندرس عن ال diabetic nephropathy ، يلي هو واحد من الامراض يلي تعتبر من ال systemic diseases يلي بتعمل secondary nephropathy ، يعني هي مش مرض ببدا من الكلية ، ،
لا هو مرض ما اله علاقة بالكلية لكن ممكن يأثر عليها و يعملي مشاكل بالكلية
طيب بدكم امثلة على systemic diseases برضه بتعمل SGP ؟

1. systemic lupus erythematous
2. amyloidosis
3. multible myeloma
4,5,. . . etc

طيب ال diabetes شو بعمل بالكلية ؟ (pathogenesis)

Diabetes can detroy the renal pelvis causing acute or chronic pyelonephritis , and diabetes can injure your papilla causing Papillary Necrosis .

Diabetes will destroy your vessels and will start destroying the efferent arteriole before the affernt arteriole

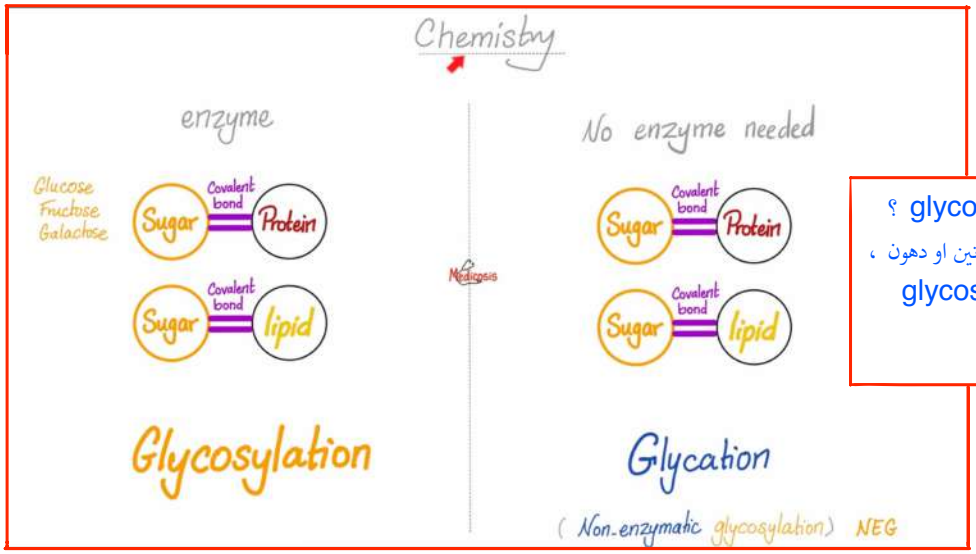
Diabetes will make your capillary basement membrane very thick due to deposition of type 4 collagen

Diabetes will cause hyper filtration injury (too much pressure ,too much blood filterd), this hyper filtration is going to injure your mesangium causing mesangial sclerosis , which can lead to proteinuria .
Glomerulus will get very sclerosed and hardened and you can even see something called nodular glomerular sclerosis or the climb steel wilson nodule .

وقل رب زدني علماً

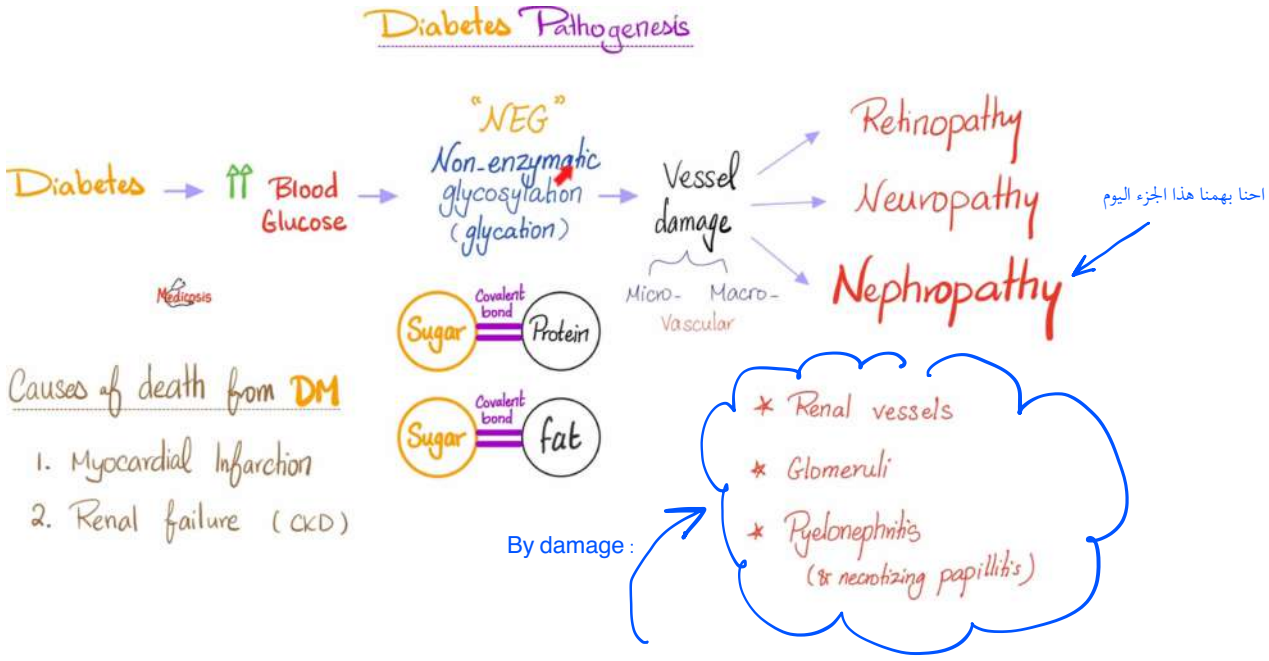
GENITOURINARY SYSTEM

بدنا نحكي شوية chemistry فطلعولي نضال الهندي يلي جواكم ، ،



شو الفرق بين ال glycation و ال glycosylation ؟
ال glycation هي بس اربط glucose ببروتين او دهون ، بدون استخدام enzyme ، اما ال glycosylation باستخدام انزيم

Diabetes damage the kidney by glycation



How does diabetes damage my kidney?

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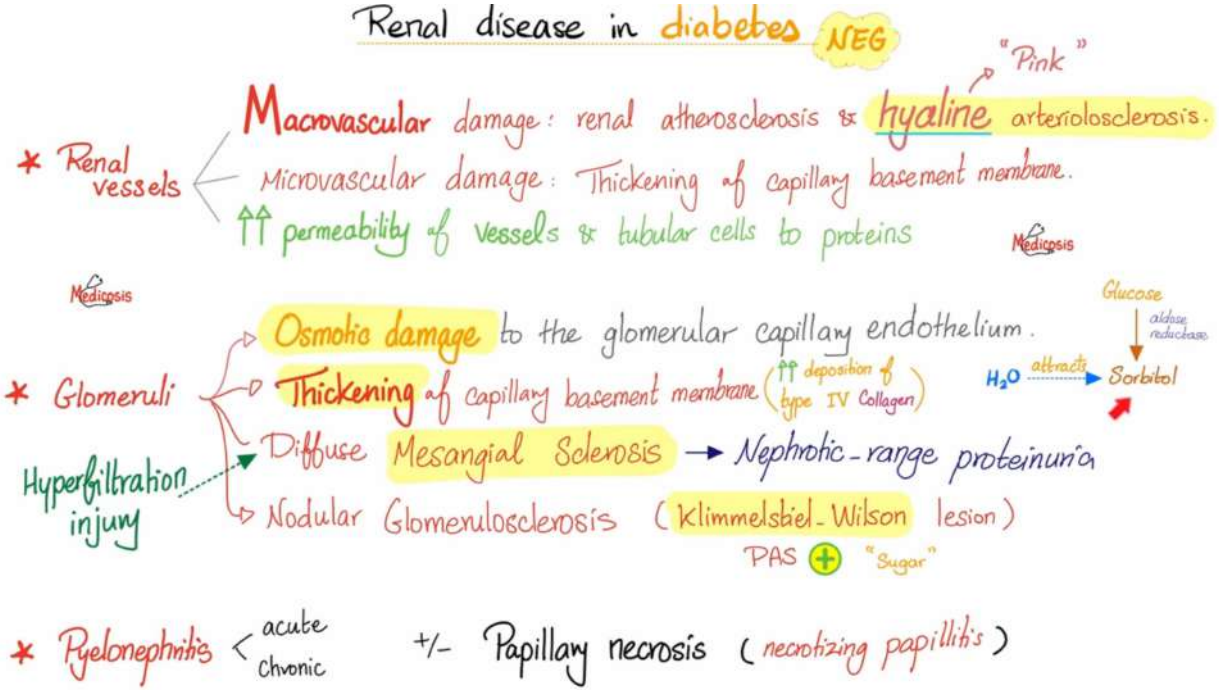

Diabetes damage your renal vessels , your glomeruli and your renal pelvis .

1. Renal vessels (big vessels and small vessels) causing renal atherosclerosis and hyaline arteriosclerosis (hyaline means pink because of proteins)

2.Glomeruli : A.osmotic damage to the glomerular capillary endothelium because glucose gets converted to sorbitol (osmotically active) which is gonna attract water and this is osmotic damage to your kidney
B. diabetes will increase the deposition of type 4 collagen in the basement membrane making it thick
C. Diffuse mesangeal sclerosis (due to hyper filtration injury) lead to nephrotic range proteinuria (severe) > 4 grams per day
D.nodular glomerulosclerosis(klimmelstiel wilson lesion) PAS+

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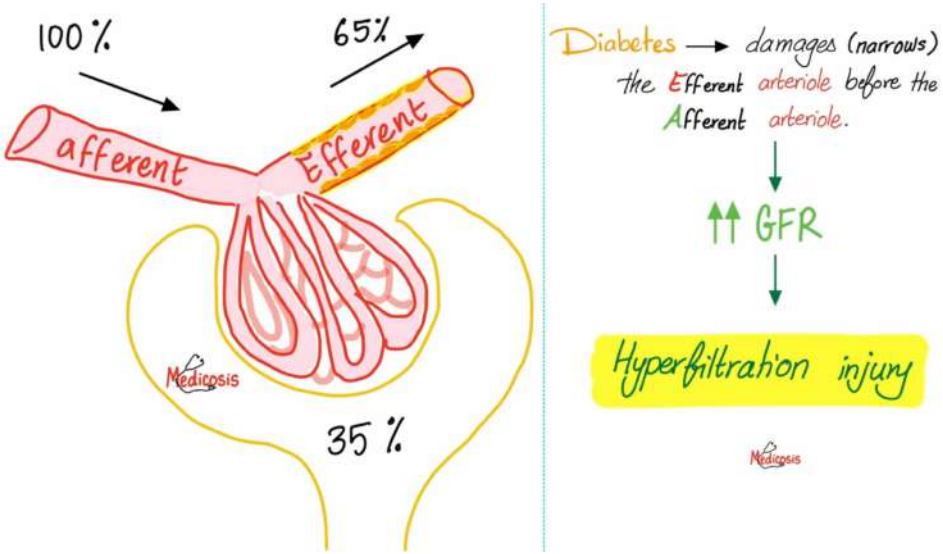
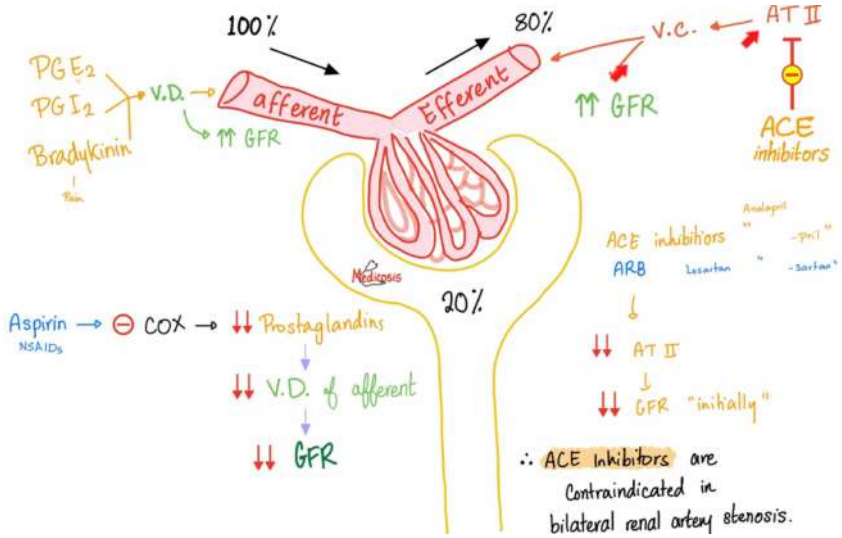


هسة ليش بصير عنا hyper filtration injury ، لانه بصير في عنا تدمير لل efferent arteriole قبل ال afferent arteriole و هذا بخلي يصير عندي تضيق في ال EA و بالتالي زيادة الفلترة



عشان هيك ال ACE inhibitor بتساعد الناس يلي معهم سكري لانها بتعمل تثبيط لانتاج ال Angiotensin II

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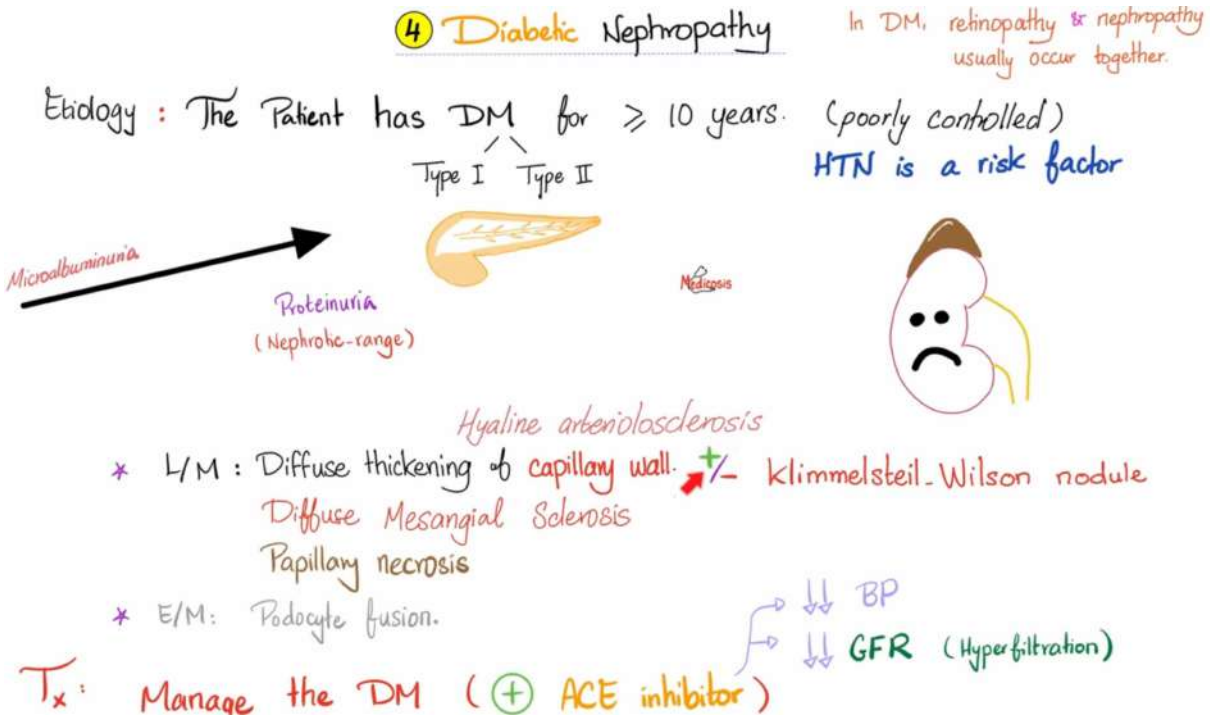
GENITOURINARY SYSTEM



The patient is diabetic (type1or2) ,This is a poorly controlled diabetes.
hypertension is another risk factor .
When you see diabetic nephropathy check the patient's retina because retinopathy and nephrology usually happen together.
This is a very slow progression, it is a very chronic disease , we start with microalbuminuria and we end up with nephroti range proteiuria
First your kidney is leaking some proteins, but now the kidney is leaking a lot of proteins

light microscopy : diffuse thickening of the capillary wall
you can see klimmelsteil-wilson nodule, diffuse mesangeal sclerosis, and papillary necrosis
Electromicroscopy: some podocyte fusion

How do I manage this?
Manage the underlying condition which is diabetes and ACE inhibitors

وقل رب زدني علماً

بسم الله نبلش بالسلايدات . .

Diabetic nephropathy

- is a common complication of type 1 and type 2 diabetes.
- Over time, diabetes that isn't well controlled can damage blood vessels in the kidneys that filter waste from the blood. This can lead to kidney damage and cause high blood pressure.
- High blood pressure can cause more kidney damage by raising the pressure in the filtering system of the kidneys.
- Histopathology :

- The characteristic histologic changes of DN includes thickening of glomerular and tubular basement membrane
- increase in mesangial matrix, Kimmelstiel-Wilson nodules sometimes combined with microaneurysms, exudative or hyalinosis lesions, capsular drop and afferent and efferent arteriolar hyalinosis.

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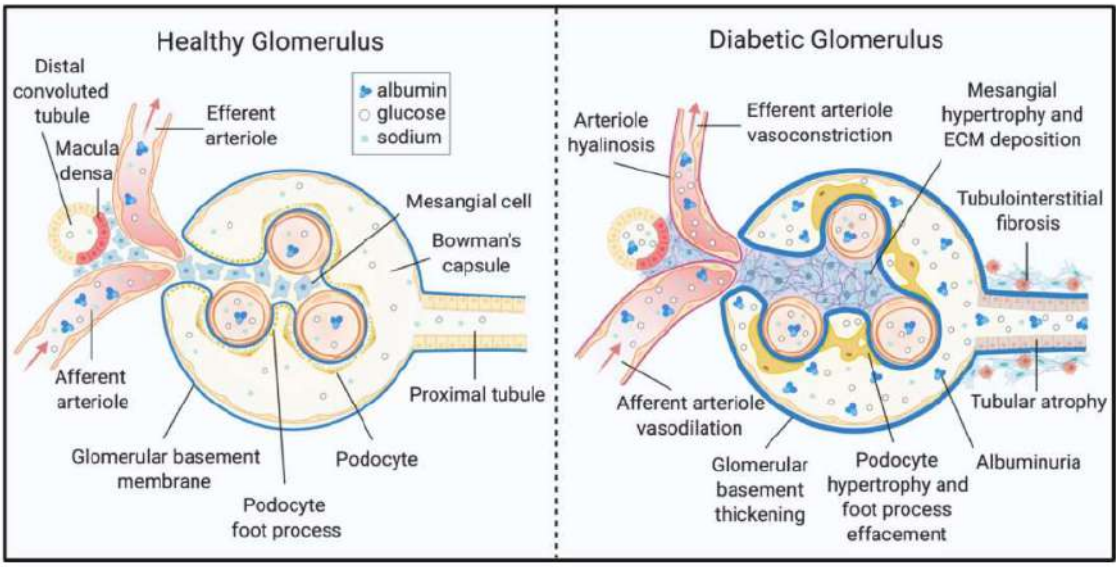
كله حكيناه بالشرح يلي قبل . .

Risk factors for developing Diabetic Nephropathy

Poor control of blood glucose,
Long duration of Diabetes,
Presence of other diabetic complication,
Ethnicity (Asian, Pima Indians),
Pre-existing High BP,
Family h/o of Diabetic Nephropathy,
Family h/o Hypertension.

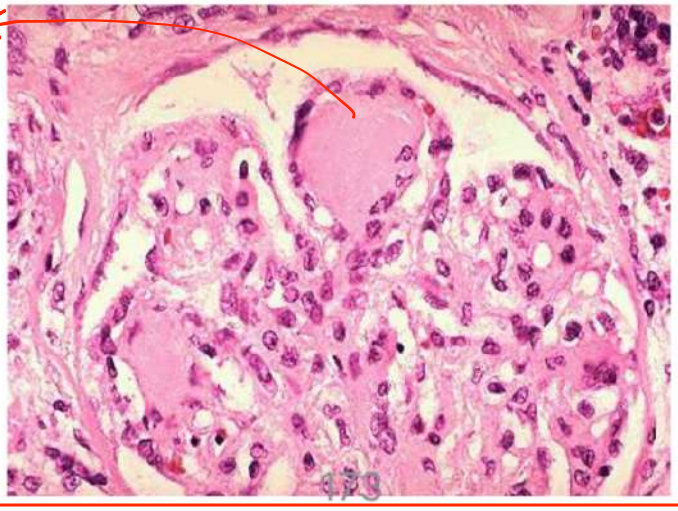


شو بنشوف بال Diabetic glomerulus ؟

بنشوف hyalinosis بال arterioles ، بنشوف mesangeal matrix increased
و بنشوف podocyte effacement و بصير في thickening في ال basement membrane
بصير في proteinuria نتيجة ال defect في ال basement membrane

This is nodular glomerulosclerosis (the Kimmelstiel-Wilson lesion) of diabetes mellitus. Nodules of pink hyaline material form in regions of glomerular capillary loops in the glomerulus. This is due to a marked increase in mesangial matrix from damage as a result of non-enzymatic glycosylation of proteins. This is one form of chronic kidney disease (CKD) with loss of renal function over time.

Characteristic feature



كل اشي هون مشروح في بداية التفريغ

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GENITOURINARY SYSTEM

بنيجي لموضوع جديد ، ،

Thrombotic microangiopathy

ال thrombotic microangiopathy عبارة عن حالة بنشوفها بأكثر من مرض ، يعني هي بحد ذاتها مش مرض ، هي مصطلح بنطلقه على حالة ، طيب شو بنشوف بهاي الحالة ؟

(a) morphologically by widespread thrombosis in the microcirculation(DIVC)
(b) clinically by microangiopathic hemolytic anemia, thrombocytopenia,&, in certain instances RF.

Common diseases that cause these lesions include:
- (1) Childhood Hemolytic Uremic Syndrome (HUS),
- (2) various forms of adult HUS,
- (3) Thrombotic Thrombocytopenic Purpura (TTP).

هسة بدنا نفرق بين ال HUS و ال TTP

Pathogenesis

- ❑ Although clinically overlapping, HUS & TTP are pathogenically distinct. Central to the pathogenesis of HUS is endothelial cell (EC) injury & activation, with resultant intravascular thrombosis; while the…
- ❑ TTP is now known to be caused by an acquired defect in proteolytic cleavage of von Willebrand factor (vWF) multimers

في ال HUS بكون في endothelial cell injury بسبب toxins او بكتيريا ، و بالتالي بصير في activation لل platelet ، لانه احنا بنتذكر انه ال activation of platelets بتصير لمايصير في endothelial cell injury لأي سبب كان . .و بالتالي اخيرا رح يصير في thrombosis نتيجة هذا ال activation
اذا في platelet activation + injury و بكمل عنا ال cascade يلي بنعرفه

اما ال TTP بكون بسبب مشكلة بتمنع انه يصير في cleavage بال vWF multimers
(لانه الطبيعي انه يصير في cleavage مشان ينتجلي vWF monomers

Childhood HUS

- ❑ 75% of childhood HUS cases follow intestinal infection with Shiga toxin-producing E. coli, such as occurs in epidemics caused by ingestion of infected ground meat (e.g., hamburgers) & infections with Shigella dysentery type I.

٧٥٪ من ال CHUS بكون بسبب intestinal infection ب shiga toxin producing E. coli او shigella dysentery type I

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يتبع . .

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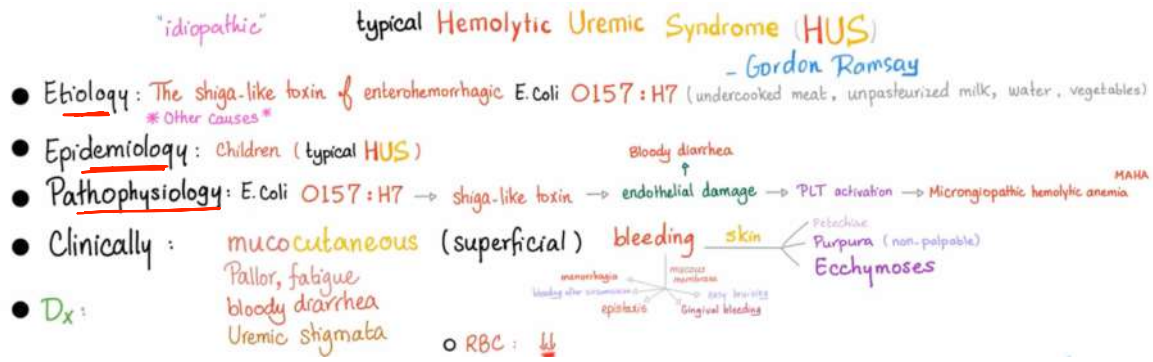

تمام يعني بيجي ال shiga toxin بروح على ال renal glomeruli epithelial cells و بعمل injury بعدين بصير في activation لل platelet و بصير في thrombotic microangiopathy

- **Pathogenesis**: Shiga toxin is carried by neutrophils in the circulation, targeting the renal G EC , because they express the membrane receptor for the toxin.
- The toxin has multiple effects on the EC, including
  - **(I) Cytotoxic, the toxin gains entry to the cells & directly causes cell death.**
  - **(II) (in the presence of cytokines, such as TNF) EC damage.**
  - **(III) ↑ adhesion of WBCs, ↑ endothelin production, & loss of EC nitric oxide (both favoring vasoconstriction) The resultant EC damage leads to thrombosis, most prominent in➡interlobular arteries,➡ afferent arterioles,➡G capillaries, as well as microangiopathy.**

تمام هسة هون عنا تأثير ال shiga toxin في ال تأثير رقم ٣ يلي شرحناه فوق و يلي اله علاقة بموضوع ال thrombosis و اله تأثير ١ و ٢ هذول تاثير اضافة للسم

- 10% of the cases of HUS in children are not preceded by diarrhea caused by Shiga toxin-producing bacteria

Morphology:

- In childhood HUS, there is fibrinoid necrosis, similar to lesions of classic thrombotic microangiopathy, with fibrin thrombi predominantly involving G & extending into arterioles & larger arteries in severe cases.
- Cortical necrosis may be present.

شو بتتوقعوا انه تشوفوا ؟

رح نشوف thrombosis و necrosis و fibronoid necrosis و بتشبه ال classic thrombotic microangiopathy ، مع fibrin thrombi

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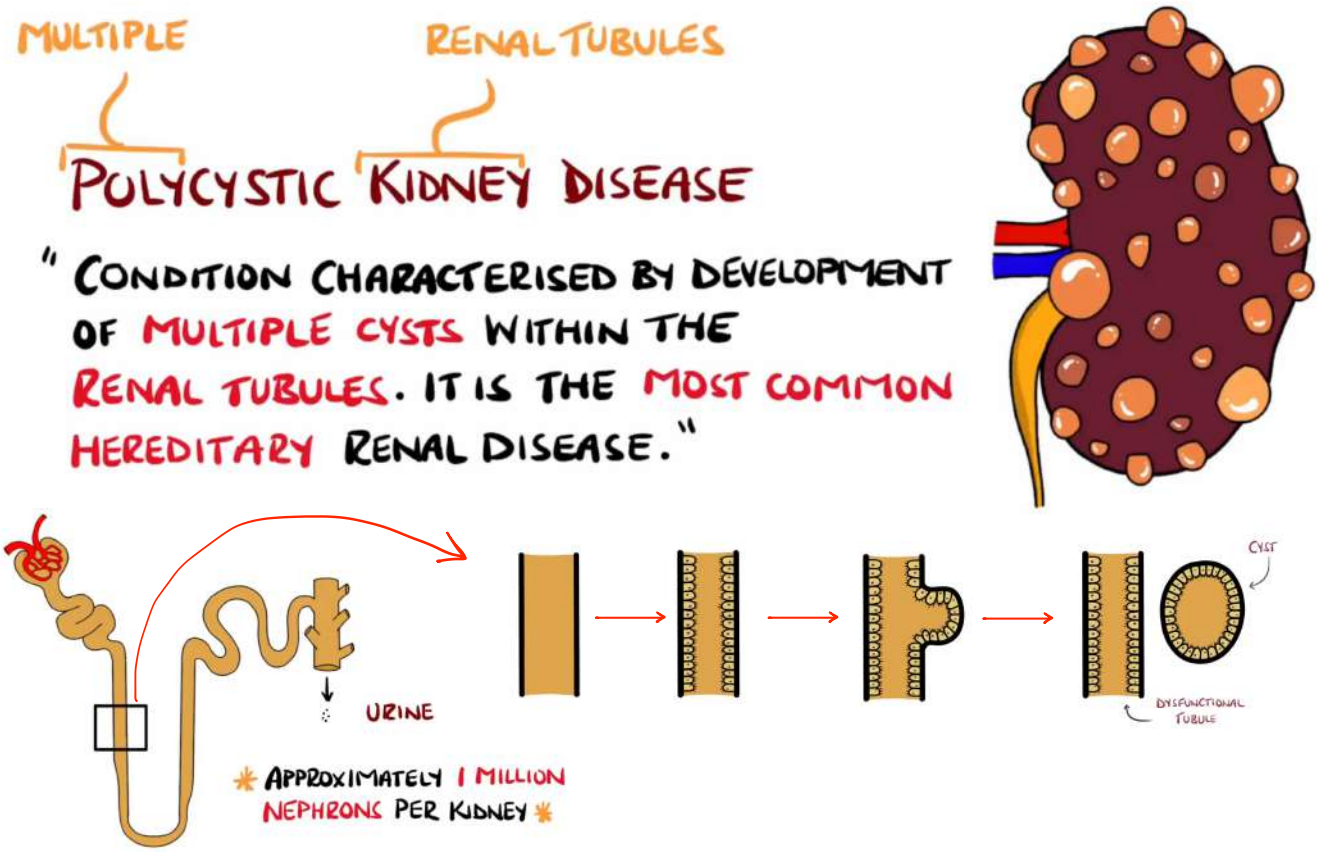
Clinically,

1-typical childhood HUS characterized by the sudden onset.
2-usually after GIT infection or flulike prodromal episode.
3- severe oliguria.
4-bleeding manifestations (hematuria) &
5- microangiopathic hemolytic anemia (DIC) .
6-This disease is one of the main causes of acute RF in children. However, if managed properly with dialysis, most patients with childhood HUS recover in a matter of weeks

Cystic disease of the kidney

شرح خارجي



in polycystic kidney disease, these tubules develop into cysts which become filled with fluid and could range in size from being microscopic to several centimetres in size the process can start even in utero

as the tubules become cysts ,they cannot carry out the normal filtering function ,therefore the number of functioning nephrons begins to decrease , this is worsened by the fact that as the cysts grow decompress nearby nephron , also making them dysfunctional.

Initially, this may not be seen to have any clinical impact as the remaining number of nephrons may increase their function to maintain the glomerular filtration rate but as the disease progresses and more nephrons are affected, the remaining ones cannot make up the difference and overall renal function, then deteriorates eventually reaching end-stage renal disease.

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GENITOURINARY SYSTEM

PATHOPHYSIOLOGY

1. MAY BEGIN IN UTERO
2. SIZE RANGES – MICROSCOPIC TO CM
3. CYST FORMATION + COMPRESSION
   ↳ DYSFUNCTIONAL TUBULES
   ↳ INITIALLY COMPENSATED

BUT OVER TIME GFR FALLS
↳ END STAGE RENAL DISEASE

* OR NEED FOR RENAL REPLACEMENT THERAPY

EVEN WITH A NORMAL GFR THERE IS STRUCTURAL DAMAGE

STAGE:	(ml/min/1.73m²)
1	>90
2	60-89
3a	45-59
3b	30-44
4	15-29
5	<15

By definition the presence of structural injury makes polycystic kidney disease, a form of chronic kidney disease with end-stage renal disease being defined as needing renal replacement therapy like dialysis or a transplant or GFR below 15 ml per minute.

CAUSES

AUTOSOMAL DOMINANT

1. PKD1 (Ch 16) – POLYCYSTIN 1 (85%)
   ↳ CELL-CELL INTERACTION, CELL CYCLE REGULATION, CALCIUM TRANSPORT
2. PKD2 (Ch4) – POLYCYSTIN 2
   ↳ VOLTAGE GATED CATION CHANNELS
3. GANAB (Ch11) – GLUCOSIDASE II α SUBUNIT

* AFFECT RENAL TUBULAR EPITHELIUM *

مش مطلوب معنا

- "SECOND HIT PHENOMENON" – NEAR 100% PENETRANCE
- 25% NO FAMILY Hx – SUBCLINICAL OR NEW MUTATION
- AT AGE 75Y, 50-75% NEED RRT

There are two main polycystic kidney disease both caused by genetics. The first is autosomal dominant with two main types, one coming from mutations in PKD 1 on chromosome 16, which codes for the protein polycystic 1. This is affected in around 85% of cases and is involved in cell to cell or cell matrix interaction, cell cycle regulation and calcium transport .

The second coming from mutations in PKD 2 on chromosome 4 coding for polycysteine 2 which codes for voltage gated cation channels

around 25% of cases do not have a family history which could be due to subclinical disease in the relatives or it could be a new mutation by age 75 between 50 and 75% of patients require renal replacement therapy

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GENITOURINARY SYSTEM

CAUSES

AUTOSOMAL RECESSIVE

- 1:20,000 (AD 1:1,000)
- PKHD1 (Ch6) - FIBROCYSTIN
  - RENAL EPITHELIUM CILIA AND LUMEN FORMATION
- 30% MORTALITY IN NEWBORNS

The other type is autosomal recessive which is significantly rare than autosomal dominant , it often involves PKHD 1 on chromosome 6 which is a gene coding for fibrocystic a protein involved with the generation of cilia in renal epithelial cells and has a role in forming the lumen of the tubule , it is estimated that mortality is around 30% in newborns with this version.

SIGNS AND SYMPTOMS

* MAY INITIALLY BE ASYMPTOMATIC *

1. HYPERTENSION (50-70%)
   - LARGELY DUE TO RAAS ACTIVATION
2. HAEMATURIA
3. PAIN / FULLNESS (ABDOMEN + FLANK)
4. POLYURIA
5. RECURRENT UTI

initially polycystic kidney disease may be asymptomatic but with time hypertension can develop due to the renin angiotensin aldosteron system activation

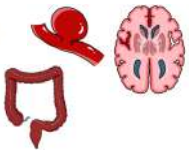
Hematuria can be present due to vessels damage within the cysts, as well as pain of fullness which is most commonly in the abdomen

polyuria meaning in excessive urine output can be a feature, because the cysts can make it more difficult to concentrate the urine

there is an Increased risk of urinary track infections and renal stones

SIGNS AND SYMPTOMS

ASSOCIATED COMPLICATIONS:



- ANEURYSM (10%)
- HEPATIC CYSTS
- PANCREATIC CYSTS
- MITRAL VALVE PROLAPSE (25%)
- DIVERTICULAR DISEASE
- AORTIC DISSECTION
- LIVER FIBROSIS
- HEPATIC BILE DUCT WIDENING

SUGGESTIVE OF AUTOSOMAL DOMINANT PKD

SUGGESTIVE OF AUTOSOMAL RECESSIVE PKD

and there is also a link between autosomal dominant polycystic kidney disease and the presence of aneurysms, for example, in arteries of the brain which can predispose to intracranial haemorrhage which is estimated to be in 10% of

Other extra renal findings, a liver and pancreas cysts, mitral valve prolapse in 25% , diverticulosis , and even aortic dissection, which could be related to the aneurysms thes can be a clue to suggest autosomal dominant rathar than autosomal recessive polycystic kidney disease as the latter typically

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نرجع للسلايدات

Cystic diseases of the kidney are a heterogeneous group, which are important for several reasons: (1) Adult polycystic disease causes 10% of all CRF cases, (2) Cysts are common& often present diagnostic problems for clinicians, radiologists, & pathologists and ,rarely, they can be confused with malignant tumors.

في عنا كثير انواع من التكيسات يلي ممكن تصير في الكلية منها وراثي منها بسبب مشكلة جينية في جينات محددة ، ممكن تكون عند الكبار او الصغار و ممكن تكون مكتسبة خلال الحياة ، ممكن تكون مرتبطة بال dialysis ، و ممكن تكون عبارة عن simple cyst with no significant diagnositic problem ، هي شائعة و تعتبر لانها عبارة عن cyst ، و ال cyst ممكن لما تنفحص بال radiologiological examination ان كان بال X ray او بال ultrasound بكون عبارة عن cyst لكن ممكن يصير تشخيص خاطئ على انها tumor ، فهذا الاشي يعتبر مشكلة عن الدكاترة ، لهيك لازم نوصل لتشخيص دقيق مشان نحدد اذا هاي cyst و لا tumor

- **Types of cysts**

1-Simple Cysts
2-Dialysis-associated acquired cysts
3-Autosomal Dominant (Adult) Polycystic Kidney Disease
4-Autosomal Recessive (Childhood) Polycystic Kidney Disease
5-Medullary Cystic Disease

رح نناقشهم وحدة وحدة

❑ Simple Cysts

عبارة عن cyst عادي ممكن يكون بأي مكان في الجسم ، و هو عبارة عن cystic lesion lyning by the cuboidal epithelium or flattened epithelium ممكن يكون فيه fluid (serous or hemorrhage) ، ممكن يكون multible او single

- **❑Multiple or single**
- **❑1-5 cm in diameter**
- **❑ translucent filled with clear fluid & lined by a gray, glistening, smooth**

  membrane composed of a single layer of cuboidal or flattened epithelium .
- **❑ confined to the cortex.**
- **❑ no clinical significance.**
- **❑ Usually discovered incidentally or because of hemorrhage and pain**
- **❑ Importance: to differentiate from kidney tumors**

❑ Cysts associated with chronic dialysis

في cysts بتصير خلال الحياة و ما بتكون مرتبطة بالجينات ، بتصر في المرضى يلي عندهم chronic kidney disease يلي بعملوا dialysis ، بزيد ال risk of carcinomas

وقل رب زدني علماً

- **Dialysis-associated acquired cysts**
- **in patients with renal failure who have prolonged dialysis.**
- **both cortex and medulla**
- **Complications: hematuria; pain**
- **Increased risk of renal carcinomas (10 times greater than in the general population)**
- **Occasionally, renal adenomas or even adenocarcinomas(RCC) arise in the walls of these cys**

عنا نوعين من ال genitiely cystic disease in the kideny يلي هم ADPKD و ARPKD انت لازم تقدر

❑ Autosomal Dominant (Adult) Polycystic Kidney Disease

- multiple bilateral cysts
- eventually destroy the renal parenchyma.
- Incidence (1: 500-1000) persons
- 10% of chronic renal failure.

كلية المريض كلش كبيرة و بكون في Multible cystic bilateral cysts

Pathogenesis

The disease can be caused by inheritance of one of at least two autosomal dominant genes of very high penetrance. In 85% to 90% of families, PKD1, the defective gene is on the short arm of chromosome 16. This gene encodes polycystin-1.

(1)- PKD1: 85-90% (encodes polycystin-1)
(2)- PKD2 : 10-15% (encodes polycystin-2).

ببساطة مشان يصير عندك هذا المرض لازم يكون عندك مشكلة بواحد من هالجينين ، و احفظ هاي الجينات كويس لانه عليه سؤال يا حلو

CAUSES

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2. PKD2 (Ch4) - POLYCYSTIN 2
   - VOLTAGE GATED CATION CHANNELS

وقل رب زدني علماً

GENITOURINARY SYSTEM

❑Autosomal Dominant (Adult) Polycystic Kidney Disease – cont.

❑**Clinical presentation :**

- **asymptomatic until the 4 th decade**
- **Symptoms: flank pain , heavy dragging sensation, abdominal mass, hemorrhage, obstruction, Intermittent gross hematuria**

ممكن عادي المريض يعيش عادي طبيعي لحد عمر ال ٤٠ بعدين بجيك بهاي الأعراض

❑**Grossly, the kidneys** may reach enormous size (weights of up to 4 kg for each kidney).

- These **very large kidneys are readily palpable** as abdominally masses.
- Both kidneys composed solely of cysts, up to 4 cm in Ø with no intervening parenchyma.

The cysts are filled with fluid, which may be clear, turbid, or hemorrhagic

لما يجي الدكتور يفحص بطنه بتكون الكلية كثير كبيرة و بتقدر تتحسسها بيدك
، و بفكر الدكتور انه في abdominal mass و بخاف ، ،

❑ **Complications**

1-Most important complications are **uremia &** hypertension(which develops in 75% of cases)

2- urinary infection.

3- Saccular aneurysms of the brain circle of Willis are present in **10% to 30% of patients, & these individuals have a high incidence of subarachnoid hemorrhage.**

4-Although the disease tends to progresses very slowly, but it is ultimately **fatal** from **uremia or hypertensive complications.**

طبعا متوقع يكون في مضاعفات ، بصير عنده rupture او pain او hematuria
بصير عنده uremia ، لانه اصلا الكلية بتكون فاقدة لل paryncyma كلها فأكيد حيصير uremia عنده

10.4 Polycystic kidneys (adult type)

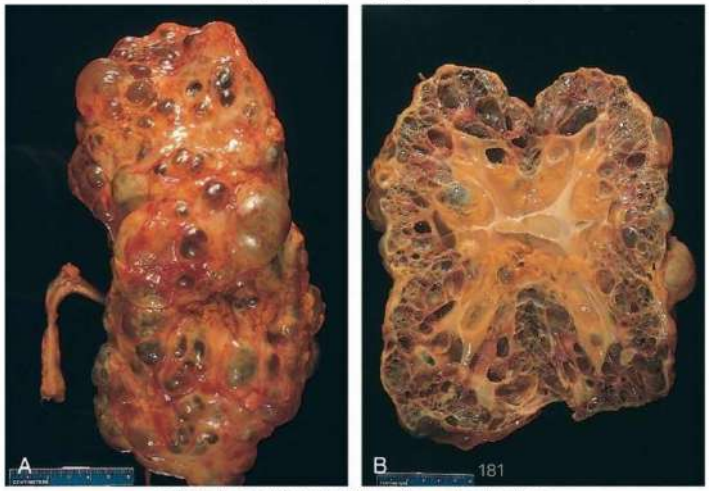
نقطة ثلاث كثير مهمة ، ممكن يجي عليها سؤال بالامتحان
شرح نقطة ٣ : ١٠ ٪ – ٣٠ ٪ من المرضى بصير عندهم saccular aneurysms يلي هو عبارة عن dilitation of the one of the blood vessels بتصير في جدران ال circle of willis in the brain

❑ Treatment is by renal **transplantation.**

وقل رب زدني علماً

GENITOURINARY SYSTEM

Autosomal Dominant (Adult) Polycystic Kidney Disease



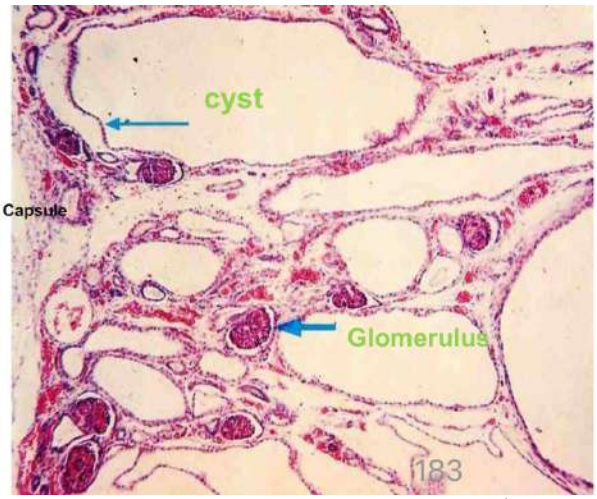
سؤال للاب :

Which one of the following diseases is associated in this type of kidney disease in about 10–30% of patient

بكون الجواب الصورة B ، يلي هي عبارة عن aneurysm in circle of wills

10.4 Polycystic kidneys (adult type)

Polycystic Kidneys (Adult type). massively enlarged **4000 g** kidney,**(Normal 300g),**consists of numerous small & large cysts bulging through the capsule.
★Some cysts contain clear urine, others are bluish-black from old hemorrhage



Adultpolycystic Kidneys X55.
Cortex of the kidney, with the capsule on the left.
No normal tubules are present, & instead, the kidney bulk consists of various size **cysts**, lined by flattened epithelium (**thin** arrow).
However, many normal looking **glomeruli (thick** arrow) remain between the cysts.

كلها عبارة عن cysts(simple) ،كلها موجودة في ال cortex ، و ما في normal tubules

The kidney bulk consists of various size cysts , lined by flattened epithelium

ممكن نلاقي شوية normal glomeruli

وقل رب زدني علماً

❑Autosomal Recessive (Childhood) Polycystic Kidney Disease

AUTOSOMAL RECESSIVE
- 1:20,000 (AD 1:1,000)
- PKHD1 (Chr6) - FIBROCYSTIN
  - RENAL EPITHELIUM CILIA AND LUMEN FORMATION

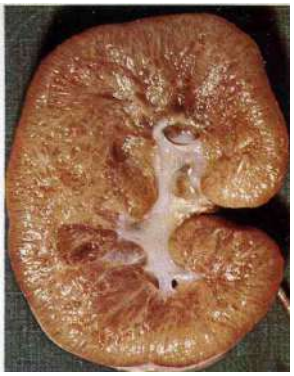
- Autosomal recessive
- Rare ,1:20,000 live births.
- Depending on time of presentation & the presence of associated hepatic lesions, there are perinatal, neonatal,infantile, & juvenile subcategories have been defined;
- **all result** from mutations in a gene PKHD1,coding for a putative membrane receptor protein (fibrocystin)localized to chromosome 6p.
- Fibrocystin may be involved in the function of cilia in tubular epithelial cells .

❑Grossly

- the disease is invariably (consistently)bilateral, with numerous small cysts in the cortex & medulla give the kidneys as sponge-like appearance .
- the medulla & cortex are completely replace by dilated & elongated channels & cysts.
- These cysts originating from the collecting tubules & are lined by cuboidal cells.
- **In all cases (100%),** there are multiple cysts in the liver as well as proliferation of portal bile ducts.

بكون bilateral، و بتكون موجودة في ال cortex و ال medulla
بحيث بكون ال cortex and medulla مليانات cysts جايين من ال collecting tubules

Autosomal Recessive (Childhood) Polycystic Kidney Disease.
★A bilateral renal defect which is **incompatible with life.**
★Sponge-like enlarged kidney from the presence of large number of small cysts, in the cortex & medulla which are abnormally, enlarged collecting tubules


Infantile polycystic kidneys

وقل رب زدني علماً

الدكتورة حكت انه ال cystic disease جاي عليه
ماكسمم سؤالين ، وانه هي رح تركز على الأشياء العامة و ما
دخلت بالتفاصيل

❑ Medullary Cystic Disease

• 2 major types:

1-medullary sponge kidney

2-nephronophthisis-medullary cystic disease complex → Associated with renal

1-medullary sponge kidney

• common and innocent (Harmless ,Inoccuous) condition.

2-nephronophthisis-medullary cystic disease complex

• almost always associated with renal dysfunction.

• usually begins in childhood.

• Cysts are at cortico-medullary junction → التشخيص تاعه بكون متأخر ، ، لانه موجود بهاي

• **In aggregate**, the various forms of nephronophthisis are now thought to be the **most common genetic cause of end-stage renal disease in children & young adults.**

• Four variants of this disease complex are recognized on the basis of the time of onset: **infantile, juvenile, adolescent, & adult.**

• **The juvenile form is the most common.**

• **5% to 20% of individuals with juvenile nephronophthisis have extra-renal manifestations, which mostly appear as retinal abnormalities.**

• **Grossly, the kidneys are small & contracted.**

• Histopathology:, numerous small cysts lined by flattened or cuboidal epithelium are present, **typically at the cortico-medullary junction.**

❑Clinical features:

• polyuria and polydipsia (↓tubular function).

• renal failure over 5-10-year

❑The disease is difficult to diagnose, Because

(1) no serologic markers &

(2) the cysts may be too small to be seen with radiologic imaging or

(3) cysts may not be apparent on renal biopsy if the cortico-medullary junction is not well sampled.

• **A positive family history & unexplained CRF in young patients** should lead to suspicion of **nephronophthisis-medullary cystic disease complex.**

وقل رب زدني علما

GENITOURINARY SYSTEM

URINARY OUTFLOW OBSTRUCTION

لما يصير في عنا انسداد في الكلية ، ممكن يكون السبب حصوة بتتكون داخل الكلية ، طبعا بدك تعرف انه سبب تكون الحصوة بالكلية يا اما بكون من الكلية نفسها او بتتكون في المثانة ، اما الحالب ما بتكون فيه حصوة لكن ممكن تمر الحصوة من الكلية عبر الحالب و تسوي انسداد

❑Renal Stones (Urolithiasis)

- Stone formation at any level in the urinary collecting system.
- Most common in kidney.
- (1%) of all autopsies.
- Symptomatic more common in men .
- Familial tendency toward stone formation.
- Unilateral in 80%.
- Variable sizes.
- Stone = inorganic salt (98%) + organic matrix (2%)

❖Types are according to inorganic salt:

1- calcium oxalate/ calcium oxalate+ calcium phosphate-- (80%) .
2- Struvite (magnesium ammonium phosphate)
3- uric acid (6-7%)
4- cysteine stones (2%)

طيب شو اسباب تكون هاي ال stones ؟

انتوا بتعرفوا انه البول سائل بس مش زي المي يعني مش نقي ، فيه كريستال و فيه املاح ، لكن هاي المواد كلها موجودة بنسب محددهة بحيث انه البول مش مشبع بهاي المواد ، فما بصير عني ترسبات ، يعني في حالة من الاتزان و اي سبب بخرب من حالة الاتزان هاي بخلي يصير في ترسبات رح يعملي stones ، و من الاسباب يلي ممكن تعمل خلل في هذا التوازن هي انه في infection او ال dehydration و اسباب اخرى ، ،

➢Causes of Renal Stones

1-increased urine concentration of stone's constituents exceeds solubility in urine (supersaturation).

- 50% of calcium stones pts have hypercalciuria with no hypercalcemia.
- 5% to 10% hypercalcemia and hypercalciuria due to hyperparathyroidism, vitamin D intoxication, or sarcoidosis.

❑2-The presence of a nidus

- **Urates provide a nidus for calcium deposition.**
- **Desquamated epithelial cells**
- **Bacterial colonies**

بتكون عن واحد عنده infection ، بكيريا او غيرها ، هاي بتصير زي ال nidus ، يعني زي نواة بتتجمع عليها هاي الاملاح و الكريستال و بعملك حصو

❑3-urine pH

لما يصير في infection بصير ph البول قاعدي اكثر ، وهذا بعملي stones

❑4-infection

- Magnesium ammonium phosphate (struvite) stones staghorn shaped stones (**almost always occur in persons with persistently alkaline urine due to UTIs, specially, due to urea-splitting bacteria, such as Proteus vulgaris& the staphylococci.**
- Uric acid stones form in acidic urine (under pH 5.5).

الناس يلي عندهم alkaline urine بكون عندهم stones بتشبه قرن الغزال موجودة في ال renal pelvis و بتاخذ شكله ، و طبعا بصير هذا الاشي بسبب infection بخلي البول قاعدي

طيب شو هي البكتيريا يلي بتعمل هيك ؟ اخذناها بالمايكرو يا حلو و دكتور حافظ حكى عنها معلومة مهمة

هي ال proteus بالدرجة الاولى و برضه ال staph

- **Gout** & diseases involving rapid cell turnover, such as the leukemia's, lead to high uric acid levels in the urine & the possibility of **uric acid stones**.

بالنسبة لمرضى النقرص بصير عندهم uric acid stones لانه بكون عندهم مستويات عالية من ال uric acid و برضه بكون في uric acid stones عند المرضى يلي عندهم امراض زي ال leukemias لانه بكون عندهم rapid cell turover

- However **50% of the individuals with uric acid stones have neither hyperuricemia nor urine urate but, an unexplained persistent excretion of acidic urine.**
- **Cystine stones** are almost invariably **associated with a genetically determined defect** in the renal transport of cysteine amino acid.

10.10 Oxalate calculus

Oxalate calculus. Large, hard, spherical stone with rough **spiny** surface

Hydronephrosis

هو عبارة عن

dilatation of renal pelvis and calyces due to obstruction

- Is dilation of the renal pelvis and calyces due to obstruction, with accompanying atrophy of kidney parenchyma.
- Sudden or insidious
- Obstruction at any level from the urethra to the renal pelvis.

مهم جدا تميز مين ال hyronephrosis يلي بصير بدون ما يكون في infection ، يعني هو aseptic ، لازم تميزه عني ال pyonephrosis يلي هو عبارة عن dilation في ال renal pelvis and calyces with pus ، يعني في infection

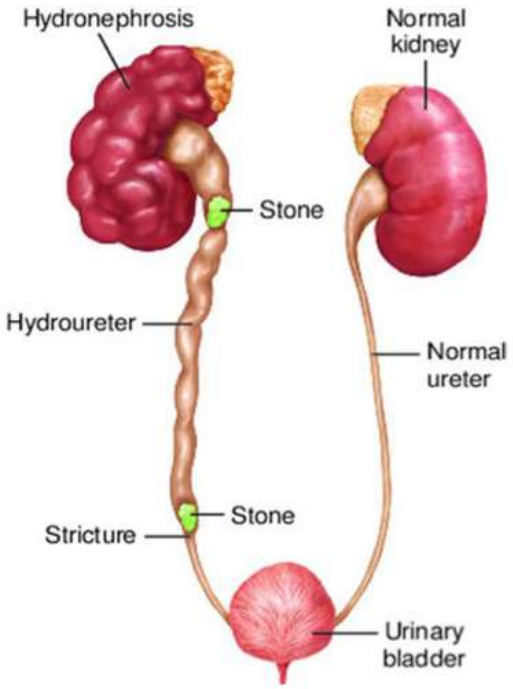
وقل رب زدني علماً

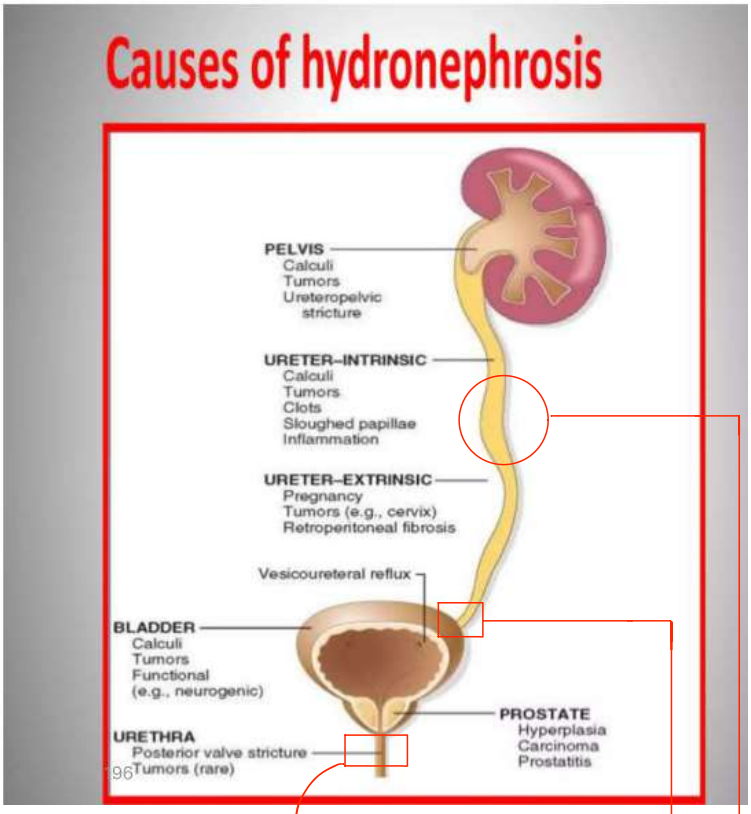
GENITOURINARY SYSTEM

رح نناقش اول الاسباب ال congenital

هسة بدنا نناقش الأسباب يلي بتعمللنا ال hydronephrosis

• 1-Congenital: examples





١ •Atresia of urethra

٢ •Valve formations in ureter or urethra

٣ •Aberrant renal artery compressing ureter

عبارة عن abnormal renal artery بعمل compression على ال ureter

٤ •Renal ptosis with torsion or kinking of ureter

هذا بصير لما ال perinephric fat يلي بتكون موجودة حولين الكلية هاي لما تذوب بتنزل الكلية ، طبعا هذا بصير لما الواحد يعمل sever diet ، فبقل ال support of the kidneys و بس تنزل الكلية ممكن تعمل انثناء بالحالب و تعمل انسدادات

وقل رب زدني علماً

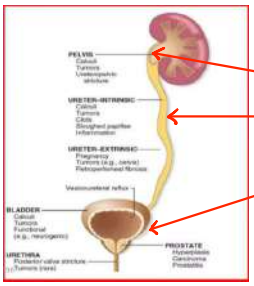
GENITOURINARY SYSTEM

• 2-Acquired:

• Examples:

- Foreign bodies
- Calculi,
- necrotic papillae

مريض عنده اي نوع من ال nephropathy يلي ممكن تعمللنا papillary necrosis



اي calculi ، انه اذا تواجدت في اي مكان رح تعمل hydronephrosis

برضه ال tumors ممكن تكون موجودة داخل ال ureter او خارج ال ureter و بتعمل ضغط عليه

- Tumors: prostatic hyperplasia, prostate cancer, bladder tumors, cervix or uterus cancer.
- Inflammation: Prostatitis, ureteritis, urethritis,
- Neurogenic: Spinal cord damage
- Normal pregnancy: rare, mild and reversible
- If blockage is at the ureters or above, the lesion is **unilateral**.
- **Bilateral HY** occurs only when the obstruction is below the level of the ureters.

❑Pathogenesis

- **Even with complete obstruction, GF persists for some time,**& the filtrate subsequently diffuses back into the renal interstitium & prerenal spaces,. Because of the **continued filtration, the** affected calyces & pelvis become dilated**.**
- The unusually high pressure thus generated in the renal pelvis, as well as that transmitted back through the collecting ducts, causes compression of the renal vasculature, with both venous stasis & arterial insufficiency.
- The most severe effects are seen in the papillae, because they are subjected to the greatest increase in pressure.
- Accordingly,**(a) the initial functional disturbances are largely tubular, manifested primarily by impaired concentration**

Only (b) later does G filtration begin to diminish.

ببساطة بكون عندي obstruction بخلي ال filtrate يرجع للوراء و يعمل dilation بال calyces و ال pelvis

وقل رب زدني علماً

GENITOURINARY SYSTEM

هاي الكلية صار فيها hydronecrosis ، و هي مبين انه صار في dilation بالكلية

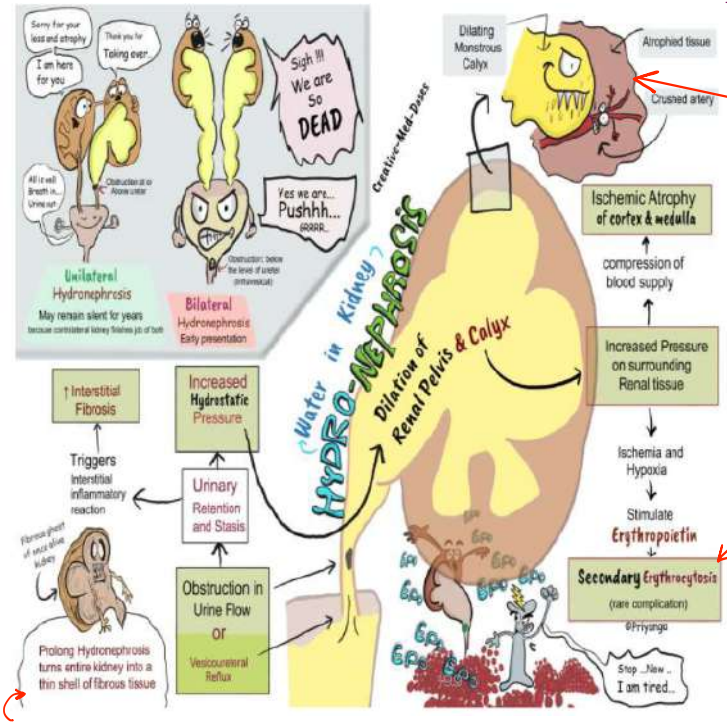
شوفوا كيف هذا ال dilation بعمل ضغط على ال blood vessels

لما يضغط على الشرايين بصير في عندي ischemic changes ، يعني بتأثر ال blood supply للكلية ، وبالتالي بصير عندي ischemia و hypoxia

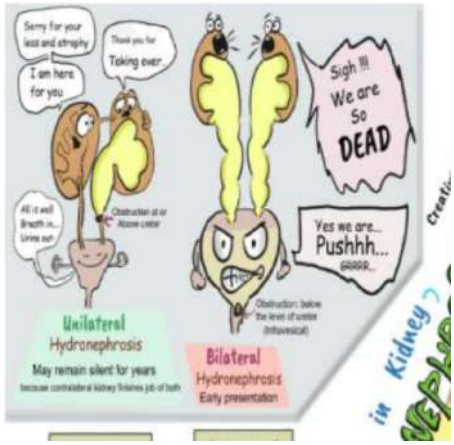
و بصير عندي stimulation لل erythropoietin و بصير في secondary erythropoiesis

و برضه كمان بصير في hypertension

Complication



اذا صار في ischemic changes ما رح نقدر نلحق الكلية و رح يصير في atrophy

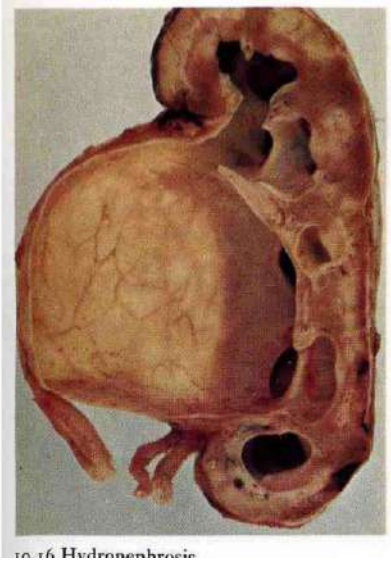


خلينا نيجي هنايا ، شو نشوف هنايا ، شاكو ماكو؟

انتبهوا هون كيف ممكن يكون ال obstruction في ال ureter بكون المرض unilateral و الكلية الثانية ما بتتاثر و بتغطي عن الكلية الأولى اما بس تكون

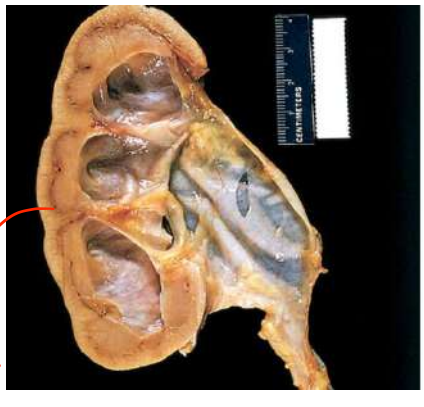
وقل رب زدني علماً

GENITOURINARY SYSTEM



Hydronephrosis.
Bisected kidney, showing:
(I) An **aberrant accessory renal artery** to the lower kidney pole (lower center, arrowed), which, by pressing upon & obstructing the upper end of the ureter, has caused.....
(II) **hydronephrosis,** with dilation of the pelvis, calyces, & upper ureter. ☺The lower ureter, below the obstruction, is normal

لاحظوا هون ال renal pelvis كيف صايرة
طبعا هاي بسبب ال aberrent blood vessels



Hydronephrosis of the kidney,
★with marked dilation of the pelvis & calyces &

★thinning of the renal parenchyma

لاحظوا هون في atrophic changes