Cystic diseases

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,

رح نحكي عنها لقدام

(2) Cysts are common & often present diagnostic problems for clinicians, radiologists, & pathologists and ,rarely, they can be confused with malignant tumors.

لانو ال RCC ممكن يصير فيه cystic degenerationالي ممكن تلخبطنا عن ال cyst

▪ Types of cysts:

1-Simple Cysts

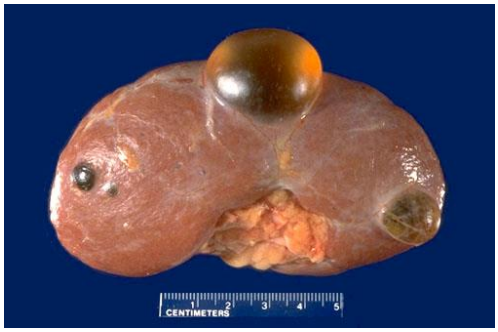
2-Dialysis-associated acquired cysts

3-Autosomal Dominant (Adult) Polycystic Kidney Disease

4-Autosomal Recessive (Childhood) Polycystic Kidney Disease

5-Medullary Cystic Disease

1. SIMPLE CYSTS



من اسمهم : اكياس المي هاي بسيطه و لا تشكل خطورة

الشي الوحيد المميز فيها انو ممكن الاخطاء بتميزها عن الكانسر

▪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*

2. CYSTS ASSOCIATED WITH CHRONIC DIALYSIS

هاد النوع من اكياس المي بظهر بعد ما الكلية توصل لاخرها زي بال

CKD And Renal failure و هم الي بسببو ظهور هاي الاكياس ,

و هدول المرضى يتم غسل الكلى لهم عند وصولهم لهذه المرحلة المتأخره, لهذا يمكن تسميتهم ب dialysis cyst patients .

و يجب معرفة دام انه هدول المرضى عندهم CKD ف هم معرضين بشكل كبير لتطور السرطان فيهم .

▪Seen in patients with renal failure who have prolonged dialysis.

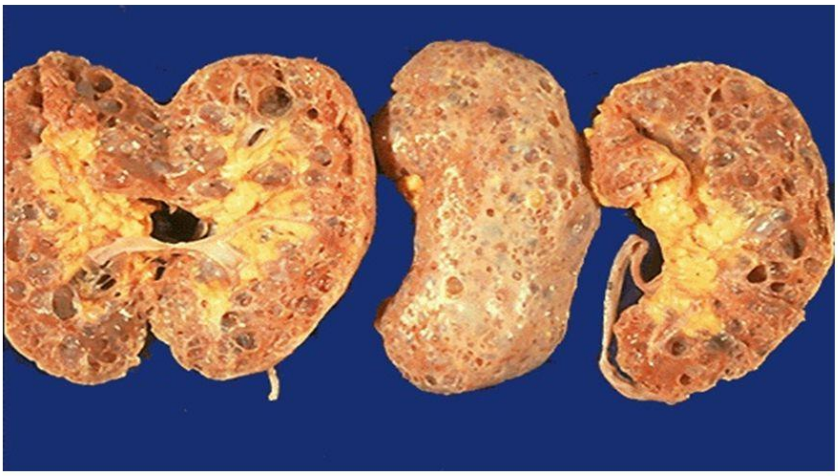
▪ In both cortex and medulla

▪Complications: hematuria; pain

▪Increased risk of renal carcinomas (100 times greater than in the general population)

▪ Occasionally, renal adenomas or even adenocarcinomas(RCC) arise in the walls of these cysts.

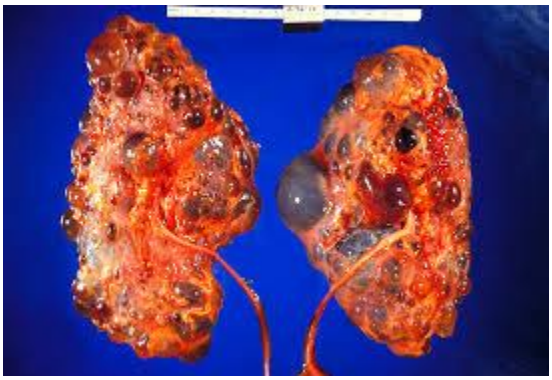
Cystic change associated with chronic renal dialysis.



Polycystic kidney diseases (PKD):

من اسمه (polycystic) بنستنتج انو بكون في عنا مجموعة من اكياس المي موجودة في الكلى والتي ادت الى المرض

و عنا نوعين منهم و كلاهما وراثي



3. Autosomal Dominant (Adult) Polycystic Kidney Disease

ما الذي ادى لتكون كيس الماء ؟

دام المرض وراثي , ف اكيد رح يكون عنا طفرة بجين معين و بهاي الحالة

بكون في عنا طفرات بجينين خوات ← PKD-1 + PKD-2

الي بنتجو بروتين اسمه polycystin protein1+2 respectively

و هاي البروتينات بتكون موجوده باعضاء مختلفه ب اغلب الخلايا عال cilia : من وظيفائهم انهم بمنعو تكاثر الخلايا .

فبهاد المرض الي بصير : الجين تاعهم يختل بالتالي لا يوجد مانع للتاكثر بالتالي الخلايا بتكتر و يتم انتاج معهم بروتنات بتساعد على ادخال المي ,

و الناتج بكون تكون كيس الماء .

اكياس الماء تنتج في كل و اي مكان ب كلى الكلى.

▪Pathogenesis:

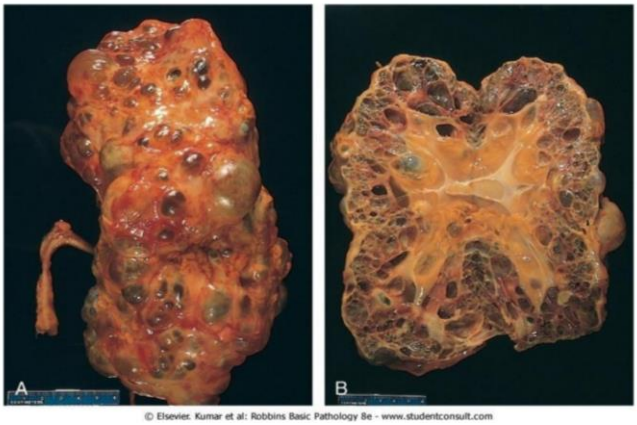
The disease can be caused by inheritance of one of at least two autosomal dominant genes of very high penetrance.

▪In 85% to 90% of families, PKD1,the defective gene is on the short arm of chromosome 16. This gene encodes polycystin-1.

▪In 10-15%, PKD2: encodes polycystin- 2.

- Multiple bilateral cysts
- Eventually destroy the renal parenchyma.
- Incidence (1: 500-1000) persons (not common)
- 10% of chronic renal failure.

AUTOSOMAL DOMINANT (ADULT) POLYCYSTIC KIDNEY DISEASE



❑Clinical presentation:

▪Asymptomatic until the 4th decade.

يمكن لنا تخيل الاعراض من تخيلنا لسير المرض

▪Symptoms: flank pain , heavy dragging sensation, abdominal mass, hemorrhage, obstruction, Intermittent gross hematuria

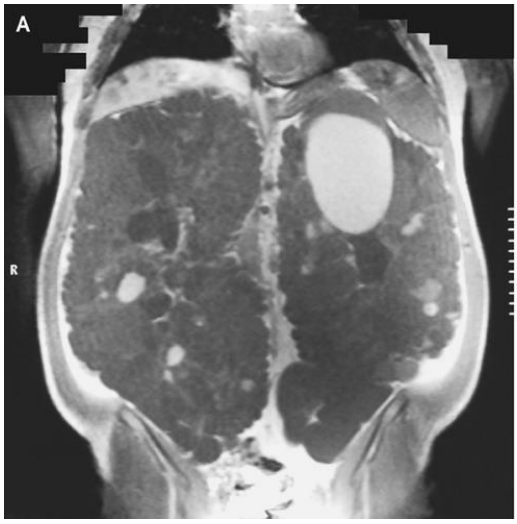
▪Grossly:

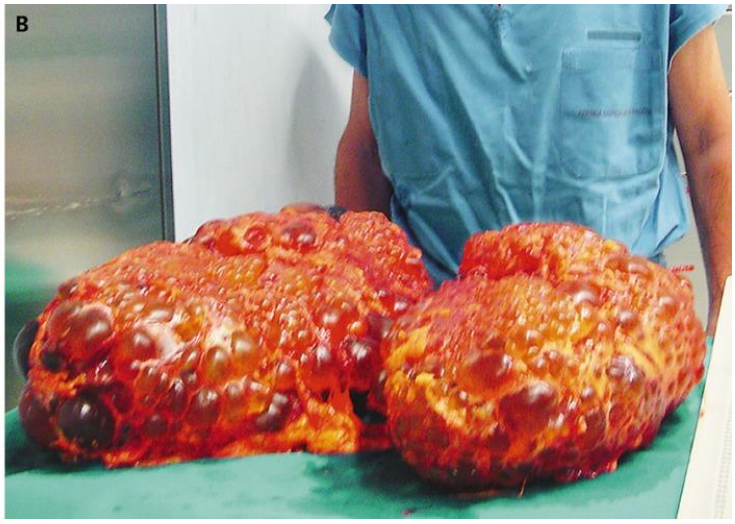
▪ The kidneys may reach enormous size (weights of up to 4 kg for each kidney).

▪These very large kidneys are readily palpable as abdominally masses.

▪ Both kidneys composed solely of cysts, up to 4 cm with no intervening parenchyma. (totally replaced by cysts)

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





❑ Complications:

ما المضاغفات المحتمله ؟

- ارتفاع ضغط الدم هو من الاعراض المهمه جدا و بساعدنا بالتشخيص

كيف بصير؟

كيس المي لما يتكون اعداده ممكن تكتر او انه كيبر لدرجة اعاقة مجرى سريان الاوردة الي حواليه

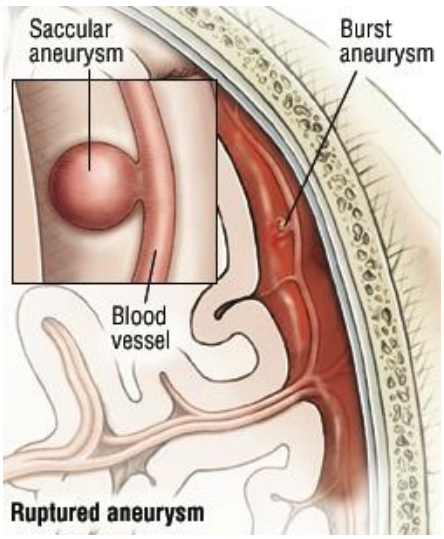
بالتالي : تقل التروية ← يقل الاكسجين← يفرز ال renin بكثرة الي بالتالي رح يساعد في زيادة ضغط الدم

و من نفس المبدأ بعمل uremia

بسبب قلة تروية ← قلة فلترة الخ

1. Uremia & hypertension (which develops in 75% of cases)
2. Urinary infection. (caused by the numerous cysts or obstruction)

كمان برضو ممكن يؤدي ارتفاع الضغط لمضاعفات اخرى من ضمنها ال saccular aneurysm

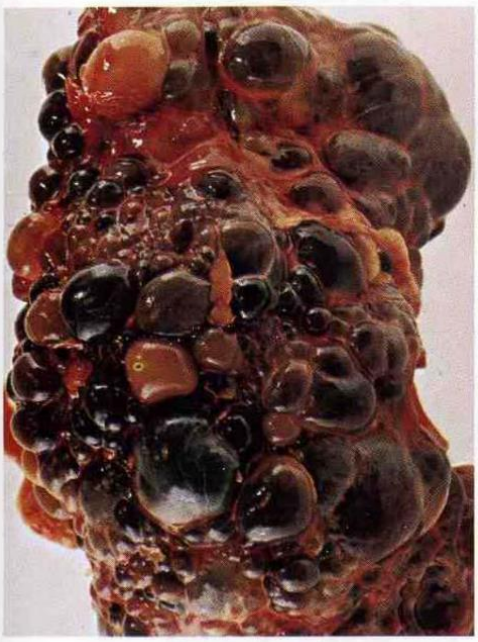


3. Saccular aneurysms of the brain circle of Willis are present in 10% to 30% of patients, & these individuals have a high incidence of subarachnoid hemorrhage.

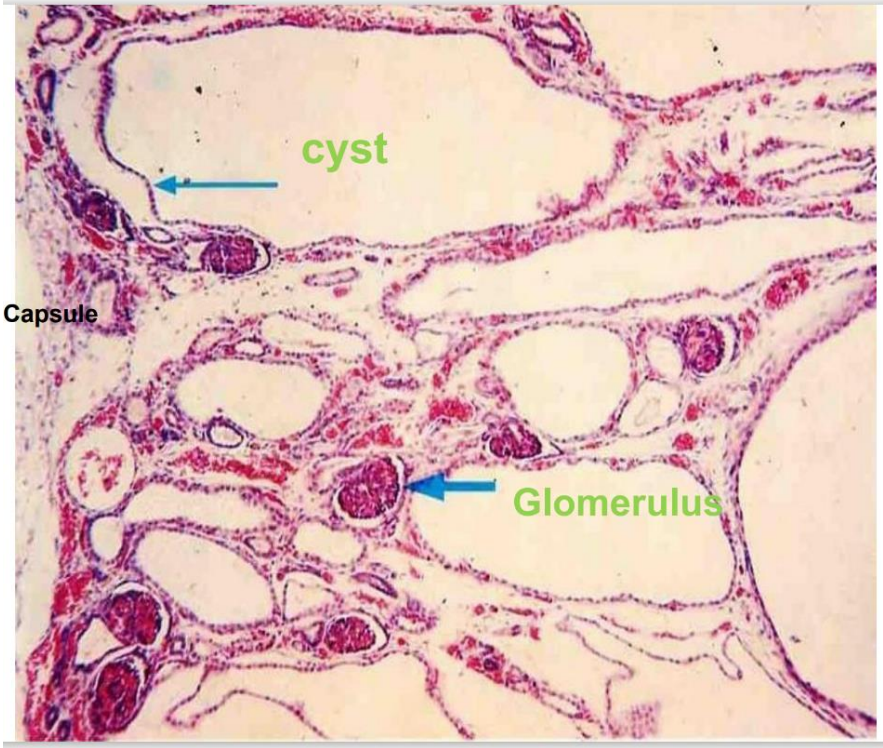
(he may have it as the first presentation in which patient comes with a severe headache , worst ever, in which is caused by PKD)

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

• Treatment is by renal transplantation (caused cyst involved whole kidney)



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



Adult polycystic Kidney.
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.

4. Autosomal Recessive (Childhood) Polycystic Kidney Disease

هاد المرض نفس اخوه بتكونه

طفرة بجين ← عطل عمل بروتين ← ادى لتكون كيس ماء

وبهاي الحاله هو ال fibrocystin الي بساهم ب وظيفة ال cilia and tubular epithilial

▪ results 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

هاد المرض متخص بالاطفال الرضع و الاجنة

بصير في عنا كتير اكياس مي بكلى الكليتين بكل مكان و بسرعة بصير في عنا فشل كلوي عند البيبي

(البيبي لما يكون ببطن امه و عنده فشل كلوي , هاد الشي رح يؤدي لكتير اضرار منها نقصان السائل الاميوني لانه الكلى خربت عنده و ما عم يخرج المي الي بلعه oligohydramnios

و من ورى نقصان السائل الاميوني ادى هاد لعدم نمو الرئه بالشكل المطلوب لانه السائل الاميوني مكون مهم في توسع و نمو الرئه ف بيبي بنولد و هو مش عارف يتنفس لانو صار في اعاقة بنمو الرئه تاعته و غيرها من مشاكل pulmonary hypoplasia

شوفو لاي مدى اثر اختلال الجين

ف الموض جدي و خطير و ممكن الطفل يموت ببطن امه)

▪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

▪Autosomal recessive

▪Rare ,1:20,000 live births.

في حكي بنحكى انو متى ما شفت كيس مي بالكلى شك ايضا بوجودها بالكبد

و غير ذلك يوجد حالات يتم اضرار الكبد و بصفي عند البيبي كمان congenital hepatic fibrosis بال portal regions

▪Depending on time of presentation & the presence *of associated hepatic lesions*, there are: perinatal, neonatal, infantile, & juvenile subcategories have been defined.

ممكن ييجي و هو بطن امه او عالولاده او و عمره سنه او بالطفوله

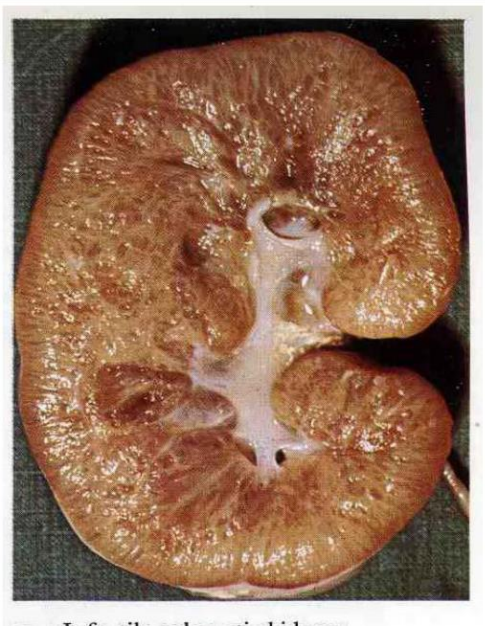
❑Grossly:

▪The disease is invariably bilateral, with numerous small cysts in the cortex & medulla give the kidneys as sponge like appearance.

▪ The medulla & cortex are completely replaced 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. مهم نعرف شو كل واحد منهم برتبط مع مين



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

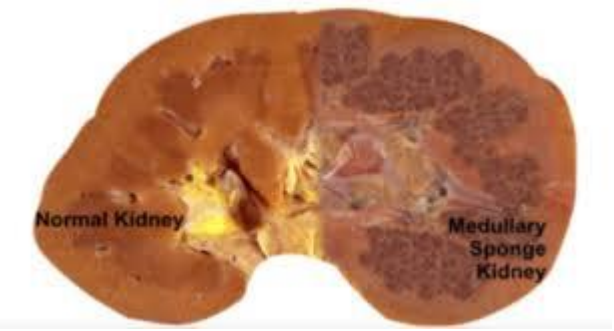
5. Medullary Cystic Disease

▪2 major types:

1-medullary sponge kidney:

▪ *Common* and innocent(Harmless) condition.

اكياس المي بتكون كتيره و صغيره وشامله فقط ال medulla



بفرق الmedullary sponge kidney عن ال nephronophthisis - medullary cystic disease complex

انه غير مؤذي اما التاني تقريبا دايما يؤدي الى فشل كلوي

2-nephronophthisis - medullary cystic disease complex:

هم يفرقو كمرضين بس الدكتورة اعتبرتهم مرض واحد للشبه الي بينهم

الي بصير في هاد المرض: انو في جين بيختل ← باثر ع بروتينات معينه ← الي بالتالي يؤدي الى ضرربالانسجة الي رح تؤثر بالكلى

و من الاضرار : انو بعمل ضمور بال renal tubules و باثر و بعمل التهاب و تليف بالانسجه الي حواليهم الي رح مع الوقت يوصل الضرر لل glomerulus و يؤدي الى تصلبها

و الناتج النهائي لكل هاد هو ضعف ب اداء الكلى و ممكن يوصل الى فشل كلوي

مع مرور الوقت بساوو اكياس مي خاصه في منطقة ال corticomedullary junction

▪Grossly:

▪The kidneys are small & contracted.

▪Numerous small cysts lined by flattened or cuboidal epithelium are present, typically at the cortico-medullary junction

▪Almost always associated with renal dysfunction.

▪Cysts are at cortico-medullary junction.

هلا بالنسبه الى ال nephronophthisis فهو عادة يوثر بالاطفال و تيكبرو ليوصلو لمرحلة الفشل الكلوي

عكسه ال medullary cystic disease الي يوثر بالكبار

و هاي من احدى الفروقات الي بينهم

▪Usually begins in childhood.

▪ 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.

من الفروقات الاخرى انو ال nephronophthisis ممكن يوثر بالاعضاء الاخرى عكس ال medullary cystic disease المقتصر على الكلى

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

❑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

و الكليه بتكون منكمشه و صغيره

Or

3. The cysts may not be apparent on renal biopsy if the corticomedullary junction is not well sampled.

لانهم بكونو موجودين من ال junction الى الداخل و غير موجوجين بال cortex بالتالي ممكن ما يبين معنا لا اذا شفنا ولا اذا اخدنا خزعه حدودها ال cortex

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

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 .(cause urethra and ureter are longer)

▪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. Cystine stones (2%)

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

حصوات الكلى ممكن انها تصير بكل مكان بالجهاز البولي و الاكثر شيوعا بالكلى نفسهم

كيف بتكونو ؟

بالوضع الطبيعي البول بيتكون من مي و مواد ذائبه ,

الي بصير انو المي رح تتشبع بالمواد الذائبه اما بسبب وجودها بكميه اكبر من المعتاد او بسبب نقصان المي لزي في حالة جفاف و هاد رح يؤدي الى ترسبها و تكون كريستالات منها و هاد ما ينتج حصى الكلى.

حسب نوع المادة الذائبه رح يتكون نوع من الحصى و اشيعهم هو حصى الكالسيوم

▪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.

ممكن تتكون هاي الحصى بسبب ارتفاع افراز الكالسيوم بالكلى و تشبعها (50%)

او بسبب ارتفاع الكالسيوم بالجسم من ورا مرض معين الي كمان ادى لارتفاعه بالكلى

2- The presence of a nidus

ال nidus هو جاذب للمواد الذائبه لترسبها به خاصه الكالسيوم

كحمض اليوريا او انفصال/ تقشر ال epithilial cells او مستعمرات الباكتيريا

➢Urates provide a nidus for calcium deposition.

➢Desquamated epithelial cells

➢Bacterial colonies

3- Urine pH

حمضية البول بتاثر على اي من المرسبات ان تتكون

كمثال التهاب المسالك البوليه تكون بول قاعدي التي تساعد على انتجاع انواع حصى معينه

كمثال ال cysteine stone و calcium oxalate بتكون بالبيئه الحمضيه

اما ال calcium phosphate و ال struvite بتكون بالبيئه القاعدية

4- Infection

Recurrent uti may lead to sone formation cause bacteria colonis causes nidus that gather organic salts and form stones

▪Magnesium ammonium phosphate (struvite) stones:

ممكن يتسمو ل infection stones لانو الحصى تكون بسبب وجود الباكتيريا

كيف ؟

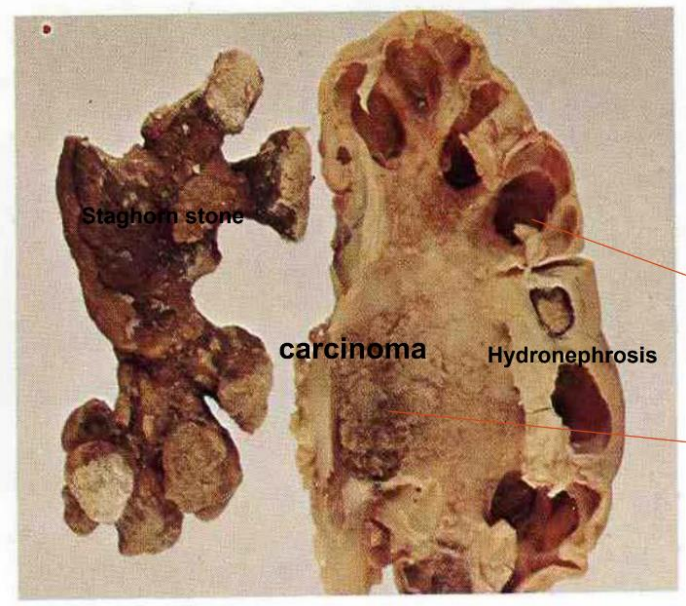
الباكتيريا تحتوي على انزيم ال urease الي رح تكسر اليوريا الى co2 و امونيا

و الامونيا بتخلي بيئة البول اكثر قاعدية مما يؤدي الى ترسب الماغنيسيوم و الفوسفات و الامونيوم

Staghorn shaped stones

بكون شكلها هيك لانها دايما بتتشعب الى ال renal calyles

with persistently alkaline urine due to (almost always occur in persons to urea-splitting bacteria, such as Proteus vulgaris& UTIs, specially, due staphylococci. the



Staghorn stone (MgNH3PO4):
(I) **struvite stone** removed from the kidney where it formed a cast of the dilated pelvis & calyces.

The kidney shows:

(II) **hydronephrosis,** extensive destruction & extreme atrophy of the renal parenchymawith calculus debris present within some calyces.

(III) **sessile papillary tumor** in the pelvis **(adenocarcinoma)**following glandular metaplasia secondary to chronic stone irritation.

so if the chronic stone persists and is not removed it would lead to chronic irritation, metaplasia in the area, and dysplasia that may lead to carcinoma

in here we have papillary carcinoma that came from the irrititve staghorn stone that obstructed the kidney

we also have severe hydronephrosis , dilation of the cortex .most is atrophied

we also have destructed renal parenchyma

▪**Uric acid stones**

form in acidic urine (under pH 5.5):

هاي الحصوات بتتشكل بشكل اساسي من حمض اليوريا

متى ممكن تصير؟

حمض اليوريا هو ناتج لهدم ال purines الي ممكن يصير اثناء الكيماوي من خلال هدم خلايا السرطان, ف احنا كمان عم نساعد على تكسير البيورينز الي رح تنتجلنا حمض اليوريا

او ممكن تصير بسبب نقص لانزيمات معينه الى رح تؤدي لانتاج حمض اليوريا بشكل كبير

او ممكن من خلال اكل اللحوم الحمراء او شرب الكحول الي برضو رح يؤدي لنفس الشي و الى gout

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

▪However, 50% of the individuals with uric acid stones have neither hyperuricemia nor urine urate but, an unexplained persistent excretion of acidic urine.

So some patients may have increased uric acid not disease caused

▪**Cystine stones:**

▪Are almost invariably associated with a genetically determined defect in the renal transport of cysteine amino acid.

transportation of cysteine in kidney will be disturbed leading to its accumulation

HYDRONEPHROSIS

هاد المرض هو ناتج انسداد في مكان ما في مجرى الجهاز البولي

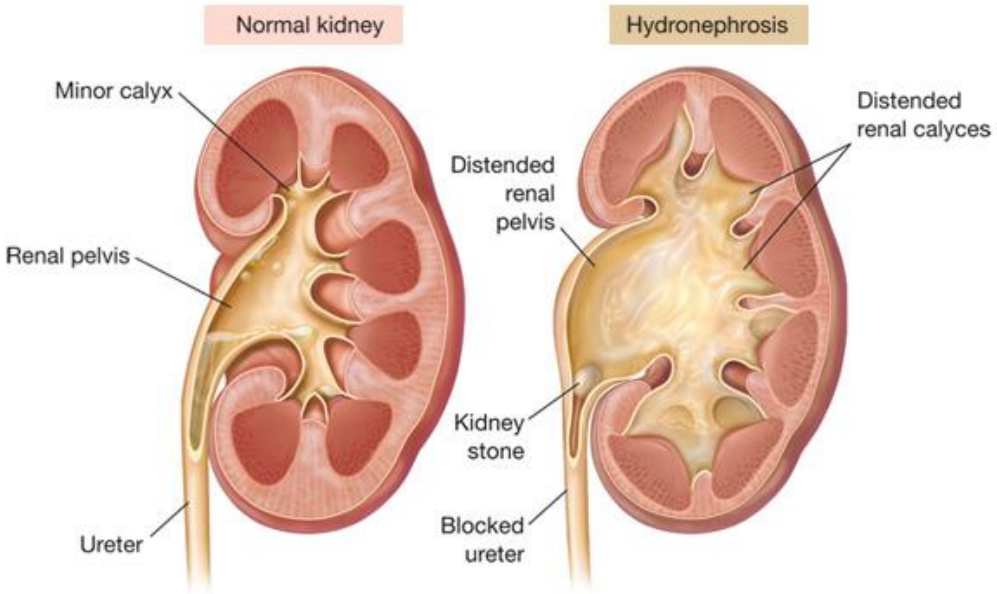
و هاد الانسداد ادى الى اعاقة جريان البول , بالتالي البول بكون بدو يمر بس ما بمر منيح بسبب الانسداد و يكون ببالنا انو انتاج البول مستمر

بالتالي بدال ما البول يكمل مساره رح يضل موجود مكانه بالكلى او برجع بدال ما يتقدم و بالاخيرمع الوقت رح يؤدي الى توسع الكلى

▪ 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.



▪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.

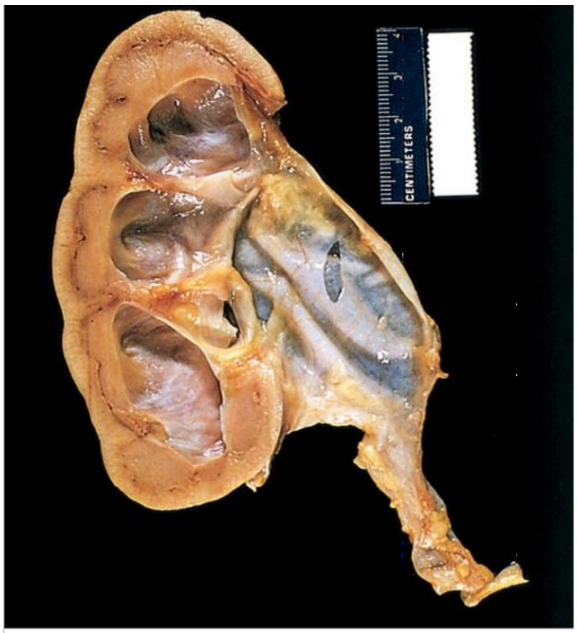
▪The unusually high pressure thus generated in the renal pelvis, as well as that transmitted back through the collecting ducts, causes compression of the renal vasculature, with both venous stasis & arterial insufficiency.

▪The most severe effects are seen in *the papillae*, because they are subjected to the *greatest increase in pressure.*

▪ Accordingly, the initial functional disturbances are

-1largely tubular, manifested primarily by impaired concentration

-2and later the G filtration begins to diminish.



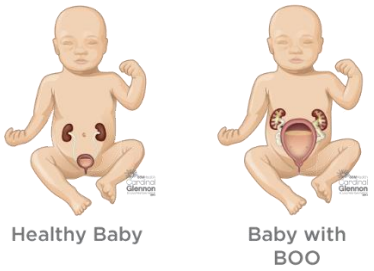
Hydronephrosis of the kidney:

★Marked dilation of the pelvis & calyces

&

★Thinning of the renal parenchyma

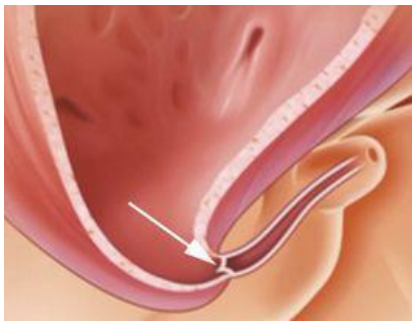
❑ The most common causes are:



1- Congenital:

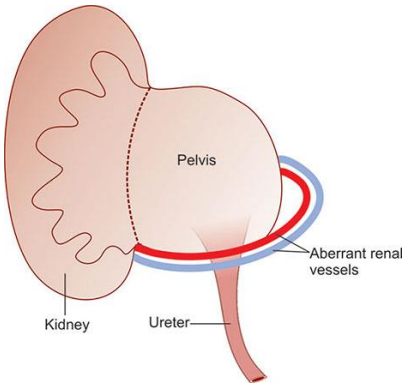
▪Atresia of urethra

▪Valve formations in ureter or urethra



الولد بكون منولد و عندو انسجه زايده عملت زي صمام بالمجرى

▪Aberrant renal artery compressing ureter



هو عبارة عن شريان موجود عند 30% من الناس و يؤغذي الكلى بدون مروره بال hilum

▪Renal ptosis with torsion or kinking of ureter

هو عدم تشبت الكلى بالشكل المطلوب الي يؤدي الى وقوعها للحوض عند الوقوف

2- Acquired:

❖ Foreign bodies

❖ Calculi (stone)

❖ Necrotic papillae (patients with papillary or urothelial cancer that lead to necrotic sluffing of the papillae from the tumor of the inflammation of the papillae that cause obstruction)

❖ Tumors: prostatic hyperplasia, prostate cancer, bladder tumors, (that obstruct urethra) cervix or uterus cancer. (that compress bladder and obstruct ureter)

❖ Inflammation: Prostatitis, ureteritis, urethritis (it cause thickening of the walls , narrowing of the lumen, and cause erythema and congestion that lead to obstruction)

❖ Neurogenic: Spinal cord damage (as paralyzed patients , loss of control of urine , obstruction happens , loss of peristalsis movement no smooth muscles movement , all leading to stasis of the urine and hydronephrosis)

❖ Normal pregnancy: rare, mild and reversible

(if it compresses the bladder or ureter , recurrent uti that may cause hydronephrosis

Its usually mild and reversible after pregnancy)

❑ If blockage is at the ureters or above, the lesion is unilateral.

(on one kidney cause it involved one ureter)

❑ Bilateral HN occurs only when the obstruction is below the level of the ureters.

(on the bladder or urethra , would affect both kidneys cause they would affect reversibley both ureters , both kidneys)