Kidney diseases can be divided into those affecting the 4 basic components

glomeruli

tubules

Blood vessels

interstitium

because some components seem to be more vulnerable to specific forms of renal injury; e.g. glomerular(G) diseases are often
whereas tubular & interstitial disorders are ؛immunologically mediated ،more likely to be caused by toxic or infectious agents

# CLINICAL MANIFESTATIONS OF RENAL DISEASES

<table>
<tr>
<td>Azotemia</td>
<td>is another word that refers to high levels of urea and is used primarily<br>when the abnormality can be measured chemically but is not yet so severe as to<br>produce symptoms</td>
<td colspan="3">
<table>
<tr><td>Renal azotemia</td><td colspan="2">azotemia may also<br>arises from extra renal disorders</td></tr>
<tr><td rowspan="2">is produced by many renal disorders</td><td>Prerenal azotemia</td><td>Postrenal azotemia</td></tr>
<tr><td>is encountered when there is hypoperfusion of the ‹kidneys<br>which decrease GFR in the absence of renal parenchymal damage</td><td>can result when urine flow is obstructed below the level of<br>the kidney. Relief of the obstruction is followed by correction of the azotemia</td></tr>
</table>
</td>
</tr>
<tr>
<td>Uremia</td>
<td>**means progression of the azotemia to clinical manifestations & systemic biochemical abnormalities<br>**Uremia is the condition of having high levels of urea in the blood.<br>**Urea is one of the primary components of urine.<br>**It can be defined as an excess of amino acid and protein metabolism end products, such as urea and creatinine, in the blood that would be normally excreted in<br>the urine</td>
<td colspan="3" rowspan="2">**Both uremia and uremic syndrome have been used interchangeably to<br>denote a very high plasma urea concentration that is the result of renal<br>failure<br><br>.<br>**Signs and symptoms<br>Classical signs of uremia are:<br>*progressive weakness and easy fatigue, loss of appetite ‹‹due to nausea and vomiting, muscle atrophy, tremors anemia, hemostasis disorders, , granulocytic, lymphocytic and platelet dysfunction , osteomalacia, β2-microglobulin amyloidosis, bone disease( via vitamin D deficiency, secondary,hyperparathyroidism and<br>itching, skin dryness, polyneuritis, ‹(hyperphosphatemia restless legs, cramps, peripheral neuropathy, abnormal mental function diurnal somnolence, night<br>memory and concentration disorders, asthenia, ‹insomnia headache, confusion, fatigue, seizures, coma, encephalopathy<br>*frequent shallow respiration and metabolic acidosis.<br>Without intervention via dialysis or kidney transplant, uremia due to renal failure will progress and cause stupor, coma and death.<br>Because uremia is mostly a consequence of kidney failure, its signs and symptoms often occur concomitantly with .other signs and symptoms of kidney failure</td>
</tr>
<tr>
<td>Uremic syndrome</td>
<td>**can be defined as the terminal clinical manifestation<br>of kidney failure (also called renal failure).<br>** It is the signs, symptoms and results from laboratory tests which result from inadequate ‹excretory<br>regulatory and endocrine function of the kidneys</td>
</tr>
</table>

## Diagnosis

A detailed and accurate history and physical will help determine if uremia is acute or chronic.

In

the cases of acute uremia, causes may be identified and eliminated, leading to a higher chance

.for recovery of normal kidney function, if treated correctly

## Blood tests

basic metabolic panel with

**basic metabolic panel** (**BMP**) is a blood test consisting of a set of seven or eight biochemical tests and is one of the most common lab tests ordered by health care providers. Outside the United States, blood tests made up of the majority of the same biochemical tests are called **urea and electrolytes** (**U&E** or "**Us and Es**"), or **urea, electrolytes, creatinine** (**UEC** or **EUC** or **CUE**), and are often referred to as 'kidney function tests' as they also include a calculated estimated glomerular filtration rate.

The seven parts of a CHEM-7 are tests for:

Four electrolytes:

- sodium ($Na^+$) [2]
- potassium ($K^+$) [3]
- chloride ($Cl^-$) [4]
- bicarbonate ($HCO_3^-$) or $CO_2$ [5]
- blood urea nitrogen (BUN) [6]
- creatinine [7]
- glucose [8]

| | |
|---|---|
| serum calcium and phosphorus to evaluate the GFR | Principal abnormality is very low (<30) GFR |
| blood urea nitrogen and creatinine | Uremia will demonstrate elevation of both urea and creatinine |
| serum potassium, phosphate, calcium and sodium levels | likely elevated potassium, high phosphate and normal or slightly high sodium, as well as likely depressed calcium levels |

| | |
|---|---|
| As a basic work up a physician will also evaluate | for anemia<br>Chronic anemia may be an ominous sign of established renal failure |
| The thyroid and parathyroid functions/ panels | will help work up any symptoms of fatigue, as well as determine calcium abnormalities as they relate to uremia vs longstanding or unrelated illness of calcium metabolism |

Urine tests

*A 24-hour urine collection for determination of creatinine clearance may be an alternative, although not a very accurate test due to the collection procedure

*Urinalysis with microscopic examination for the presence of protein, .casts, blood and pH

The clinical manifestations of renal disease can be grouped into 8 major syndromes

 Some are peculiar to diseases of G; others are present in diseases that affect any one of the 4 components. These are:

| | |
|---|---|
| Acute nephritic syndrome | is a G syndrome characterized by acute onset of **gross** hematuria(RBCs in urine), **mild to moderate** hypertension ;it is &،proteinuria, edema,azotemia the classic presentation of acute poststreptococcal GN |
| The nephrotic syndromeis | a G syndrome characterized by **heavy** proteinuria ،(excretion of >3.5 grams of protein/day in adults *normal : less than 150 mg hypoalbuminemia,severe edema, **hyperlipidemia, & lipiduria**(lipid in the urine) |
| Asymptomatic hematuria or proteinuria,or both | , is usually a manifestation of subtle (mild) G abnormalities |
| Rapidly progressive GN | manifested by **microscopic** hematuria, **dysmorphic RBC** RBC **casts** in the urine & **mild-to-moderate** & proteinuria, resulting in loss of renal function in a few days or weeks |
| Acute renal failure(RF) or (Acute Kidney Injury) | is dominated by oliguria or anuria (no urine flow) |
| Chronic renal failure(CRF) = Chronic Kidney Disease (CKD) | is the end result of all chronic renal diseases It characterized by ،prolonged signs & symptoms of uremia and in which, to maintain life, patient needs either long term 12 hours/week haemodialysis or renal transplant |
| Urinary tract infection(UTI) | & characterized by bacteriuria& pyuria(bacteria leukocytes in the urine respectively)). The infection may be symptomatic or asymptomatic, & it may affect the kidney (pyelonephritis)or the bladder (cystitis) |
| Nephrolithiasis(renal stones) | is manifested by renal colic, hematuria, & recurrent stone formation UT obstruction& renal tumors represent specific anatomic lesions that often have varied manifestations |
| UT obstruction& renal tumors represent specific anatomic lesions that often have varied manifestations | |

GLOMERULAR DISEASES

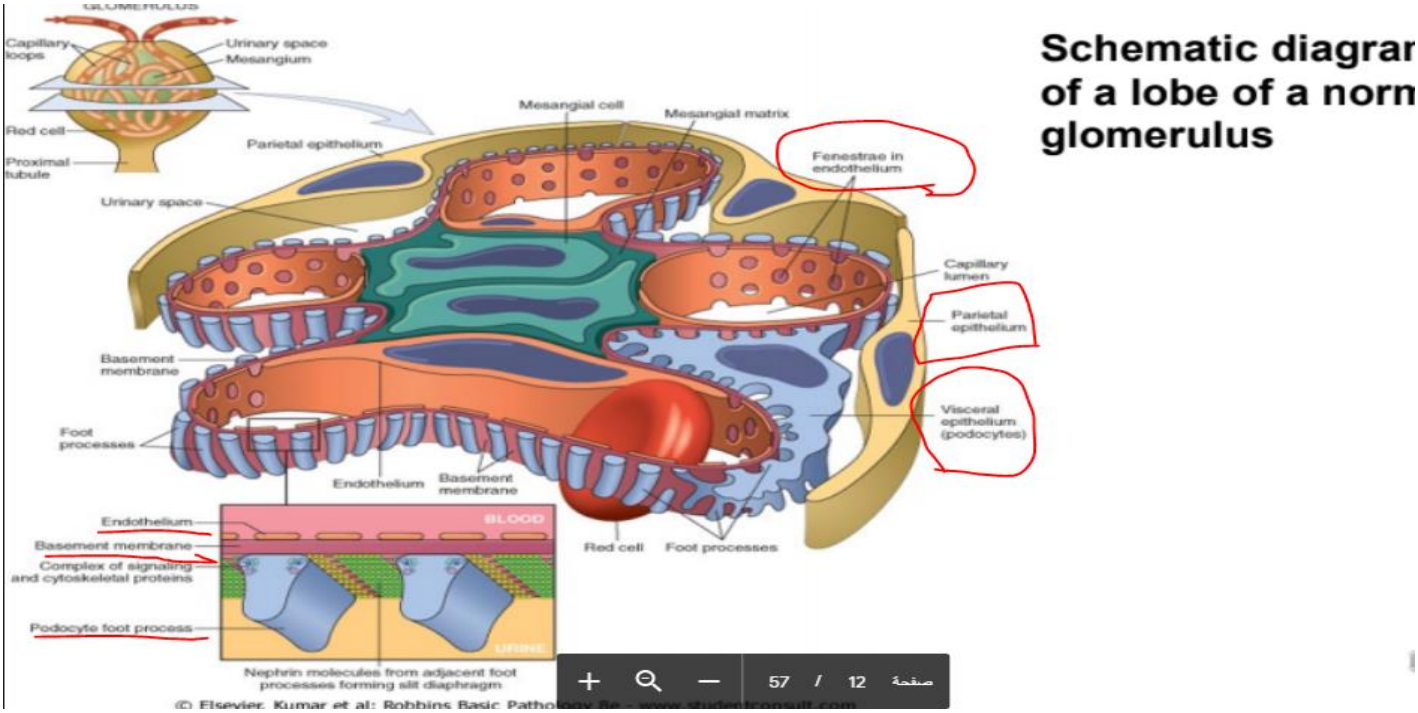
One of the most common causes of chronic kidney disease and is major problems encountered in nephrology; and chronic GN is one of the most common causes of chronic kidney disease in humans

The glomerulus normally consists of an anastomosing network of capillaries, invested by two layers of epithelium. The visceral epithelium (podocytes) is an intrinsic part of the capillary wall , whereas the parietal epithelium lines Bowman space(urinary space), the cavity in which plasma ultrafiltrate first collects

*Ultrafiltrate :

هاي معناها انه كل شي بالدم يمر ( glucose +AA + electrolyte +water ) ما عدا ptns and RBCs + WBCs + platelet

بالتالي لوخرب احد ال barriers يلي رح نحكي عنهم رح يصير عنده hematuria or proteinuria or both



**The G capillary wall is the filtration unit & consists of the following structures:

(I) A thin layer of fenestrated endothelial cells (EC)

II) A glomerular basement membrane(GBM)

*Layers :

1- lamina rara interna :

هاي المواجهة لل endothelium

2- the lamina densa : thick, electron-dense central layer thinner

3-lamina rara externa:

هاي المواجهة لل podocytes

1+3: thin electron-lucent peripheral layers

نوت خارجي :

١+٣ > يعتبروا charge barrier اما ٢ > لانها سميكة تعتبر size barrier

*The GBM consists of collagen (mostly type IV), laminin proteoglycans, fibronectin, & several other glycoproteins

III) The visceral epithelial cells(podocytes),structurally complex cells that possess interdigitating foot processes embedded in & adherent to the lamina rara externa of the GBM

**The entire G tuft is supported by mesangial cells (of mesenchymal origin) lying between the capillaries

**The major characteristics of GF are an extraordinarily high permeability to water & small solutes& an almost <u>complete impermeability to molecules of the size & molecular charge of albumin(size: 3.6 nm)</u>

**This selective permeability, called glomerular barrier function

discriminates among protein molecules depending on their size (the larger, the less permeable), their charge (the more cationic (+), the more permeable), & their configuration

لانه BM شحنته سالبة

**Glomeruli may be injured by diverse mechanisms, which are either a:

| Primary G diseases | Secondary G diseases |
|---|---|
| those in which the kidney is the only or predominant organ involved | in which the G may be injured in the course of a number of systemic diseases |
| *(Minimal-change disease (MCD<br>*Focal and segmental glomerulosclerosis (FSGS)<br>*Membranous GN = Membranous nephropathy MN<br>*Membranoproliferative GN (MPGN)<br>*Acute postinfectious GN<br>*IgA nephropathy<br>*Chronic GN | *Systemic Diseases Lupus (SLE) nephritis<br>*Diabetic nephropathy<br>*Goodpasture syndrome<br>*Microscopic polyangiitis<br>*Wegener's granulomatosis<br>*Henoch-Schönlein purpura<br>*Thrombotic microangiopathy<br>*Amyloidosis<br>*Bacterial endocarditis-related GN<br>*GN secondary to extrarenal infection<br>*GN secondary to lymphoplasmacytic disorders |

Pathogenesis of Glomerular disease -usually immune mediated via antibody deposition, cell mediated injury or activation of alternative complement pathway Antibodies deposited are either to in situ antigen (intrinsic or planted) or are circulating immune complexes

<table>
<tr><td colspan="3">immune mediated</td><td rowspan="2">NON immune mediated</td></tr>
<tr><td>1- Intrinsic<br>Ag يعني الجهاز المناعي يهاجم موجود اصلا مكانه بالكلية وجزء منها</td><td>Ex :<br>*Goodpasture disease antigens are in basement membrane;<br>*Heymann nephritis antigens are<br>on visceral epithelial cells;</td><td>produce linear immunofluorescence patterns</td></tr>
<tr><td>2-Planted antigens<br>يهاجم Ag موجود بالكلية بس هو اصلا مكانه مو بالكلية غريب عنها مزروع فيها</td><td>are deposited in basement membrane<br><table><tr><td>may be exogenous</td><td>endogenous</td></tr><tr><td>drugs, infectious agents</td><td>DNA, immunoglobulin, immune complexes</td></tr><tr><td colspan="2">their cationic proteins bind to glomerular anionic sites</td></tr></table></td><td>produce granular lumpy staining by immunofluorescence</td><td rowspan="3">Podocyte injury</td></tr>
<tr><td>3-Circulating immune complexes<br>Ag ارتبط مع Ab ب<br>circulation وبعدها عملوا<br>complex وراحوا ارتبطوا ب<br>mesangial<br>or subendothelial<br>activation of وعملوا<br>complement</td><td><table><tr><td>endogenous</td><td>exogenous</td></tr><tr><td>(DNA, tumors)</td><td>(infectious products)</td></tr></table>(Hepatitis B / C, lupus)</td><td>they usually localize within glomeruli and activate complement; deposits are usually mesangial<br>or subendothelial and resolve by macrophage phagocytosis, unless there are repeated cycles of formation</td></tr>
<tr><td>4-Cell mediated immune injury</td><td>is by sensitized nephritogenic T cells</td><td></td></tr>
</table>

**Progression to end stage renal disease occurs when the glomerular filtration rate (GFR) is 30 – 50% of normal, due to compensatory hypertrophy of remaining glomeruli and systemic hypertension (inhibited by angiotensin converting enzyme inhibitors), eventually causing glomerulosclerosis)

**The Nephrotic Syndrome

لتوضيح على اي اساس بصير مع الشخص nephrotic or nephritic ؟؟

المحدد الرئيسي هو site of glomerular injury

Podocytes injury >>>protein loss only >>> nephrotic

Endothelial / mesangial injury >>>

لانهم هدول الشغلتين بكونوا exposed to blood elements

So they are also exposed to inflammatory cells >>> nephritis (nephritic syndrome )

*a clinical complex resulting from glomerular disease & includes the Following :

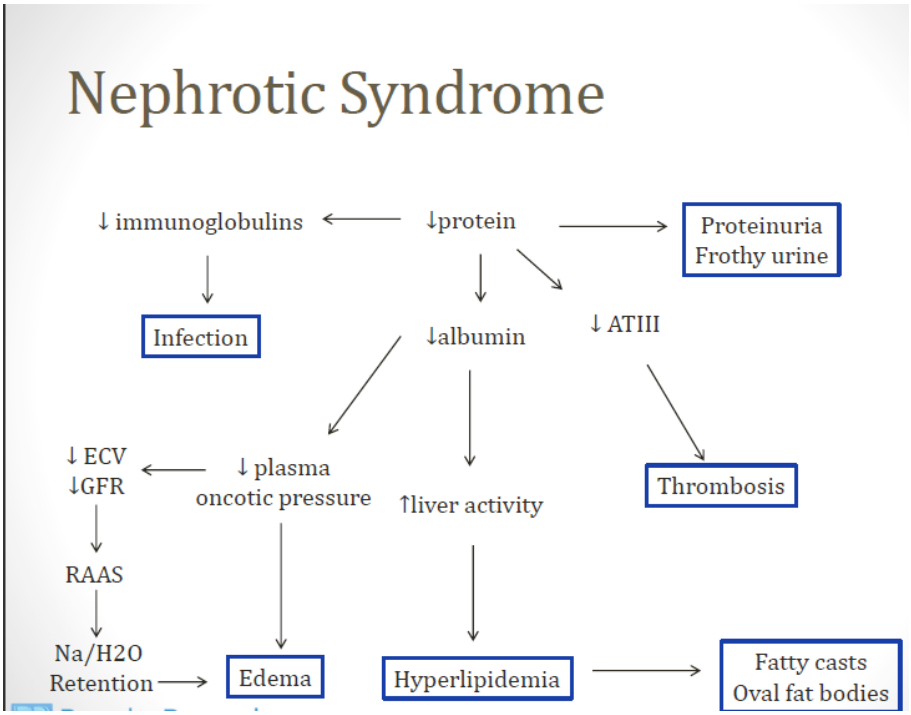
1- massive proteinuria 3.5 gm /day in adults

2- hypoalbuminemia (≤ 3 gm/dL

3-generalized edema

4- hyperlipidemia and lipiduri

5- little or **no** azotemia, **hematuria,** or h hypertension



Causes of Nephrotic Syndrome

| Primary Glomerular Diseases that Present Mostly with | Secondary Systemic Diseases with Renal Manifestations |
|---|---|
| ***Minimal-change disease**<br>***Focal segmental glomerulosclerosis(FSGS)**<br>*Membranous nephropathy<br>Membranoproliferative GN type 1 (usually a combination of nephrotic/ nephritic syndrome) | ***Diabetes mellitus**<br>***Amyloidosis**<br>*Systemic lupus erythematosus drugs (gold, penicillamine, "street "heroin)<br>*Infections (malaria, syphilis, hepatitis B, HIV)<br>*Malignancy (carcinoma, melanoma)<br>*Miscellaneous (e.g. bee-sting allergy) |

نوت خارجية للفهم :

نعتمد بتشخيص ال glomerular dz على biopsy بشكل كبير عشان هيك لازم نعرف العينة بتلت ادوات وكل اداة او كل صورة على شو بنتطلع بزبط :

Light microscope : type of injured cell / is there any crescentic (parietal cells +fibrin + monocyte ) that indicate sever G injury

EM : to see the site of accumulation of Ag – Ab complexes (subepithelial / subendothelial / mesangium ) .....

غير هيك بنشوف فيه structures تبعون الخلايا بتفاصيلها

Immunofluorescence :

شكل ترسيب ال Ab – Ag complexes هل هو linear or granular ??

شو نوع Igs / complement

# **Minimal Change** Disease (Lipoid Nephrosis)

**MCD is the most frequent (about 65%) cause of the nephrotic syndrome in children. Although it may develop at any age, MCD is most common between ages 1 and 7 years.

** It is characterized by G that have a **normal appearance by light microscopy**

ومن هنا جاء اسمه **Minimal** Change

** but when viewed with the EM it shows (**mechanism/ Pathogenesis :)

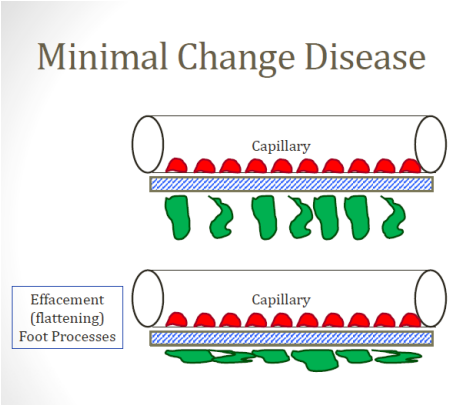
1-diffuse effacement of podocyte foot processes

معناها تصير ممسوحة ويبطل في SLITS بينهم

غير هيك بصير عنا injury عن طريق تراكم cytokines ويفقد ال GBM ال

charges – تبعونه وهاي المعلومة مهمة ويترتب عليها احداث .. غير مذكورة

صورة توضح المقصود :




2- without antibody deposits

يعني ما رح نستفيد من IF

*The pathogenesis of podocyte injury, which is the underlying mechanism of proteinuria in MCD is **unknown** & it may be the result of nonimmune causes

**Morphology:

| LM | IF | **EM** |
|---|---|---|
| the glomeruliappear normal | Negative ( no immune complexes ) | **uniform and diffuse effacement of the foot processes of the podocytes**<br>No immune deposits |

**MCD Clinical Course

• nephrotic syndrome in an otherwise healthy child

•no hypertension

•renal function preserved

•**selective proteinuria (albumin) =only albumin in the urine not Igs**

not selective ،،،،، nephrotic diseases باقي ال

**Ttt , prognosis and fate of Dz :

•prognosis is good

طب ليه ؟ النقطة يلي تحت

•**Treatment : corticosteroids 90 % of cases**

nephrotic diseases وهاي برضه ميزة لهاي المرض مو موجودة بغيره من امراض

•< 5 % develop chronic renal failure after 25 years

•In Adults with minimal change disease the response is slower and relapses are more common

# Focal and Segmental Glomerulosclerosis (FSGS)

G lesion characterized histologically, by sclerosis ( pink collagen deposition in glomerulus ) affecting **some, but, not all G** (focal involvement) & **involving only some (segments)** of each affected G

**cause :

*often associated with the nephrotic syndrome& can occur

1-in association with other known conditions, e.g., HIV nephropathy, ؛heroin nephropathy

2-(As a secondary event in other forms of GN(e.g., [IgA] nephropathy

3- as a maladaptation after nephron loss

4- in inherited or congenital forms resulting from mutations affecting cytoskeletal or related proteins expressed in podocytes (e.g., nephrin), ؛i.e., nonimmune cause

((Nephrin a transmembrane glycoprotein, is the major component of the slit diaphragms between adjacent foot processes))

5- as an primary or idiopathic FSGS, which accounts for 20% to 30% of all cases of the nephrotic syndrome

**Epidemiology :

*It is becoming an increasingly common cause of nephrotic syndrome (in adults (35%

*remains a frequent cause in children

#In children it is important to distinguish FSGS cause of the nephrotic syndrome from MCD, because the clinical courses are markedly different :

خلينا نحكي انه

FSGS : sever form of MCD

-Unlike MCD, patients with FSGS have

(1) Nonselective proteinuria, &

(2) Higher incidence of hematuria & hypertension

(3) Generally, a poor response to corticosteroid therapy,

(4) with 50% of cases developing RF within 10 years of diagnosis.

Adults in general feel even less well than children

**Pathogenesis

*The pathogenesis of primary FSGS is unknown

*In any case, nonimmune injury to the podocytes is thought to represent the initiating event of primary FSGS (as with MCD)& is the underlying mechanism of proteinuria

*The permeability-increasing factors produced by lymphocytes have been proposed in both MCD & FSGS

هاي قصدهم فيها ال cytokines

*The recurrence of proteinuria in some persons with FSGS, who receive renal allografts, sometimes within 24 hours of transplantation, supports the idea that a circulating **mediators** is the cause of the damage to podocytes

*The deposition of hyaline masses in the G in FSGS represents the entrapment of plasma proteins & lipids in foci of injury where sclerosis develops.

*IgM & complement proteins commonly seen in the lesion are also believed to result from **nonspecific entrapment in damaged G**

**Morphology:

| LM | IF | EM |
|---|---|---|
| *both **focal & segmental lesions** occurring in some segments within a G & sparing of the others (hence the term "segmental) ,<br>*the disease first affects only some of the G(hence the term "focal)<br>FSGS is characterized by<br>**The affected G exhibit<br>(a)INCREASE mesangial matrix,<br>(b) **deposition of hyaline masses hyalinosis)** & lipid droplets in the affected G, causing<br>C) obliteration of the capillary lumens | immunofluorescence M often reveals **nonspecific trapping of immunoglobulins** usually IgM, & complement, in the areas of hyalinosis | On EM, **as in MCD**, the podocytes exhibit effacement of foot processes |

**Clinically,there is little tendency for spontaneous remission of idiopathic

**Ttt , prognosis , fate of the Dz :

*FSGS, & responses to corticosteroid therapy are poor

*Progression of FSGS, with time, leads to global sclerosis of the G with pronounced tubular atrophy & interstitial fibrosis, a picture difficult to differentiate from other forms of chronic Gdisease, with progression to RF occuring in 50% of FSGS patients after 10 years

| | MCG | FSGN |
|---|---|---|
| Hematuria | _ | + |
| Hypertension | _ | + |
| Proteinuria | Selective | Non-selective |
| Respond to corticosteroid therapy | Good | Poor |

**Collapsing glomerulopathy

1- A morphologic type of FSGS

2-poor prognosis

3-collapse of glomerular tuft and podocyte hyperplasia

4- It may be

. idiopathic

.associated with HIV infection

.drug-induced toxicities

## Membranous GN(MGN)=Membranous Nephropathy MN

*A slowly progressive disease, **most common in the 30-50** years age ،group >> **most common form in adult**

**characterized by the presence of:

I)diffuse **thickening** of the capillary wall

هون صح بصير thickening بس ما بصير hypercellularity ،

II)**subepithelial** immunoglobulin-containing deposits

يعني على BM الخارجي من ناحية podocyte.

نوت خارجية مهمة :

Most Ab disorders are nephritic except membranous nephropathy is nephrotic

**Pathogenesis

*MGN is a form of chronic immune complex nephritis. Although circulating complexes of known exogenous (e.g., hepatitis B virus) or endogenous (DNA in SLE) Ag can cause MGN, it is now thought that most idiopathic MGN are induced by Abs reacting in situ to endogenous, or, planted G Ags

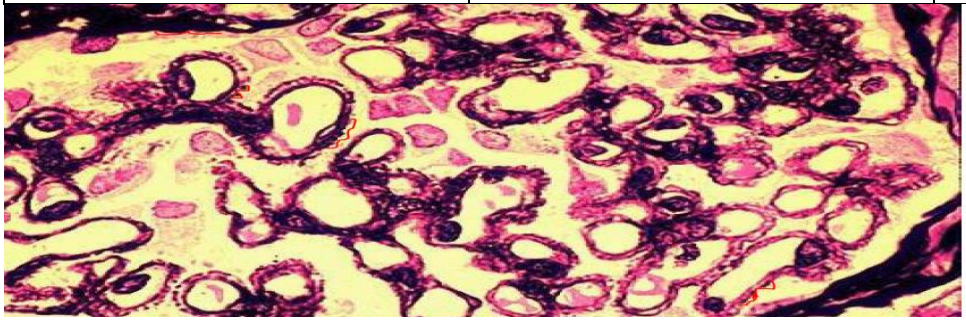
**Types of Membranous glomerulonephritis

cause من حيث ال

| **Idiopathic** | Secondary membraneous nephropathy |
|---|---|
| (**85%** of cases) | |
| antibodies against **podocyte antigen phospholipase A2 receptor (PLA2R)antigen** | ***autoimmune diseases as SLE**<br>لانه احنا بنعرف انه ب SLE في عنا production of Abs وممكن هاي Abs<br>Potentially deposits in subepithelial<br>***infections** (HBV, syphilis, malaria،schistosomiasis)<br>*malignant **tumors** (lung, and melanoma colon)<br>*inorganic salts exposure (**gold**, mercury)<br>drugs (**penicillamine**, captopril,**NSAID)**<br>لتسهيل حفظ الادوية كل يلي ب bold ادوية حكيناهم بعلاج RA |

**Morphology

| LM | IF | EM |
|---|---|---|
| **diffuse thickening of the GBM** | deposits of immunoglobulins and complement along the GBM **IgG** | (1) the podocytes show ,effacement of & ،foot processes<br>(2) the diffuse thickening of the GBM is caused in part by **subepithelial** dome deposits that nestle against the GBM & are separated from each other by small, spike like protrusions of GBM matrix that form in reaction to the dome deposits, resulting in a **(spike dome pattern)** As the disease progresses, these spikes close over the deposits, incorporating them into the GBM |



A silver stain (black). Characteristic "spikes" seen with membranous glomerulonephritis as projections around the capillary loops.

**Clinical Course

Clinically, idiopathic MGN characterized by insidious development of the nephrotic syndrome, usually without antecedent illness.

*In contrast to MCD:

(I) the proteinuria is nonselective

(II) does not usually respond to corticosteroid therapy

.poor response to corticosteroid therapy•

.Secondary causes of MGN should be ruled out

**Prognosis:

| **60% of cases** | **about40%** | **30%** |
|---|---|---|
| **proteinuria persists** | **progressive disease and renal failure 2 to 20 yr.** | **partial / complete remission of proteinuria** |

| | |
|---|---|
| 1. Minimal change disease | Cytokines |
| 2. FSGS | Podocyte Damage |
| 3. Membranous | Immune Complexes |
| 4. Diabetic | Glucose |
| 5. Amyloidosis | Amyloid |
| 6. Membranoproliferative glomerulonephritis | |

## The Nephritic Syndrome

Pathogenesis: inflammation

*proliferation of the cells in glomeruli& leukocyte

Infiltrate >>>

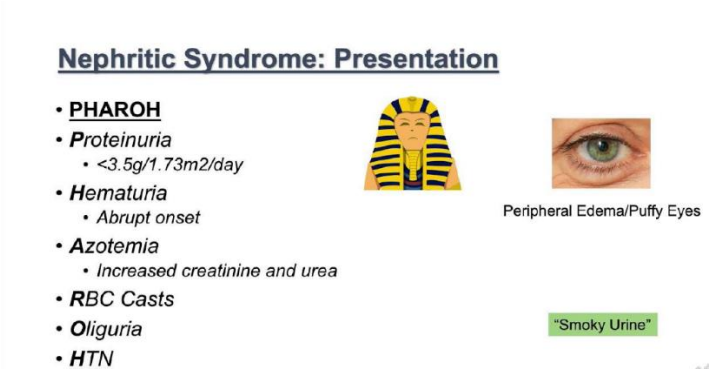
Injured capillary walls escape of RBCs into urine

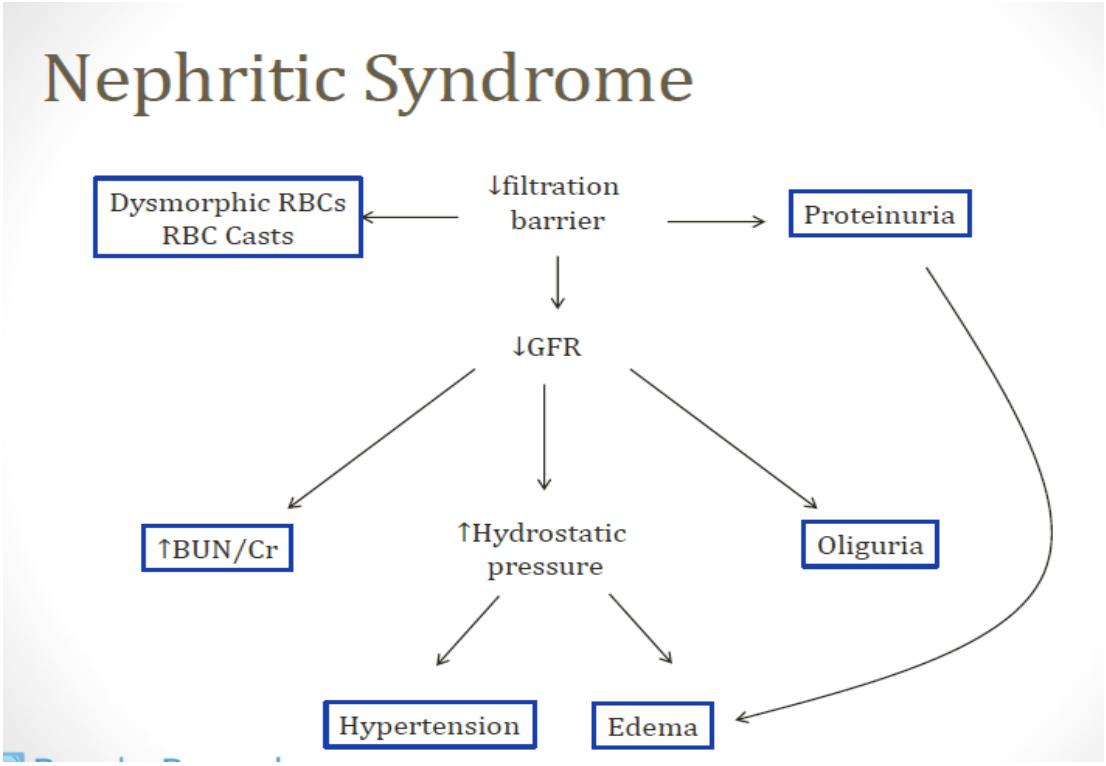
>>> GFR↓>>>

*oliguria, fluid retention, and azotemia

*Hypertension(a result of both the fluid retention and

some augmented renin release from kidneys)






سوف يتم تأجيل موضوع MPGN لاخر التلخيص لانه موضوع متعلق ب NEPHRITIC +NEPHROTIC

## Acute diffuse Postinfectious (Poststreptococcal) Glomerulonephritis(PSGN)

**A frequent GN, typically caused by deposition of **immune complexes** in the G, resulting in diffuse **proliferation** & swelling of resident G cells & frequent infiltration by **neutrophils**

**CAUSE : The inciting Ag may be exogenous or endogenous

Not direct infection of the kidney

**

| The prototypic exogenous pattern | Endogenous antigens |
|---|---|
| is seen in poststreptococcal GN, & a similar proliferative GN may occur in association with infections by other organisms, including certain pneumococcal & staphylococcal infections, several common viral diseases such as mumps, measles, chickenpox, & hepatitis B & C | occur in SLE |

**post streptococcal GN :

Classically, poststreptococcal GN develops in children 1 to 4 weeks* after they recover from a group A, "nephritogenic**" strains of β-hemolytic streptococcal infection.

*هاد الوقت بلزم لحتى ينتج Abs ويتراكموا بالكلية

**Nephritogenic شو يعني ؟؟ هاي البكتيريا اخدناها برضه بالكارديو يوم حكينا عن RF

..... وهاي البكتيريا السلالات يلي تستهدف الكلية لا تستهدف HEART يعني ما بتعمل 2 complications سوا بس وحدة منهم ...

**In most cases the initial infection is in the pharynx or skin*

*برضه جبنا سيرتها ب mss يوم حكينا عن impetigo

* هاي المعلومة بتفيدنا بالهستوري

**Pathogenesis of Acute Post streptococcal GN

Is immune complex deposition,because the typical features of immune ،complex disease are seen, including

**1- granular** deposits of IgG & complement on the GBM

2- Hypocomplementemia

**Morphology :

| LM | IF | EM |
|---|---|---|
| *proliferation of endothelial and mesangial cells and neutrophilic infiltrate<br>يعني hyper cellularity لكل الخلايا<br>* In postinfectious GN, the most characteristic change by light microscopy is a **Diffuse** (affecting nearly all glomeruli …..>50%), **uniform increased cellularity** of the G tufts(caused both by swelling & proliferation of EC & mesangial cells & by a neutrophilic & **monocytic infiltrate**<br>*Sometimes there is necrosis of the capillary walls & In a few cases، there may also be "**crescents**" within the urinary space in response to **the severe inflammatory injury**.<br>*In general, both of these findings are **ominous**<br>مشؤومة .لانه هون بكون تحول الى RPGN رح نجيها بعدين | deposits of IgG and complement within the capillary walls<br>واحنا عارفين انه IgG ينشط complement لهيك صابه Hypocomplementemia | immune complexes "**subepithelial"humps**" in GBM<br>يعني بكون عامل ارتفاعات ملاحظة اينما وجد |

**PSGN-Clinical Course

- **acute onset .**
- **fever, nausea, and nephritic syndrome.**
- **gross hematuria with smoky brown** rather than bright red urine **.**
- **Mild proteinuria.**
- **Serum complement levels are low during the active phase of the disease.**
- **↑serum anti-streptolysinOantibody titers.**

•**Recovery occurs in most children**

## IgA Nephropathy

*one of the **most common causes of recurrent** microscopic or gross hematuria children and young adults

*is **the most common G disease revealed by renal biopsies worldwide**

burger's disease الله اسم تاني

لانه **A** ،،،، الاول هو اكتر اسباب GN شيوعا في كل العالم

**Clinically:

*IgA nephropathy usually & most often affects children & young adults

**Don't confuse with other glomerular disorders**

- **Post-strep GN: weeks after infection**
- **IgA GN: days after infection**
- **Minimal change: nephrotic syndrome after URI**

*hematuria 1 or 2 days after nonspecific upper respiratory tract infection

*hematuria lasts several days and then subsides and recur every few months

| | |
|---|---|
| More than 50%of patients | present with gross hematuria *(that occurs within 1 or 2 days of a nonspecific upper RTI, or, less commonly, GIT or UT infection); *the hematuria typically lasts for several ،days & then subsides *only to return every few months *& is often associated with loin(Specifically to the sides below the ribs that includes the .human genitals ) pain |
| 40%have only | microscopic hematuria,with or without proteinuria |
| up to 10% | develop acute nephritic syndrome |

**Pathogenesis of IgA nephropathy:

* The pathogenic hallmark is the deposition of IgA in the mesangium

*abnormality in IgA production and clearanc

*Normally, **IgA,** the main immunoglobulin in **mucosal secretions**, is at

**low levels in normal serum.**

*IgA is ⍰in 50% of patients with IgA

nephropathy due to ⍰production in the bone marrow.

*A genetic influence is suggested by it's occurrence in families & in HLA-identical siblings

*Studies suggest that INCREASE IgA synthesis in response to respiratory or GIT exposure to environmental agents (e.g., viruses, bacteria, & food proteins) may lead to deposition of IgA & IgA-containing immune complexes in the mesangium, where they activate the alternative complement pathway & initiate G injury)

في هون ملاحظة صغيرة انه احنا بنعرف انه بالوضع الطبيعي ال IgA ما بعمل activation of complement طب كيف هون عمل ؟؟؟؟ لانه اصلا احنا بوضع مش نورمال .... بس حتى لما يعمل بكون weak interaction وبالتالي

No hypocomplementemia

PSGN +MPGN + SLE NEPHRITIS ؟ hypocomplementemia مين يلي بعملوا

**Morphology:

| LM | IF | EM |
|---|---|---|
| Variable<br>The G may be normal, or may show mesangial widening & segmental inflammation confined to some G(focal proliferative GN); diffuse mesangial proliferation (mesangioproliferative); or (rarely) .overt crescentic GN | **Mesangial Granular** deposition of **IgA with C3** | deposits in the mesangium |

## Rapidly Progressive (Crescentic) Glomerulonephritis

هي وصف اكتر ما تكون مرض لانه الها many causes الها تلت انواع بس الدكتورة مش ذاكريتهم فنكتفي بالموجود

زي شو يؤدي لهاي الحالة ؟؟ PSGN+ SLE + good pasture syndrome

•characterized by the presence of **crescents**(crescentic GN).

**وهوعبارة عن fibrin + macrophages +**

•**proliferation of the parietal epithelial cells** of Bowman's capsule in response to injury and infiltration of monocyte sand macrophages

•**nephritic syndrome rapidly progresses to oliguria and azotemia**

## Hereditary Nephritis

•**a group of hereditary glomerular diseases caused by mutations in GBM proteins (most common** X-linked**).**

•**Most important type: Alport syndrome**

## Alport syndrome

•Pathogenesis:

Mutation of any one of the **α chains of type IV collagen** that present in kidney , eye , ear and others

•EM

GBM thin and attenuated

**GBM later develops splitting and lamination "basket-weave" appearance**

•clinically :

**nephritis + nerve deafness + eye disorders (lens dislocation, posterior cataracts,corneal dystrophy).**

•renal failure occurs between 20-50 yrs of age

Classic presentation :

•male with  Classic triad: • Hematuria • Hearing loss • Ocular disturbances

• Look for child with triad and family history

## MembranoproliferativeGN(MPGN)

**Is manifested H, by **alterations in the GBM** & **mesangium& by proliferation of G cells.**

****MPGN accounts for 10% of cases of idiopathic nephrotic syndrome** in children & adults.

• Some individuals present only with hematuria or proteinuria in the non-nephrotic range; others have nephritic syndrome or a combined nephrotic-nephritic picture.

**•Types of MPGN:**

**1-type I (80% of cases)-immune complex disease (The inciting antigen is not known)**

**2-type II-excessive complement activation**

| | Type I MPGN | Type II MPGN (dense-deposit (disease |
|---|---|---|
| **Pathogenesis** | *Most cases of are caused by **circulating immune complexes, but** the inciting Ag is not known.<br>*Like many other GNs, type I MPGN may also occur in association with other known disorders (**secondary MPGN**),**such as SLE, hepatitis B & C, chronic liver disease or infected A-V shunt** | ***Cause: excessive complement activation**<br>**•autoantibody against C3 convertase called C3 nephritic factor (it stabilizes the enzyme and lead to uncontrolled cleavage of C3 and activation of the alternative complement pathway).** |
| **Morphology** | **LM**<br>•both types of MPGN are similar by LM.<br>•glomeruli are large with accentuated **lobular appearance** and show **proliferation of mesangial and endothelial cells** as well as infiltrating leukocytes<br>**•GBM is thickened(double contour** or **"tram track"**)<br>•The **tram track** appearance is caused by "**splitting" of the GBM** due to the inclusion within it of processes of mesangial & inflammatory cells extending into the peripheral capillary loops<br>زي شكل سكة القطار | |
| | **EM :**<br>**Is characterized by discrete subendothelial electron-dense deposits.**<br>**Discrete**<br>**منفصلة وغير مترابطة بس النوع التاني هو dense** | In type II lesions the lamina densa & the sub endothelial space of the GBM are transformed into an irregular, **ribbon-like**, **extremely electron-dense structure,** resulting from the deposition of material of unknown composition, giving rise to the term dense-deposit disease**.**<br>**Ribbon- like :**<br>**متل الشريط متصل بكون** |
| | *By immunofluorescence M, **C3 is deposited in an irregular granular pattern, & IgG & early complement components (C1q & C4) are often also present,** indicative of an immune complex pathogenesis**.** | ***C3 alone in C3 is present in** irregular chunky & segmental linear foci in the BMs & in the mesangium but the **IgG & the early components of the classical complement pathway (C1q & C4) are usually absent GBM** |
| **Result** | | **Hypocomplementemia** |

**Clinical Course**

• Clinically, 50% of MPGN cases presented with **nephrotic syndrome**, although it may begin as acute nephritis or mild proteinuria.

•prognosis poor.

•No remission.

•40% progress to end-stage renal failure.

•30% had variable degrees of renal insufficiency.the remaining 30% had persistent nephrotic syndrome without RF.

•**Dense-deposit disease (type II) has a worse prognosis.**

•**It tends to recur in renal transplant recipients**

**Chronic GN**

**Chronic GN** is the **final outcome of various forms of G disease**, irrespective of whether there has been preceding **G** inflammatory injury.

When it is discovered, the **G** changes are so **far advanced** that it is

difficult to ascertain the original lesion.

It represents the **end stage** of a variety of entities, including Cr GN,

FSGS, MN, MPGN & IgA nephropathy,

Although it may develop at any age, it is usually first noted in young &

middle-aged adults.

It is a common & important cause of CRF, e.g.,

Among 3700 Jordanian cases **whom require chronic hemodialysis** or renal transplantation in **2011**,**30%**are **chronic GN; 30%**are **diabetic; 30%**are **hypertensive;10%** are renal **adult polycystic** disease.

It has been estimated that **20% of chronic GN cases arise with no history** of symptomatic renal disease!

**Grossly, both kidneys are symmetrically contracted**& their surfaces are red-brown & **diffusely granular.**

Histopathological E : **Advanced scarring & obliteration of the G**, sometimes to the point of complete sclerosis

**Atrophy of the tubules** in the cortex

**Interstitial fibrosis, with** marked lymphocytic cell infiltrates,

the **small & medium-sized arteries** are frequently **thick walled**& narrowed, due to **hypertension secondary to the chronic GN**

Such markedly damaged kidneys are designated **"end-stage kidneys“!**