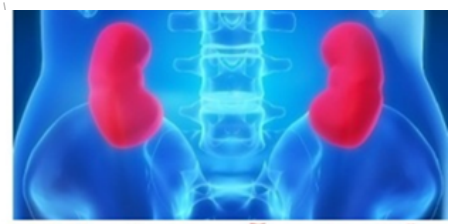


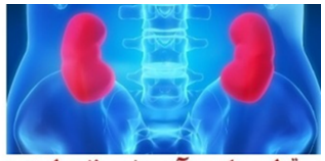
مرکز تحقیقات نفرولوژی قطب علمی آموزشی نفرولوژی

In The Name of God

Glomerular Diseases Evaluation & Diagnosis

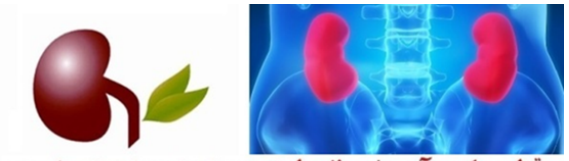
بیماری های گلومرولی
ارزیابی و تشخیص

SM Gatmiri, MD, Nephrologist, Associate Prof. of TUMS, NRC, Center of Excellence in Nephrology, 2024



Glomerular disease can be inherited or acquired & can be asymptomatic or presented as AKI or ESRD.

Occationally kidney biopsy is required, particularly in nephrotic syndrome or GN. Rarely, biopsy cannot be performed.

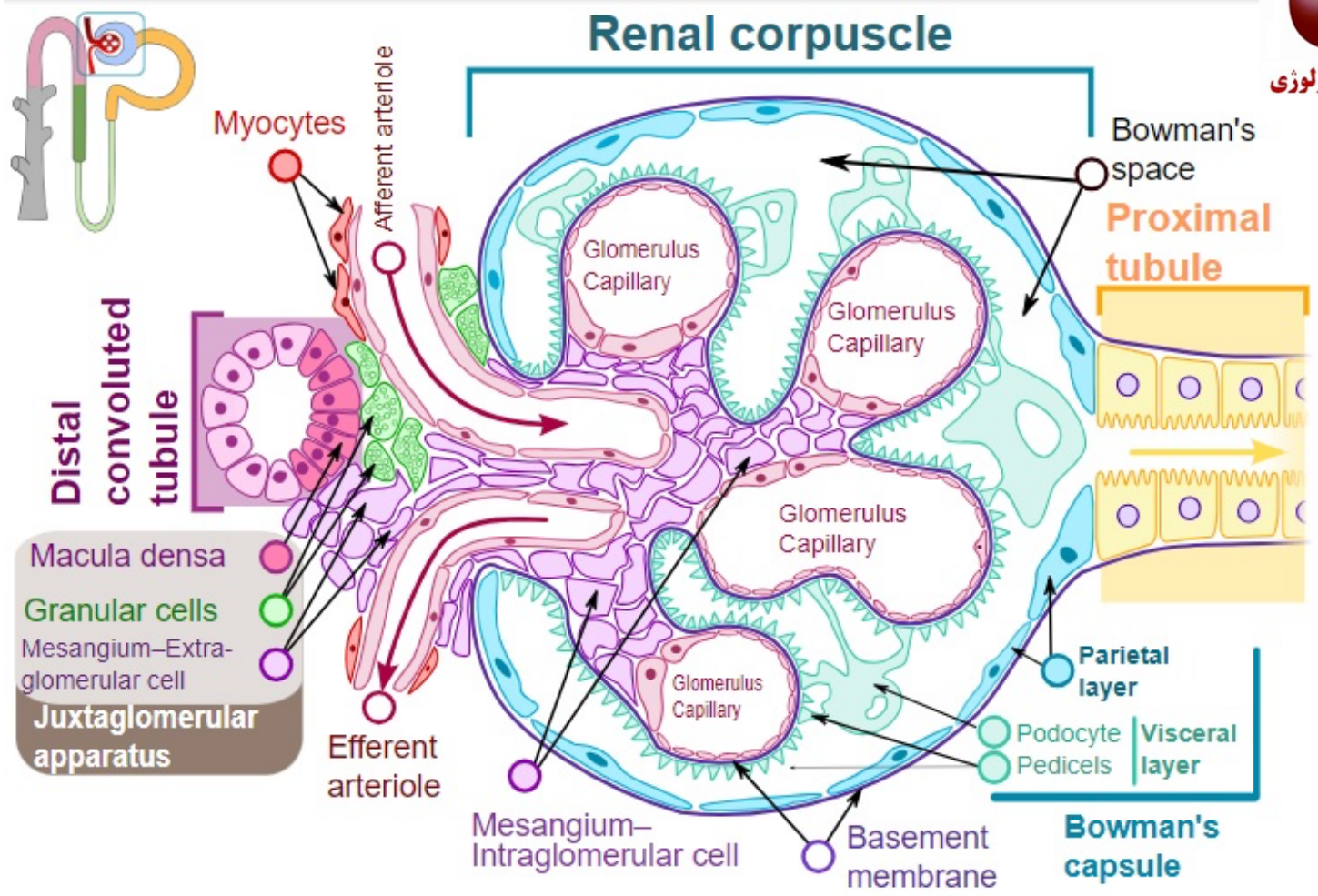


A biopsy may be deferred if the risk is prohibitive or the patient is uncooperative or unwilling.

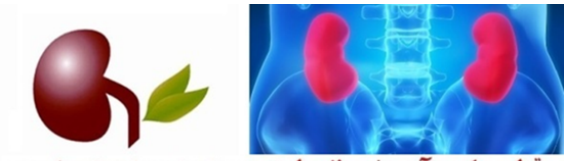
Biopsy maybe performed at a later date

(eg, after delivery in a pregnant patient).

Or may not be required if a diagnosis can be made by serology (eg, in MGN associated with anti-PLA2R Ab).



The glomerulus is the basic filtering unit of the kidney (figure 1).



On a pathological basis glomerular lesions can be

-Diffuse (all glomeruli are involved) or

-Focal (only some glomeruli are involved [typically <50%]).

At the level of the individual glomerulus, a process is

-Global if the whole glomerular tuft is involved or

-Segmental if only a portion is involved (<50%).

Histologic descriptions include the terms

-proliferative (an increase in the number of cells in the glomerulus),

-sclerosing (presence of scarring), &

-necrotizing (areas of cell death).

Proliferation may occur predominantly

-in the mesangium (mesangial proliferative GN),

-within the capillary wall (endocapillary hypercellularity), &

-in an extracapillary location or crescents.

Crescents

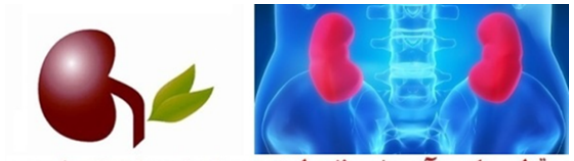
An extracapillary proliferation which is associated with accumulations of macrophages, fibroblasts, proliferating epithelial cells, & fibrin within Bowman's space & represent rupture of the glomerular membrane, signifying severe injury to the glomerular capillary wall.

Other terminology

Focal & segmental necrotizing glomerulonephritis &

Diffuse global proliferative glomerulonephritis.

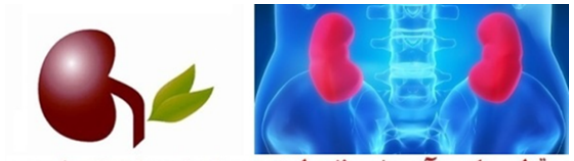
Interstitial fibrosis, which accompanies uncontrolled glomerular disease, is a poor prognostic sign.[3]



Podocyte dysfunction can occur in genetic disease, affecting key basement membrane proteins such as collagen IV mutations in Alport syndrome.

Circulating Factors

In diseases such as MCD & FSGS, putative circulating factors are thought to directly affect podocyte function & lead to proteinuria [4].



Mechanical Disruption

In DM & amyloidosis, there is mechanical disruption of the glomerulus due to accumulation of NL or abnormal protein both in the capillary loops of the glomerulus & the mesangium.

Immune Mechanisms

Include in situ immune complexes in MGN[5] or the localized effects of anti-GBM in Goodpasture's disease; in conditions such as SLE, immune-mediated kidney injury is caused by deposition of circulating immune complexes [6].

Activated neutrophils & Macrophages

Could **directly** injure the glomerulus in **ANCA-associated** vasculitis [2].

CLINICAL MANIFESTATIONS

Hematuria &/or proteinuria

Urinary RBC casts or hematuria in which a substantial proportion of RBCs are acanthocytes.

Dysmorphic RBCs & RBC casts in the urine sediment &/or nephrotic-range proteinuria (>3 to 3.5 g/day of proteinuria) **are more specific for a glomerular origin.**

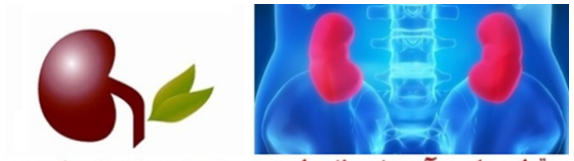
Renal insufficiency

Nephrotic syndrome do not typically present with AKI but, AKI may be seen at the time of presentation in podocytopathies such as MCD or primary FSGS.

Renal impairment is commonly seen in GNs

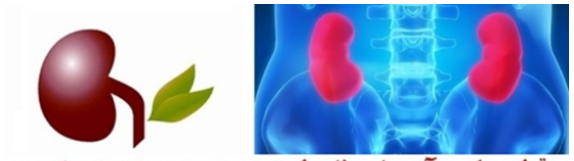
AKI may occur in acute GN especially in crescentic, which is often due to ANCA-associated vasculitis or anti-GBM disease.

Chronic glomerular diseases may develop a progressive decline in GFR & CKD.



Hypertension

Acute onset or worsening HTN in someone with preexisting, controlled HTN should raise suspicion for glomerular disease, particularly if hematuria & edema are present.



Edema –Sodium retention.

Hypercoagulability – In MGN may produce a hypercoagulable state, thrombotic events, pulmonary embolism.

Systemic findings - autoimmune disorders, malignancy, & drug reactions. Fevers, chills, weight loss, night sweats, fatigue

Eye – Retinitis or uveitis. ENT – Epistaxis, sinusitis, oral ulcers

Cardiovascular – Murmurs, pain. pericarditis, or heart failure

Lungs – Hemoptysis, infiltrates, or nodules. Abdomen – Enteritis, colitis, or pancreatitis

Nervous system – Seizures or peripheral neuropathy

Extremities – Digital ischemia or infarction. Skin – Purpura or rash. Musculoskeletal – Arthritis, arthralgias, myalgias

Infections – Particularly evidence of Staphylococcus, Streptococcus, hepatitis virus, or HIV, syphilis

EVALUATION

In the nephrotic syndrome, leakage of plasma proteins without inflammation is the primary pathogenic mechanism.

In GN, inflammation within the glomerulus leads not only to the passage of plasma proteins but also of inflammatory cells & RBCs into the renal tubule.

Some conditions may present with both patterns, & some disorders (lupus nephritis) may progress from one pattern to the other.

Some patients may present with mild manifestations such as isolated proteinuria or isolated hematuria.

Proteinuria

-Albuminuria.

-Tubular proteinuria, (low-molecular-weight proteins that are filtered but incompletely reabsorbed by the renal tubule

-Overflow proteinuria, (light chains in the patients with multiple myeloma)

-Postrenal proteinuria, which is typically associated with a UTI & leukocyturia

Proteinuria discovered by

-Semiquantitative urine dipstick typically reflects glomerular proteinuria because the dipstick is insensitive to nonalbumin proteins.

-Quantitative test

-24-hu collection or a random urine Pr/Cr,

-The origin of the proteinuria can be determined with a

Dipstick,

-24-hu collection or a random urine Alb/Cr, or with a

-urine protein electrophoresis &

-immunofixation.

Nephrotic syndrome

-A urine protein>3500 mg /24 h or, if a random urine Pr/Cr>3000 mg/g in an adult

-Hypoalbuminemia<3.5 g/dL

-Other common findings include edema (peripheral or periorbital, occasionally ascites or pleural effusions), hyperlipidemia, & lipiduria.

-Lipiduria is identified by the presence of fat droplets, which may be free within sloughed tubular cells (oval fat bodies) or inside fatty casts. Fat droplets have a characteristic "Maltese cross" appearance under polarized light.

Diagnosis

R/O DM & If amyloidosis is suspected (in a patient with a monoclonal gammopathy)

Chec anti-PLA2R for MGN

And then a kidney biopsy, certain laboratory tests, include:

-HbA1C, to ANA, antidsDNA Ab, free light chains & for HBsAg HCVAb, HIV

C3, C4, Other serologic, microbiological, genetic tests are sometimes performed in patients once a specific histologic diagnosis is established.

Secondary NS due to DM, infection, autoimmune disease, is more common than primary NS.

DKD is the most common cause of NS.

Although MCD is the most common cause of primary NS in children, MGN & FSGS are the most common causes of primary NS in adults.

MGN predominates in White & FSGS in Black patients.

C3 glomerulonephritis or other causes of a membranoproliferative pattern of injury can present as NS, GN, or both.

Isolated Transient Proteinuria

Transient proteinuria in young individuals need no further evaluation.

Orthostatic proteinuria

Can be diagnosed by performing a split urine collection.

Isolated Persistent Proteinuria

Ultrasound

Evaluate VUR, serum free LCs, protein electrophoresis, immunofixation to evaluate for a monoclonal gammopathy.

And Kidney biopsy

Rarely, a biopsy show findings suggestive of systemic disease (eg, amyloidosis, Fabry disease).

Proteinuria that is not isolated (accompanied by hematuria or reduced kidney function) should be biopsied.

Except DKD or atrophic kidneys.

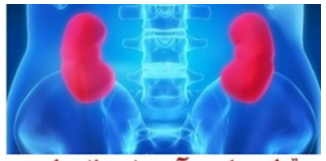
Glomerular hematuria

Hallmark: dysmorphic RBCs & RBC casts.

The nephritic syndrome (GN):

Glomerular inflammation with hematuria, proteinuria, & leukocyturia in the absence of UTI.

HTN, renal insufficiency & pulmonary hemorrhage, palpable purpura, arthritis.



GN can present rise in PCr & proteinuria (leading to advanced CKD & ESRD).

RPGN & is typically associated with **extensive crescents** on the kidney biopsy.

Lab tests in GN:

C3, C4, ANCA; ELISAs specific for proteinase-3 & myeloperoxidase), GBMAbs, ANA, Anti-dsDNA, HCV, HBV, HIV, Serum free LCs & serum immunofixation

A cryocrit in patients with cryoglobulinemia or a known history of HCV. Blood cultures in nfections.

Differential diagnosis of GN

C3 & C4 are NL in anti-GBM disease & pauci-immune GN but low in immune complex-mediated GNs (except of IgA nephropathy). Kidney biopsy is required.

In microangiopathic hemolytic anemia, thrombocytopenia, & kidney failure, the diagnosis of thrombotic microangiopathy (TMA) is a clinical one, & typically do not need a kidney biopsy. However, patients with subacute & chronic TMA may exhibit minimal or no hematological or systemic abnormalities but present with progressive kidney failure with or without proteinuria & hematuria (eg, in drug-induced TMA) [8,9]. Such patients should be biopsied.

Gross hematuria

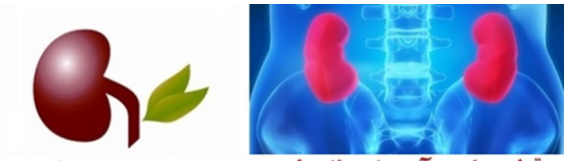
may accompany with upper respiratory infection.

If a latent period of 7 to 10 days occurs between the onset of infection & gross hematuria, ***PSGN*** is the usual culprit.

And if occurring concurrently with the onset of infection (synpharyngitic GN) is typical of ***IgA*** nephropathy.

Palpable purpura or a petechial rash suggest ANCA-associated ***vasculitis***, **IgA vasculitis** [Henoch-Schönlein purpura], **or cryoglobulinemia & Rarely, lupus nephritis & Pulmonary hemorrhage.**


قطب علمی آموزشی نفرولوژی
مرکز تحقیقات نفرولوژی
thanks



REFERENCES

Ellis EN, Mauer SM, Sutherland DE, Steffes MW. Glomerular capillary morphology in normal humans. Lab Invest 1989; 60:231.

Dickinson BL. Unraveling the immunopathogenesis of glomerular disease. Clin Immunol 2016; 169:89.

http://www.ajkd.org/content/atlasofrenalpathologyii (Accessed on November 25, 2016).

Nagata M. Podocyte injury and its consequences. Kidney Int 2016; 89:1221.

Ronco P, Debiec H. Membranous nephropathy: A fairy tale for immunopathologists, nephrologists and patients. Mol Immunol 2015; 68:57.

Vinen CS, Oliveira DB. Acute glomerulonephritis. Postgrad Med J 2003; 79:206.

Trachtman H, Bergwerk A, Gauthier B. Isolated proteinuria in children. Natural history and indications for renal biopsy. Clin Pediatr (Phila) 1994; 33:468.

Raife TJ, Lager DJ. Chronic thrombotic microangiopathy associated with antineoplastic therapy with minimal hematologic effects. Mayo Clin Proc 2002; 77:323.

George JN, Nester CM. Syndromes of thrombotic microangiopathy. N Engl J Med 2014; 371:654.