Medicine

Nephrology

5th year – lecture 3

الدكتور
محمد يونس العطبي
الاختصاص الدقيق بأمراض وزرع الكلى
اختصاص الطب الباطني
MBChB, FICMS (Medicine), FICMS (Nephrology), CABMS (Nephrology)

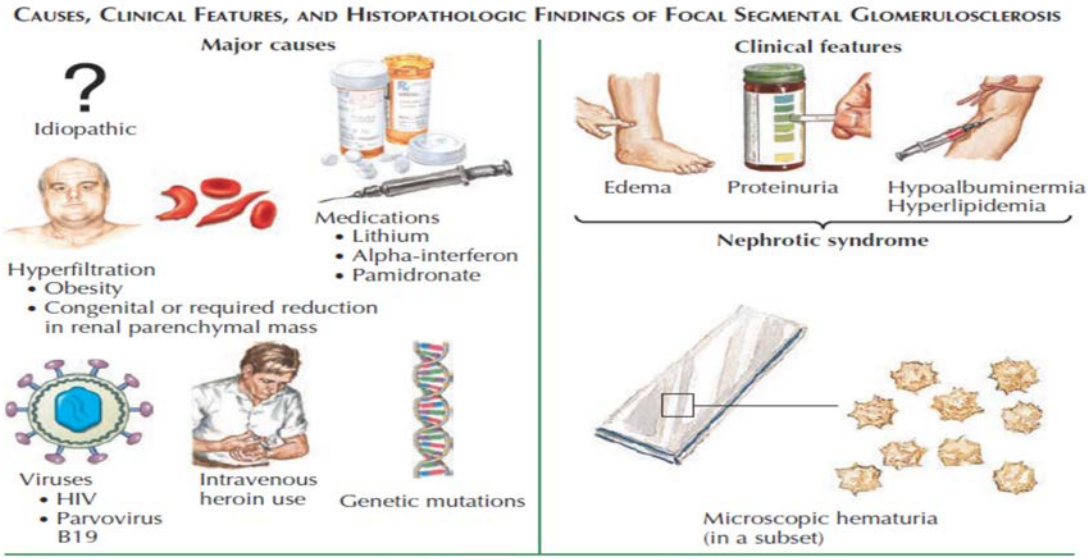
Glomerular disease specific diseases

MINIMAL CHANGE DISEASE (MCD):

- Minimal change disease is the leading cause of nephrotic syndrome in children, accounting for 90% of cases in this population, and a major cause of nephrotic syndrome in adults.
- The name of this disease refers to the seemingly normal appearance of glomeruli when visualized using light microscopy with negative immunostaining . On electron microscopy, however, diffuse foot process effacement can be seen.
- Proteinuria is usually 'highly selective', where albumin.
- **Treatment** : High-dose steroid therapy with prednisolone 60 mg/m^2 daily (2 mg/kg for children , 1 mg/kg for adults , maximum of 60 mg/d) for a maximum of 4–6 weeks, followed by 40 mg/m^2 every other day for a further 4–6 weeks, reverses proteinuria in more than 95% of children. In some cases, patients diagnosed with MCD fail to respond to treatment and, on repeat biopsy, are found to have FSGS. ACE inhibitors and statins are generally not required in steroid-responsive patients because their disease is short in duration.
- One-third of these patients regularly relapse on steroid withdrawal, so that a second-line agent should be added after repeat induction with steroids. Patients with relapsing disease are often prescribed alternative immunomodulatory therapies, such as calcineurin inhibitors (Ciclosporin or tacrolimus), mycophenolate mofetil, and cyclophosphamide.

Focal segmental glomerulosclerosis (FSGS)

- a clinical pathologic syndrome in which there is proteinuria accompanied by glomerular scarring or sclerosis that occurs in a focal (i.e., only some glomeruli are involved) and segmental (i.e., affecting only part of any glomerulus) distribution.
- FSGS is a major cause of nephrotic syndrome in adults, and it can occur as a primary, idiopathic process or secondary to numerous systemic conditions.
- Several histologic variants of FSGS can be distinguished, including 1)classic FSGS (also known as FSGS NOS ,not otherwise specified), 2)perihilar variant, 3)glomerular tip variant, 4)cellular variant, 5)collapsing variant (also known as collapsing glomerulopathy).



- Treatment :

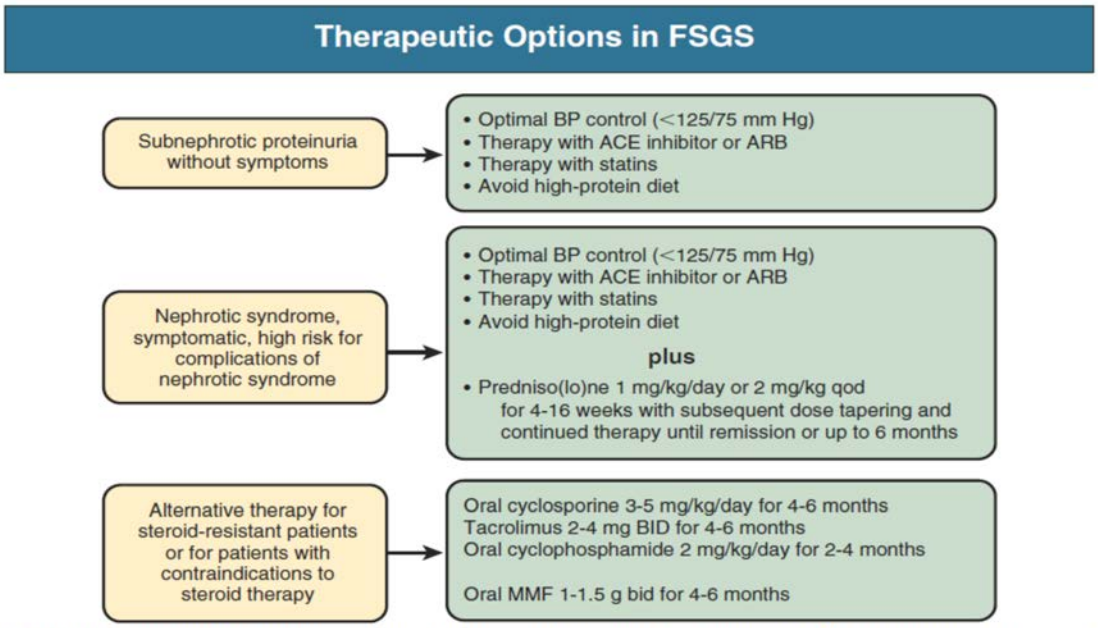
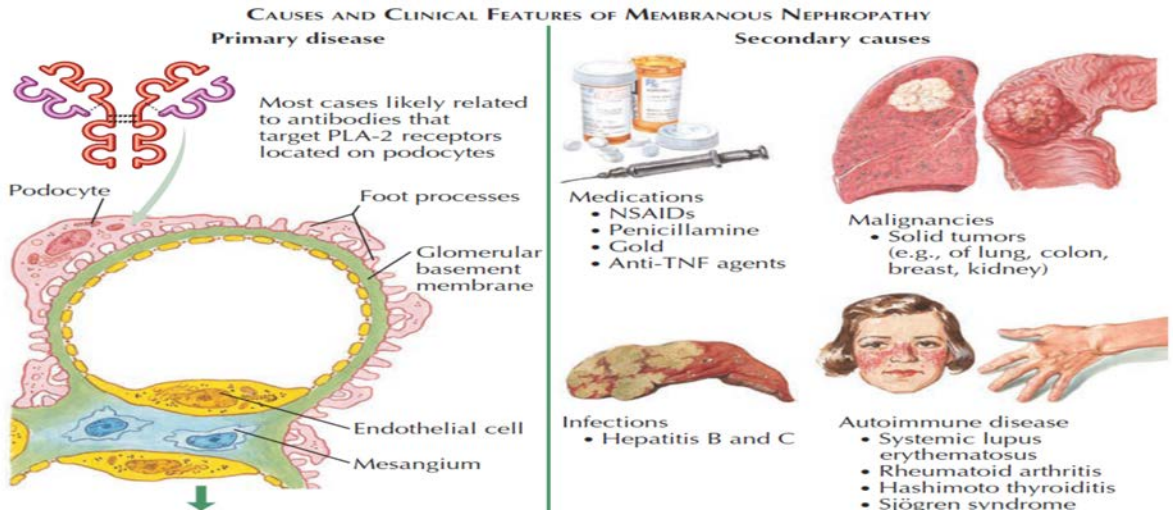


Fig. 18.19 Therapeutic options in focal segmental glomerulosclerosis (FSGS). Treatment of secondary FSGS should be directed at the underlying cause whenever possible. For HIV-associated nephropathy, treatment with highly active antiretroviral therapy (HAART); for pamidronate nephrotoxicity, discontinue the medication; and for obesity-related glomerulopathy, weight loss. *ACE*, Angiotensin-converting enzyme; *ARB*, angiotensin receptor blocker; *BP*, blood pressure; *MMF*, mycophenolate mofetil.

- Approximately 30% of patients with primary FSGS who develop ESRD and undergo renal transplantation develop recurrent FSGS in the allograft.

Membranous nephropathy (MN) :is one of the most common causes of nephrotic syndrome in adults. It isnamed for the major histologic finding of diffuse glomerular basement membrane (GBM) thickening with immune deposits of immunoglobulin G (IgG) and complement components on the subepithelial surface of the glomerular capillary wall. The peak incidence between 30 and 50 years of age. In most cases MN is a primary phenomenon. The predominant autoimmune system responsible for primary MN is that associated with autoantibodies directed at the M-type phospholipase A2 receptor (PLA2R) on podocytes. Circulating anti-PLA2R antibodies are detectable in the serum of 75% to 80% of patients with primary MN from all ethnic groups and are rarely found in secondary MN.



- **Risk Categories of Renal Disease Progression in Membranous Nephropathy:**

Low Risk	Medium Risk	High Risk
Normal serum creatinine and creatinine clearance plus proteinuria <4 g/day over 6 mo of observation	Normal or near-normal creatinine clearance and persistent proteinuria 4-8 g/day over 6 mo despite maximum conservative treatment	Deteriorating renal function and/or persistent proteinuria >8 g/day for 3 (up to 6) mo of observation

- **Treatment** : mainly supportive (ACEi , statins) .The immunossupresion had been reserved for those with persistent severe nephrotic syndrome or deteriorating renal function .The primary MN is steroid resistance , so we use combined steroid and cyclophosphamide may improve both the nephrotic syndrome and the long-term prognosis.. The two leading therapies are cytotoxic agents (cyclophosphamide or chlorambucil) and calcineurin inhibitors (cyclosporine or tacrolimus,(either of which is given in combination with oral or intravenous corticosteroids. Recently, other agents such as rituximab and ACTH (synecthin depot), and have also shown promising results, particularly in cases refractory to initial therapeutic attempts.

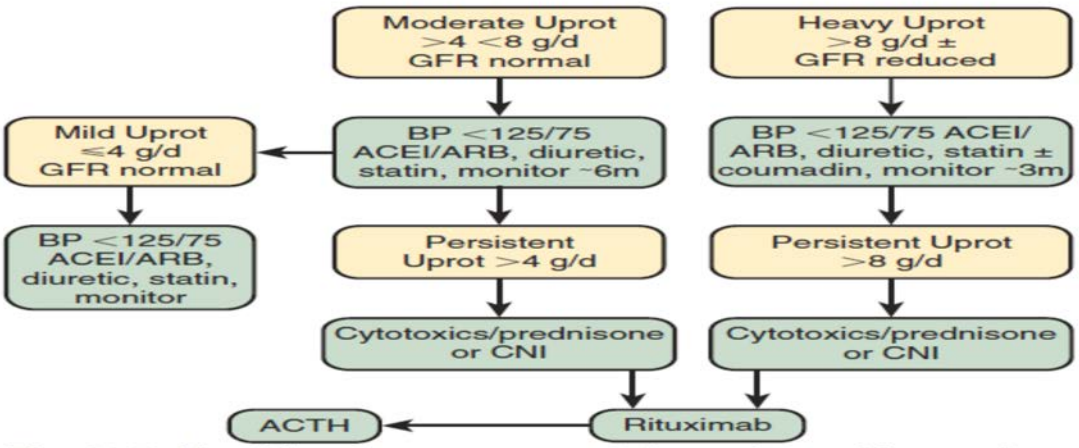


Fig. 20.7 Algorithm for treatment of the patient with membranous nephropathy (MN). Details of possible therapies are discussed in the text. *ACEi,* Angiotensin-converting enzyme inhibitor; *ACTH,* adrenocorticotropic hormone; *ARB,* angiotensin receptor blocker; *BP,* blood pressure; *CNI,* calcineurin inhibitor; *GFR,* glomerular filtration rate. Uprot, proteinuria.

Prognosis: Approximately one-third of patients with idiopathic membranous nephropathy undergo spontaneous remission, one-third remain in a nephrotic state, and one-third develop progressive CKD.

Systemic lupus erythematosus (lupus nephritis):

- nephrotic syndrome with an active sediment is most common presentation
- GN caused by immune complex deposition in capillary loops and mesangium with resulting renal injury. Immune deposits in the glomeruli and mesangium are characteristic of SLE (tubuloreticular structure in glomerular endothelial cells) and stain positive for IgG, IgM, IgA and the complement components C3, C1q and C4 (full house)on immunofluorescence. Histologically, almost all patients will have changes and shows the progression of the histological findings and the clinical picture from classes I to VI.

Class I	Minimal mesangial LN
Class II	Mesangial proliferative LN
Class III	Focal LN (<50% of glomeruli)[a]
Class IV	Diffuse LN (≥ 50% of glomeruli)[a,b]
Class V	Membranous LN
Class VI	Advanced sclerotic LN (90% of glomeruli globally sclerosed without residual activity)

ISN/RPS, International Society of Nephrology/Renal Pathology Society; LN, lupus nephritis.
[a]Specify active versus chronic.
[b]Specify segmental versus global.

- low level of serum complement (C3,C4) and high level of anti-Ds DNA levels are usually indicate active renal disease.
- Treatment: Steroids and high-dose intravenous cyclophosphamide or mycophenolate mofetil (MMF) may be used as induction therapy. In white populations, low-dose cyclophosphamide is a good alternative to high-dose cyclophosphamide, as it is similarly effective and associated with less toxicity. MMF is as effective as high-dose intravenous cyclophosphamide in the induction phase with a similar safety profile (so it is recommended for fertile female because of cyclophosphamide may induce infertility) but cyclophosphamide may be inferior to MMF in black and Hispanic people, possibly because of poor tolerance.

IgA nephropathy (IgAN) : is a mesangial proliferative glomerulonephritis characterized by diffuse mesangial deposition of IgA. A striking feature of IgAN is reduced glycosylation of the hinge region of IgA1. IgA1 carries distinctive O-linked sugars at its hinge region; IgA2 has no hinge and carries no such sugars and is found in up to 90% of individuals with IgAN.

- IgAN may occur at any age but is usually diagnosed in young adults, with a male : female ratio of at least 2 : 1.
- The clinical manifestations are diverse and can include asymptomatic hematuria and proteinuria, gross hematuria, nephrotic syndrome, and acute kidney injury.In up to one in three patients, IgAN will progress to end-stage renal disease.
- Hematuria usually follows intercurrent mucosal infection, typically in the upper respiratory tract (the term synpharyngitic hematuria has been used) or occasionally in the gastrointestinal tract. Hematuria is usually visible within 24 hours of the onset of the symptoms of infection, differentiating it from the 2- to 3-week delay between infection and subsequent hematuria in postinfectious (e.g., poststreptococcal) GN.
- Treatment : supportive (ACEi , omega-3 fatty acids), steroid in proteinuria>3g/d.