

Glomerular diseases of the kidney

Glomerulous

Glomerulus consists of a combination of

1- Cellular elements:

- Endothelial cells
- Mesangial cells
- Visceral and parietal epithelial cells

2- Extracellular matrix:

- Glomerular basement membrane (GBM)
- Mesangial matrix



Glomerulonephritis

- Glomerular disease includes glomerulonephritis - inflammation of the glomeruli and glomerulopathies when there is no evidence of inflammation.
- Glomerulonephritis is a subset of glomerulopathies

Terminology

All glomeruli are involved: Diffuse (generalized)

Some glomeruli are involved: Focal

In one glomerulus:

if the whole glomerulus is involved : Global

if only a part of the glomerules is involved: Segmental

Other terminologies in common use:

Proliferative: increase in cell number cells

Sclerosing: Hardening of the tissue

Renal failure

The causes of renal failure:

1- Pre-renal causes:

Any cause reduces blood flow to the kidney (hypovolemia, sepsis, renal artery occlusion, low cardiac output).

2- Post-renal causes:

any cause obstructs urine flow

3- Renal causes (intrinsic renal disease):

Renal failure

3- Renal causes (intrinsic renal disease):

- o Tubular disease

 - Acute tubular necrosis

 - A common cause of acute renal failure. Its a reversible injury

- o Interstitial disease

 - Acute interstitial nephritis

- o vascular disease

 - Nephrosclerosis, mostly due to hypertension

- o Glomerular disease

Is one of the common causes of chronic renal failure (15-30%)

 - Primary

 - Secondary

 - Hereditar

Glomerulonephritis

Primary glomerulonephritis (GN):

Acute (diffuse) proliferative GN

Rapidly progressive (crescentic) GN

IgA nephropathy

Nephritic syndrome

Minimal change disease (lipoid nephrosis)

Focal segmental glomerulosclerosis

Membranous GN

Membranoproliferative GN

Nephrotic syndrome

Glomerulonephritis

Secondary (systemic) GN:

Diabetes mellitus (diabetic nephropathy)

Systemic lupus erythematosus (SLE)

Amyloidosis, hypertension, vascular diseases

HIV, hepatitis,...etc

Hereditary disorders

Alport syndrome

Thin membrane disease

Fabry disease

- ***Clinical presentations of glomerulopathies***

Glomerular diseases have been classified in numerous ways. they are organized as four major **glomerular syndromes**:

- **Nephrotic syndrome** – massive proteinuria (> 3.5 g/day), hypoalbuminaemia, edema, lipiduria and hyperlipidaemia.
- **Acute glomerulonephritis (acute nephritic syndrome)** – abrupt onset of glomerular haematuria (RBC casts or dysmorphic RBC), non-nephrotic range proteinuria ,oedema, hypertension and transient renal impairment.

- Rapidly progressive glomerulonephritis – and rapidly **progressive renal failure** over weeks.
- Asymptomatic **haematuria, proteinuria or both.**

Glomerulonephritis

Glomerulonephritis is an immune-mediated renal disease induced by three mechanisms.

- Antibody-mediated
 - Antibody react with fixed glomerular antigen (i.e., IgA)
 - Circulating antigen-antibody complex that trapped by glomerulus (i.e., acute (diffuse) proliferative GN).

- Cell-mediated
caused by sensitized T-cells

- Activation of alternative complement pathway

Glomerular lesion

The lesion Consists of:

Infiltration of leucocytes.

Proliferation of endothelial, mesangial and epithelial cell.

Formation of deposits.

Also immunoglobulins and complements form deposits (granular deposits).

The formed deposits lie at three sites:

- In the mesangium (*mesangial deposits*).
- Between the endothelial cells and glomerular basement membrane (GBM; *subendothelial deposits*).
- Between the outside of GBM and podocytes (*subepithelial deposits*).

Primary glomerulonephritis (GN)

Nephritic syndrome:

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- Rapidly progressive (crescentic) GN
- IgA nephropathy

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- Membranoproliferative GN

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Acute (diffuse) proliferative GN
(poststreptococcal, postinfectious)

Definition

- Acute glomerulonephritis is the **inflammation of the glomeruli** which causes the kidneys to malfunction
- It is also called Acute Nephritis, Glomerulonephritis and Post-Streptococcal Glomerulonephritis
- Incubation period is 2 to 3 weeks

Acute (diffuse) proliferative GN (poststreptococcal, postinfectious)

- It is an immune complex-mediated disease.
- It is caused by an exogenous antigen (endostreptosin) following infection of the pharynx or skin with strain of **group A β -hemolytic streptococcus** (nephritogenic).
- It can be caused by other infectious diseases.
- It is more common in children.

Acute (diffuse) proliferative GN
(poststreptococcal, postinfectious)

Poststreptococcal Glomerulonephritis

Poststreptococcal glomerulonephritis is prototypical for acute endocapillary proliferative glomerulonephritis.

Acute poststreptococcal GN

- 90% of cases affect children between the ages of 2 and 14 years
- 10% of cases are patients older than 40

Acute (diffuse) proliferative GN
(poststreptococcal, postinfectious)

Poststreptococcal Glomerulonephritis

The classic presentation is an acute nephritic picture with hematuria, pyuria, red blood cell casts, edema, hypertension, and oliguric renal failure, which may be severe enough to appear as RPGN.

Systemic symptoms of headache, malaise, anorexia, and flank pain (due to swelling of the renal capsule) are reported in as many as 50% of cases.

Acute (diffuse) proliferative GN
(poststreptococcal, postinfectious)

Poststreptococcal Glomerulonephritis

Poststreptococcal glomerulonephritis
caused by impetigo and streptococcal
pharyngitis:

- Impetigo: 2–6 weeks after skin infection
- Streptococcal pharyngitis: 1–3 weeks after infection

Acute (diffuse) proliferative GN
(poststreptococcal, postinfectious)

Signs and Symptoms

- **Hematuria:** dark brown or smoky urine
- **Oliguria:** urine output is < 400 ml/day
- **Edema:** starts in the eye lids and face then the lower and upper limbs then becomes generalized; may be migratory
- **Hypertension:** usually mild to moderate

Acute (diffuse) proliferative GN
(poststreptococcal, postinfectious)

General Symptoms

- Fever
- Headache
- Malaise
- Anorexia
- Nausea and vomiting
- High blood pressure
- Pallor due to edema and/or anemia
- Confusion
- Loss of muscle tissue
- Enlargement of the liver

Acute (diffuse) proliferative GN
(poststreptococcal, postinfectious)

Clinical Presentation

- Nephritic urinary sediment – dysmorphic RBCs, red cell casts, leukocytes, subnephrotic proteinuria
- Nephrotic-range proteinuria not common

Acute (diffuse) proliferative GN (poststreptococcal, postinfectious)

Labs

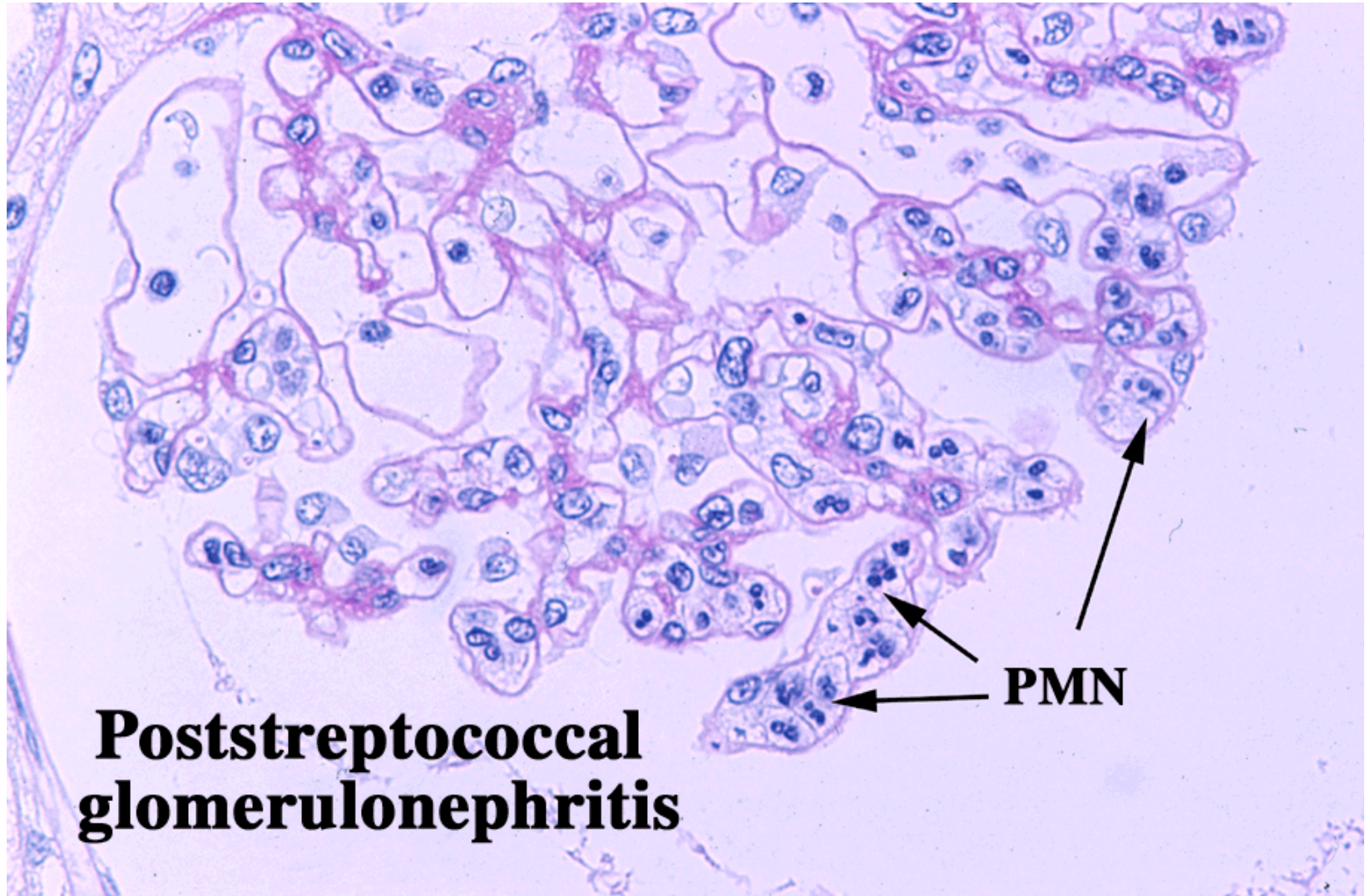
- Serum CRP can be commonly elevated at presentation, though mild
- C3 and CH50 decreased w/in 2 weeks
- C4 usually normal (complement level usually normal within 6-8 weeks)
- Most patients have directed Ab, such as ASO, anti-DNAse B, etc
- Serum IgG and IgM increased in 80% and returns to normal in 1-2 months
- Polyclonal cryoglobulinemia in 75%

Acute (diffuse) proliferative GN
(poststreptococcal, postinfectious)

Poststreptococcal Glomerulonephritis

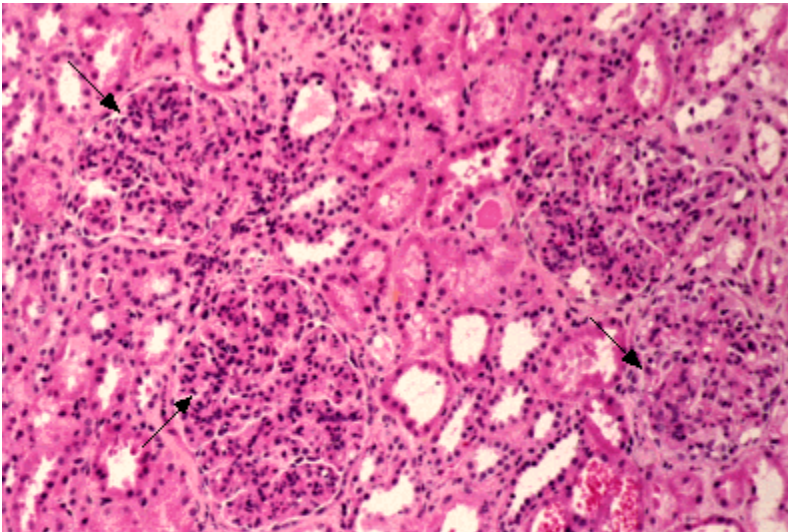
The renal biopsy in poststreptococcal glomerulonephritis demonstrates:

- Hypercellularity of mesangial and endothelial cells
- Glomerular infiltrates of polymorphonuclear leukocytes
- Granular subendothelial immune deposits of IgG, IgM, C3, C4, and C5-9
- **Subepithelial deposits**



Acute (diffuse) proliferative GN (poststreptococcal, postinfectious)

Light Microscopy

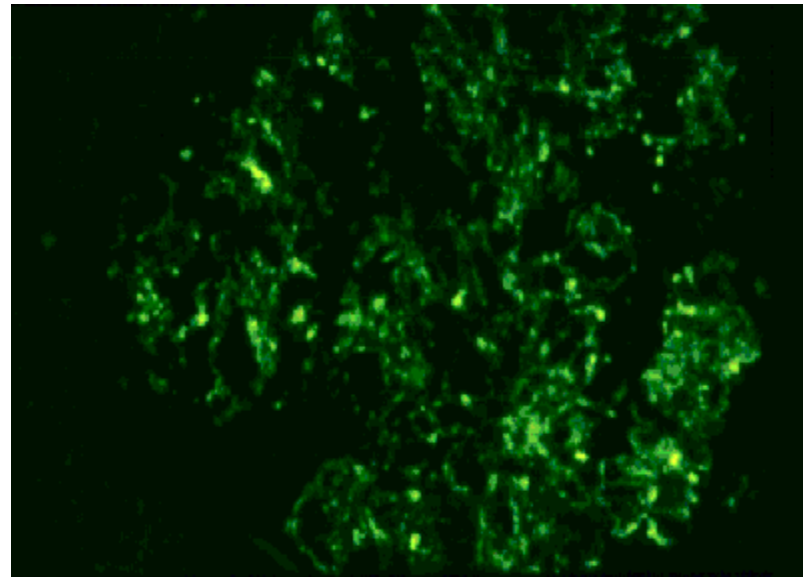


Postinfectious glomerulonephritis Low power light micrograph showing diffuse, proliferative glomerulonephritis as may be seen in postinfectious glomerulonephritis. The glomeruli are so hypercellular (arrows) that open capillary lumens cannot be seen and the glomeruli may be hard to distinguish from the surrounding interstitium. Courtesy of Helmut Rennke, MD.

On light microscopy,
usually see diffuse
proliferative GN

Immunofluorescence Microscopy

- Deposition of IgG and C3

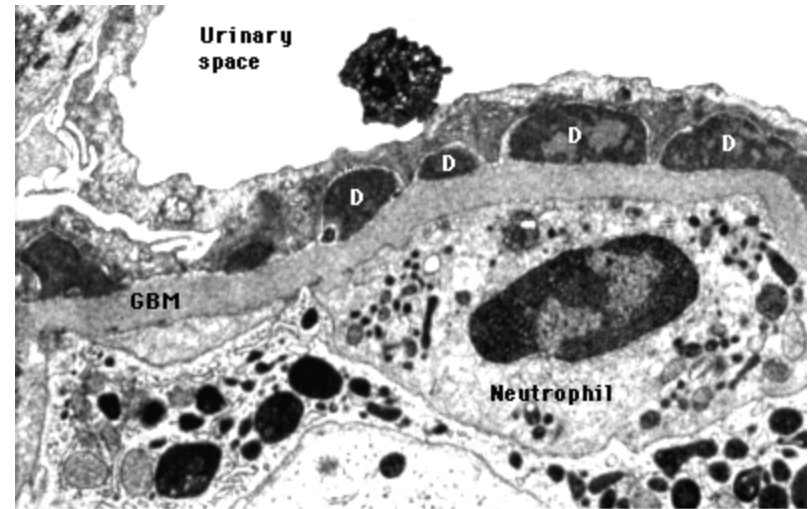


Postinfectious glomerulonephritis Immunofluorescence microscopy shows granular deposition of complement in the glomerular tuft in postinfectious glomerulonephritis. IgG can also be seen in the same distribution. Courtesy of Helmut Rennke, MD.

Acute (diffuse) proliferative GN (poststreptococcal, postinfectious)

Electron Microscopy

- large electron – dense immune deposits in subendothelial, subepithelial, and mesangial areas



Postinfectious glomerulonephritis Electron micrograph shows pathognomonic subepithelial deposits (D) with a semilunar, hump-shaped appearance in postinfectious glomerulonephritis. The humps sit on top of the glomerular basement membrane (GBM). A neutrophil is attached to the denuded GBM, contributing to the glomerular inflammation. Neutrophil attraction requires the initial presence of subepithelial immune deposits so that complement chemoattractants have access to the systemic circulation. Courtesy of Helmut Rennke, MD.

Acute (diffuse) proliferative GN

(poststreptococcal, postinfectious)

Course

- Irreversible Renal Failure rare – less than 1 % in children, slightly higher in adults
- Resolution usually quick, plasma Cr usually returns to previous levels by 3-4 weeks
- Hematuria resolves usually within 3-6 months, proteinuria falls at a slower rate
- Some patients - recurrent proteinuria, and renal insufficiency 10-40 yrs after
- > 20% of adults may have some degree of persistent proteinuria and or compromise of GFR 1 year out

Acute (diffuse) proliferative GN
(poststreptococcal, postinfectious)

Complications

- Hypertensive encephalopathy, heart failure and acute pulmonary edema may occur in severe cases
- Acute renal necrosis due to injury of capillary or capillary thrombosis

Acute (diffuse) proliferative GN (poststreptococcal, postinfectious)

Treatment

- Symptomatic therapy is recommended for patients with acute poststreptococcal glomerulonephritis, and it should be based on the clinical severity of the illness. The major goal is to control edema and blood pressure.
 - During the acute phase of the disease, restrict salt and water. If significant edema or hypertension develops, administer diuretics.
 - Loop diuretics increase urinary output and consequently improve cardiovascular congestion and hypertension.
- For hypertension not controlled by diuretics, usually calcium channel blockers or angiotensin-converting enzyme inhibitors are useful. For malignant hypertension, intravenous nitroprusside or other parenteral agents are used.
- Indications for dialysis include life-threatening hyperkalemia and clinical manifestations of uremia.
- Restricting physical activity is appropriate in the first few days of the illness but is unnecessary once the patient feels well.

Acute (diffuse) proliferative GN

(poststreptococcal, postinfectious)

Treatment

- Specific therapy for streptococcal infection is an important part of the therapeutic regimen.
 - Treat patients, family members, and any close personal contacts who are infected.
 - Throat cultures should be performed on all these individuals. Treat with oral penicillin G (250 mg qid for 7-10 d) or with erythromycin (250 mg qid for 7-10 d) for patients allergic to penicillin.
 - This helps prevent nephritis in carriers and helps prevent the spread of nephritogenic strains to others.

Acute (diffuse) proliferative GN
(poststreptococcal, postinfectious)

Prevention

- proper hygiene
- prompt medical assessment for necessary antibiotic therapy should be sought when infection is suspected
- prophylactic immunizations

Primary glomerulonephritis

Nephritic syndrome:

- Acute (diffuse) proliferative GN
- Rapidly progressive (crescentic) GN**
- IgA nephropathy

Nephrotic syndrome:

- Minimal change disease (lipoid nephrosis or nil)
- Focal segmental glomerulosclerosis
- Membranous GN
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Rapidly progressive (crescentic) glomerulonephritis (RPGN)

It is immune-related disease characterized by:

- ✓ Rapid and progressive loss of renal function (within weeks to months).
- ✓ Extensive extracapillary proliferation (**crescent formation**) in a large number of glomeruli.

The proliferation cells are composed of parietal epithelial cells and inflammatory cells (monocytes and macrophages)

Rapidly progressive (crescentic) glomerulonephritis

Divided into three types

Type 1; Anti-GBM disease caused by circulating antibodies and characterized IgG and C3 deposits on the GBM.

The disease known as Goodpasture's syndrome, when pulmonary manifestation (hemorrhage) are associated

Patients can reach dialysis-requiring level within days or weeks.

The patients respond well to plasmapheresis, steroids and cytotoxic drugs, if treatment start early.

Rapidly progressive (crescentic) glomerulonephritis

Type II; characterized by immune-complex deposition (SLE, poststreptococcus GN, IgA).

Plasmapheresis and treatment of underlying etiology is helpful.

Rapidly progressive (crescentic) glomerulonephritis

Type III; Characterized by absence of immune deposits or anti-GBM antibodies (pauci-immune). However, most patients have antineutrophil cytoplasmic antibody (ANCA) in their blood.

Mortality/Morbidity

- Renal failure at presentation carries an increased risk for [end-stage renal disease](#) and death despite immunosuppressive therapy. Death or dialysis occurs in 73% of patients who are treated with conventional therapy and in 88% of patients if they are oligoanuric at time of presentation.

Race

- No racial predilection exists.

Sex

- For RPGN types I and III, a predilection for males.

Age

- RPGN has a broad age distribution, as follows:
- RPGN type I generally occurs in young adults.
- RPGN types II and III generally occur in older adults; the peak incidence occurs in the fourth to sixth decades of life.

Clinical

History

Clinical and laboratory presentations of all types of acute RPGN are quite similar.

- Some patients present with signs and symptoms of renal disease, for example, anemia, hematuria, fluid retention, oliguria, or even uremia.
- Symptoms of weakness, nausea, and vomiting (indicative of azotemia) usually dominate the clinical picture.
- Other patients present with signs and symptoms of their primary etiology (Goodpasture syndrome, Wegener granulomatosis, systemic lupus erythematosus [SLE]).
- Still others give a history of a flulike or viral prodrome. Vague aches and pains or frank arthritis, sinusitis, otitis, episcleritis, skin rash, neuritis, or encephalopathy are uncommon and are more common with a multisystem disease (suggesting secondary form).
- Oliguria, abdominal or flank pain, and hemoptysis may occur (Goodpasture syndrome).
- Peripheral swelling may be present.
- Fifteen percent of patients may be asymptomatic.

- Physical
- Blood pressure may be normal or slightly elevated.
- Peripheral edema may be present in 10% of patients.
- Pallor is common.
- Skin rash: A lesion suggesting leukocytoclastic vasculitis may be present.

Treatment & Medication

- Early and aggressive treatment is warranted to preserve renal function
- A nephrologist should be involved early in the disease course
- Renal diet: Provide a low-salt, low-protein (0.8 g/kg/d) diet, if renal dysfunction is present. Restrict potassium if the patient has hyperkalemia. Avoid malnutrition
- No specific limitations are necessary other than limiting activity after renal biopsy

Medication - Principles of therapy

- **Supportive therapy** involves control of infection, control of volume status (providing dialysis if required), and smoking cessation
- **Specific therapy** is directed toward providing immunosuppressive therapy (eg, glucocorticoids, cyclophosphamide, azathioprine, mycophenolate [MMF]), plasma exchange (in patients presenting with life-threatening pulmonary hemorrhage or advanced renal failure, ie, creatinine level of $>500 \mu\text{mol/L}^1$), and anticoagulant agents

- Recently, monoclonal antibodies (infliximab, rituximab), alemtuzumab (reduces TNF), mizoribine (a purine synthesis inhibitor), and antithymocyte globulin have been used with encouraging results in a small number of patients, but controlled trials are needed
- At present, the mainstay of therapy remains cyclophosphamide and steroids for induction of remission

Glucocorticoids

- **Pulses of intravenous methylprednisolone (5-20 mg/kg) followed by high-dose oral prednisone (2 mg/kg) daily or on alternate days for 2-3 months have shown improved 1-year renal survival rates of 40-70%**

Immunosuppressive agents (cytotoxics)

- Cyclophosphamide 3 mg/kg/d for 12 weeks is a common recommendation, but the duration of therapy may be longer (4-6 mo) in patients with pauci-immune glomerulonephritis.
- This therapy should be followed by the administration of azathioprine (1.5-2 mg/kg/d) or methotrexate (5-20 mg wk as a single dose) until the patient is in remission for at least 6-12 months.
- The duration of azathioprine therapy to prevent further relapses is unknown, but it should be at least for 2 years

Primary glomerulonephritis

Nephritic syndrome:

- Acute (diffuse) proliferative GN
- Rapidly progressive (crescentic) GN
- IgA nephropathy

Nephrotic syndrome:

- Minimal change disease (lipoid nephrosis or nil)
- Focal segmental glomerulosclerosis
- Membranous GN
- Membranoproliferative GN

IgA nephropathy

- The most common type of primary GN worldwide (15-40%).
- It is associated with abnormal synthesis and clearance of IgA.
- It presents with gross hematuria.
- The disease affects children and young adults with worse prognosis in older age.
- Presents with episodic gross hematuria preceded by a recent (1-2 days) of nonspecific throat infection.

IgA Nephropathy

Deposits of IgA are also found in the glomerular mesangium in a variety of systemic diseases, including:

- Chronic liver disease
- Crohn's disease
- Gastrointestinal adenocarcinoma
- Chronic obstructive bronchiectasis
- Idiopathic interstitial pneumonia
- Dermatitis herpetiformis
- Mycosis fungoides
- Leprosy
- Ankylosing spondylitis

IgA nephropathy

- The course of the disease is variable and may take decades to reach chronic renal failure.
- Characterizes by IgA mesangial deposits as well as C3 and Ig G deposits.
- By electron microscopy, electron-dense deposits are found in mesangial and paramesangial areas.
- Absence of C1q and C4 in glomeruli suggests activation of alternative complement pathway.
- No specific treatment. The effect of immunosuppressive drugs and steroids is far from clear.

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Minimal change disease (lipoid nephrosis or nil)

- The most common pattern of nephrotic syndrome (NS) in children; and compromises 5% of nephrotic syndrome in adults.
- It may follow upper respiratory tract infection or routine immunization.

Minimal change disease (lipoid nephrosis or nil)

Also called **Lipoid Nephrosis or Nil**.

Most frequent cause of nephrotic syndrome in **children**

The disease sometimes follows a **respiratory infection**

Causes :

1- **NSAIDs**,

2- **Hodgkin lymphoma** (most commonly)

Minimal change disease (lipoid nephrosis or nil)

In minimal change disease the glomeruli appear **normal** on light microscopy.

The only abnormality seen on electron microscopy is **fusion** of the foot processes of epithelial cells (podocytes) ((not specific abnormality)).

Absence of immune deposits in the glomerulus.

Minimal change disease (lipoid nephrosis or nil)

The basic change in minimal change disease:

Loss of basement membrane polyanions → reduces the negative charge in the membrane (T-cell cytokines) → decreases the filtration barrier to anionic molecules in the plasma (albumin) → permitted to pass through (large amount)

Minimal change disease (lipoid nephrosis or nil)

Clinical features

- Proteinuria (albuminuria) is usually highly selective in childhood
- Oedema is present and in children this may be facial
- No hypertension in children, which is common in 50% of adults.
- Commonly no hematuria.
- Renal function remains good

Minimal change disease (lipoid nephrosis or nil)

Treatment

Glucocorticoid therapy is the treatment of minimal change disease (MCD), leading to complete remission of proteinuria in over 85 to 90% of cases.

Minimal change disease (lipoid nephrosis or nil)

- The changes are reversible
- 90% respond to steroid
- May recur
- 5% progress to CRF

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Focal segmental glomerulosclerosis

- Similar to minimal change disease, but it affects adults.
- It is either primary or secondary disease (HIV, heroin addiction nephropathy, sickle cell nephropathy).

Focal segmental glomerulosclerosis

- Idiopathic or secondary to:
 - Other glomerular disease (IgA)
 - Other renal disease (chronic reflux / pyelonephritis / interstitial nephritis)
 - Systemic disorder (HIV)
 - Drugs (Heroin)
- Characterised by:
 - Sclerosis of portions of some, not all glomeruli
 - Often progresses to chronic renal failure (CRF)
 - Recurs in 25-50% renal transplants

Focal segmental glomerulosclerosis

- Unlike minimal change disease, patients with this disease have higher incidence of hematuria (25-75) and hypertension (30-50%) and proteinuria is non-selective.
- the disease characterized by sclerosing of some, but not all, glomeruli (*focal*).
- Initially the disease affects a segment of the glomerulus (*segmental*).



Focal segmental glomerulosclerosis

- The lesion shows:
 - sclerosis of focal glomerular segments.
 - fusion or loss of foot processes of visceral epithelial cells and epithelial cell detachment with denudation of the underlying GBM.
 - IgG and C3 deposits in sclerotic area.
- Has little tendency for spontaneous remission.
- Response to corticosteroids is poor.
- Progression to chronic renal failure is high (>50%) and relapse after transplantation is common.

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Membranous glomerulonephritis

- The most common cause of nephrotic syndrome in adults.
- It is associated with thrombotic events.
- Characterized by unselective proteinuria.
- It is slowly progressive disease and the prognosis of the disease is variable.

Causes:

- Idiopathic (85%).
- Secondary (15%) to drugs (NSAIDs), malignancy (lung, colon carcinoma), systemic diseases (SLE, DM) or infectious diseases (hepatitis, syphilis).

Membranous glomerulonephritis

Membranous glomerulonephritis is an important and common cause of **nephrotic syndrome** in adults (mean age 35 years). It is rare in children.

85% of cases idiopathic.

Membranous glomerulonephritis

Other causes :

- 1- **Systemic infections**, including hepatitis B, malaria.
- 2- **Drugs** such as penicillamine, captopril, and heroin.
- 3- **Toxic metals** such as gold and mercury.
- 4- **Neoplasms**, including carcinomas, malignant lymphomas, and Hodgkin's lymphoma.
- 5- **Autoimmune disease**: SLE.
- 6- **Miscellaneous** conditions including renal vein thrombosis and sickle cell disease.

Membranous glomerulonephritis

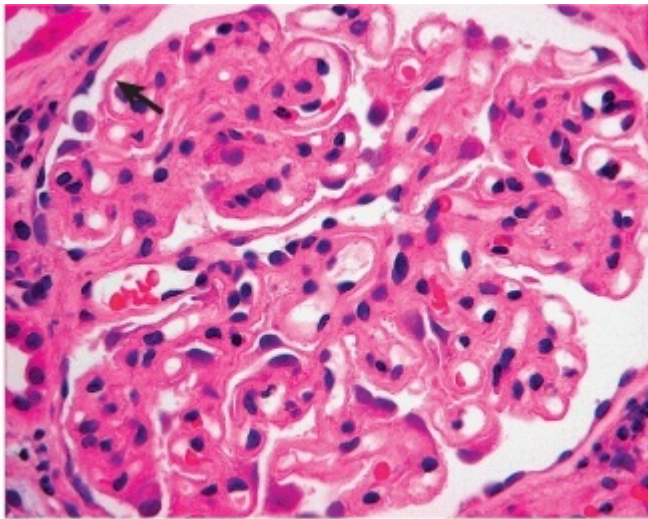
Idiopathic membranous glomerulonephritis is characterized by the presence of **IgG** and complement (**C3**) as granular deposits (Increases membrane permeability) in the **subepithelial** region indicative of a chronic antigen-antibody reaction.

Membranous glomerulonephritis

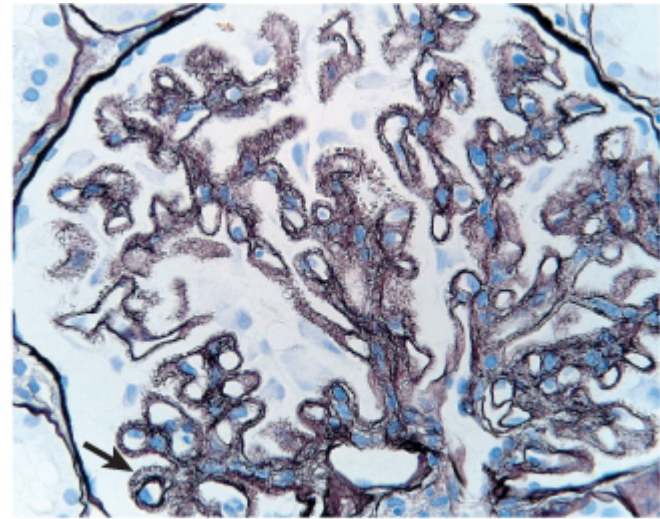
Stage I : Deposition of dome-shaped subepithelial electron-dense deposits, basement membrane is near normal, Protein leakage from the glomerulus leads to epithelial foot process fusion.

Stage II : Spikes of basement membrane.

Stage III : Spikes enlarge and fuse on the epithelial side of the deposits, basement membrane thickening.



(b)



(c)

Membranous glomerulonephritis

Clinical Features

- Asymptomatic proteinuria (nonselective)
- Hematuria is absent in the early stage.
- Hematuria and mild hypertension are present in 15% to 35% of cases

Membranous glomerulonephritis

Treatment

Cyclophosphamide, chlorambucil, and cyclosporine have each been shown to reduce proteinuria.

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Membranoproliferative glomerulonephritis

- The disease is characterized by histological changes in GBM and mesangium and there are mesangial proliferation and inflammation cell infiltration.
- Usually presents as nephrotic, but occasionally is nephritic or combined.
- Accounts for 5-10% of idiopathic nephropathy in children and adults.

Membranoproliferative glomerulonephritis

–Types:

○ Primary

- Type I; is an immune-complex reaction, but the inciting antigen is not known.
- Type II; has a circulating factor called C3 nephritic factor, which activate the alternative complement pathway.

○ Secondary

SLE, hepatitis B and C, HIV and malignancy

- The prognosis is poor and in type II is worse.
- Recurrence after transplantation is common.

Characteristic of primary membranoproliferative glomerulonephritis

	Type 1	Type 2
type	Immune-complex nephritis (unknown antigen)	IgG autoantibody, specific for C3 convertase
Serum C3	Normal C3 levels	Low C3 levels
Light microscope	Large and hypercellular glomeruli	Large and hypercellular glomeruli
GBM	Thick	Thick
Cell proliferation	Mesangial cell	Mesangial cell
Deposits	Subendothelial	Intramembranous
Deposits	IgG and C3	C3 (no IgG)
Inflammatory cells	Leukocytic infiltration	Leukocytic infiltration

Membranoproliferative glomerulonephritis

- Diagnosis – serum complement (depressed), hepatitis serologies, biopsy – glomeruli are hypercellular, often lobular in appearance – more detailed changes.
- Treatment – manage hypertension, ACEI/ARB, salt restriction, diuretics, treat HCV with interferon
- 50% progress to ESKD
- Tends to recur in a kidney transplant

Glomerulonephritis

Secondary (systemic) GN:

Diabetes mellitus (diabetic nephropathy)

Systemic lupus erythematosus (SLE)

Amyloidosis, hypertension, vascular diseases

HIV, hepatitis,...etc

Hereditary disorders

Alport syndrome

Thin membrane disease

Fabry disease

Systemic Lupus Erythematosus (SLE)

SLE is an autoimmune multisystem disease.

Commonly presents as nephrotic syndrome.

Morphologically, its divided into **five** categories:

Class I: Normal; there is no morphological change.

Class II: mesangial lupus GN; mild lesion characterized by increased mesangial cells, mesangial, matrix and granular deposits of immunoglobulin and complement inside mesangium.

Class III: focal proliferative GN; affects <50% of glomeruli (focal). Glomeruli are swollen with proliferation of endothelial and mesangial cells, infiltration of neutrophils, fibrinoid deposits and intracapillary thrombi.

Systemic Lupus Erythematosus (SLE)

Class IV: Diffuse proliferative GN; it's a serious type and common.

It affects the entire glomeruli.

Characterized by proliferation of mesangial, endothelial and epithelial cells.

Epithelial cell proliferation fill Bowman's space and form casts.

There is also fibrinoid necrosis and hyaline thrombi.

Extensive subendothelial immune complex deposits (called *wire loops*) are common, under light microscopy, which reflects the activity of the disease and prognosis.

Class V: Membranous GN; Morphologically is identical to primary membranous GN.

Class IV and V have the worse prognosis that may end in chronic renal failure.

Diabetic nephropathy (DN)

DM caused three major lesions in the kidney: *Glomerular lesion, renal vascular lesion and pyelonephritis.*

A- **Glomerular lesion** includes:

- 1) **Thickening of the capillary GBM** and the tubular basement membrane. Occurs early (2 yrs) regardless of the presence or absence of albuminuria or change in renal function.
- 2) **Diffuse glomerulosclerosis**; characterized by mesangial cell proliferation and mesangial matrix expansion. Occurs late (10-20 yrs) after disease onset.

Diabetic nephropathy (DN)

- 3) **Nodular glomerulosclerosis** (Kimmelsteil-Wilson disease); characterized by hyalinized nodules, which are characteristic of DN. The nodules are acellular and contain lipids and fibrin. They enlarge and compress capillaries causing ischemia leading also to tubular atrophy and interstitial fibrosis.

B- **Renal vascular lesion**

Atherosclerosis and arteriosclerosis of blood vessels. It is part from systemic effect of DM on blood vessels. Hyaline arteriosclerosis affects both afferent and efferent. These changes are associated with hypertension.

C- **Pyelonephritis**

Inflammation that usually begins in interstitial tissue and extends to tubules causing tubular necrosis.

- **Management of nephrotic syndrome**
- *General measures*
- ■ Initial treatment should be with dietary sodium restriction and a thiazide diuretic . Unresponsive patients require furosemide 40–120 mg daily with the addition of amiloride (5 mg daily), with the serum potassium concentration monitored regularly.
- Normal protein intake is advisable. A high-protein diet(80–90 g protein daily) increases proteinuria and can be harmful in the long term. Infusion of albumin produces only a transient effect.

- Hypercoagulable states predispose to venous thrombosis. The hypercoagulable state is due to loss of clotting factors (e.g. antithrombin) in the urine and an increase in hepatic production of fibrinogen. Prolonged bed rest should therefore be avoided as thromboembolism is very common in the nephrotic syndrome. In the absence of any contraindication, longterm prophylactic anticoagulation is desirable.
- If renal vein thrombosis occurs, permanent anticoagulation is required

Sepsis is a major cause of death in nephrotic patients. The increased susceptibility to infection is partly due to loss of immunoglobulin in the urine. Pneumococcal infections are particularly common and pneumococcal vaccine should be given.

- **Lipid abnormalities** are responsible for an increase in the risk of cardiovascular disease in patients with proteinuria. Treatment of hypercholesterolaemia starts with an HMG-CoA reductase inhibitor.
- ACE inhibitors and/or angiotensin II receptor antagonists (AIIRA) are used for their antiproteinuric properties in all types of GN. These groups of drugs reduce proteinuria by lowering glomerular capillary filtration pressure; the blood pressure and renal function should be monitored regularly.

THANK YOU

