BMJ Best Practice

Glomerulonephritis

The right clinical information, right where it's needed

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Summary

- Often part of a multisystem disorder.
- Oedema is a sign of severe or chronic disease.
- A renal biopsy is the test for definitive diagnosis, although it is not required in all patients.
- Treating the underlying disorder and managing HTN, hyperlipidaemia, and proteinuria is the mainstay of therapy.
- Some patients may eventually need dialysis or transplant.

BASICS

Definition

Glomerulonephritis (GN) denotes glomerular injury and applies to a group of diseases that are generally, but not always, characterised by inflammatory changes in the glomerular capillaries and the glomerular basement membrane (GBM). The injury can involve a part or all of the glomeruli or the glomerular tuft. The inflammatory changes are mostly immune mediated.[1] [2]

Epidemiology

For every patient with clinically apparent GN, approximately 5 to 10 patients have undiagnosed subclinical disease.[3] In the US, focal segmental glomerulosclerosis is the most common cause of GN, especially among black patients. Membranous nephropathy (MN) used to be the most common biopsy diagnosis in adult patients.[4] [3] Idiopathic MN is more common in white men >40 years of age. MN is associated with lupus in young women and with hepatitis B in children.[5] By comparison, studies from Australia, France, and China show that IgA nephropathy is more common there.[6] [7] [8] In the US and Europe, GN is the third commonest cause of end-stage renal disease (ESRD), after diabetes and HTN. Worldwide, GN is the commonest cause of ESRD, as the result of various infectious agents in developing countries. Focal segmental glomerulosclerosis is the most common primary glomerular disease underlying ESRD in the US.[4] [9]

Aetiology

The disease can result from renal-limited glomerulopathy or from glomerulopathy-complicating systemic disease: for example, SLE and rheumatoid arthritis.

Glomerular injury may be caused by inflammation due to leukocyte infiltration, antibody deposition, and complement activation. Poorly understood non-inflammatory mechanisms may be responsible for some conditions as well.

It is commonly idiopathic.

Other causes include:[1] [2] [10]

- Infections (group A beta-haemolytic *Streptococcus*, respiratory and GI infections, hepatitis B and C, endocarditis, HIV, toxaemia, syphilis, schistosomiasis, malaria, and leprosy)
- Systemic inflammatory conditions such as vasculitides (SLE, rheumatoid arthritis, and antiglomerulobasement disease, Wegener's granulomatosis, microscopic polyarteritis nodosa, cryoglobulinaemia, Henoch-Schonlein purpura, scleroderma, and haemolytic uraemic syndrome)
- Drugs (penicillamine, gold sodium thiomalate, NSAIDs, captopril, heroin, mitomycin C, and ciclosporin)
- Metabolic disorders (diabetes mellitus, hypertension, thyroiditis)
- Malignancy (lung and colorectal cancer, melanoma, and Hodgkin's lymphoma)
- Hereditary disorders (Fabry's disease, Alport's syndrome, thin basement membrane disease, and nail-patella syndrome)
- Deposition diseases (amyloidosis and light chain deposition disease).

Pathophysiology

Most human glomerulonephritides are triggered by immune-mediated injury exhibiting both humoral and cellular components.

The cellular immune response contributes to the infiltration of glomeruli by circulating mononuclear inflammatory cells (lymphocytes and macrophages) and crescent formation in the absence of antibody deposition. This mechanism plays a primary role in some types of GN such as minimal change nephrotic syndrome or focal glomerulosclerosis and antineutrophil cytoplasmic antibodies-positive GN.[11] [12] Some evidence also supports a role for T cells and platelets in glomerular pathology.[13] [14]

The humoral immune response leads to immune deposit formation and complement activation in glomeruli.[15] [16] [17] Antibodies can be deposited within the glomerulus when circulating antibodies react with intrinsic autoantigens (antiglomerular basement membrane disease), or with extrinsic antigens that have been trapped within the glomerulus (post-infectious GN), or by trapping of immune complexes that have formed in the systemic circulation (cryoglobulinaemia). Injury usually occurs as a consequence of the activation and release of a variety of inflammatory mediators (complement activation, cytokines, growth factors, and vasoactive agents) that initiate a complex interplay of events that ultimately result in the structural and functional characteristics of immune glomerular disease.[18]

A variety of non-immunological metabolic, haemodynamic, and toxic stresses can also induce glomerular injury. These include hyperglycaemia (diabetic nephropathy), lysosomal enzyme defects, and high intraglomerular pressure (systemic hypertension and overload of functioning nephrons following loss of other nephrons due to other causes). A few glomerular diseases are due to hereditary defects resulting in deformity of the glomerular basement membrane (e.g., type IV collagen).

Classification

Primary/secondary classification[1]

Primary disease: the pathological glomerular injury is limited to the kidney and not part of a systemic disease manifestation. The injury may or may not be idiopathic. Any systemic symptoms are a result of renal injury.

- Post-infectious GN
- IgA nephropathy
- Anti-glomerular basement membrane (anti-GBM) GN
- Idiopathic crescentic GN.

Secondary disease: renal pathology in this group is a result of systemic disease such as vasculitis, which also has other organ involvement.

- SLE
- Henoch-Schonlein purpura
- Wegener's granulomatosis
- Microscopic polyangiitis

- Cryoglobulinaemia
- Thrombotic microangiopathies
- Deposition diseases (amyloidosis, light chain deposition disease)
- Malignancies (Hodgkin's lymphoma, lung and colorectal cancer).

Nephrotic/nephritic classification

Nephrotic syndrome (nephrotic-range proteinuria, hypoalbuminaemia, hyperlipidaemia, and oedema)

- Deposition diseases
- Minimal change disease
- Focal and segmental glomerulosclerosis
- Membranous nephropathy
- Membranoproliferative GN.

Nephritic syndrome (haematuria, sub-nephrotic-range proteinuria, and HTN)

- IgA nephropathy
- Postinfectious GN
- Rapidly progressive GN
    - Vasculitis
    - Anti-GBM GN.

Nephritic and rapidly progressive GN (RPGN) classification

Nephritic and RPGN can be classified according to the immunofluorescence microscopy:

- Granular immune deposits (immune complex mediated)
- Linear immune deposits (anti-GBM)
- Pauci-immune.

Secondary prevention

Susceptible people - for example, those with SLE - should be routinely tested with urinalysis for renal involvement.

Case history

Case history #1

A 35-year-old man with no past medical history presents to the emergency department after he noted cola-coloured urine. He denies pain or fever associated with the bleed, but has had a sore throat for the past 3 days, which is getting better. He has not had a similar episode previously. Examination reveals a non-blanching purpuric rash over both his legs. There are no other abnormalities.

Case history #2

A 42-year-old man with a medical history of HIV infection presents to his general practicioner with generalised swelling progressive for the past week. HIV was diagnosed a year ago and he has been non-compliant with the therapy prescribed. He denies orthopnoea, abdominal pain, nausea, and blood in his urine. He has non-pitting oedema mostly over the lower extremities but extending up to mid-abdomen.

Other presentations

GN can present with a nephritic syndrome (haematuria, sub-nephrotic-range proteinuria, and HTN), with a nephrotic syndrome (nephrotic-range proteinuria, hypoalbuminaemia, hyperlipidaemia, and oedema), or with rapidly progressive glomerulonephritis (haematuria, proteinuria, and rising creatinine over weeks to months). Some patients present with just haematuria (macroscopic/microscopic) or proteinuria, or with both. In addition, patients have signs or symptoms of the underlying aetiological agent: for example, pharyngitis with streptococcal infection.

Step-by-step diagnostic approach

Milder forms of GN result in an asymptomatic illness. History, clinical examination, and laboratory testing may arouse clinical suspicion of the disease, but a biopsy is sometimes required for definitive diagnosis.

Early diagnosis with specialist referral, renal biopsy, and serological testing, and early initiation of appropriate therapy are essential to minimise the degree of irreversible renal injury.

Clinical assessment

Clinical features vary depending on the aetiology, and may include 1 or a combination of haematuria (macroscopic or more commonly microscopic), proteinuria, and oedema (characteristic of nephrotic syndrome).**[Fig-10] [Fig-9]** Hypertension may or may not be present; it is uncommon in nephrotic syndrome.

Patients may have features of the underlying disorder, for example:

- Joint pain, rash,**[Fig-12]** and haemoptysis in vasculitis
- Fever and sore throat in streptococcal infections
- Jaundice in hepatitis B and C
- Weight loss in malignancies
- Stigmata of IV drug use.

Laboratory tests

A urinalysis and urine microscopy is generally the first test, and further testing is prompted on the basis of the results. Other initial recommended tests include GFR and creatinine evaluation, 24-hour urine collection, FBC, metabolic profile, and lipid profile.

- Urinalysis and renal function tests show haematuria and proteinuria. In complicated disease GFR and creatinine may suggest reduced renal function.
- Proteinuria, measured by 24-hour urine collection, is generally <3.5 g/day, but if it is >3.5 g/day, patients are classified as having nephrotic-range proteinuria and may have full nephrotic syndrome (hyperlipidaemia, hypoalbuminaemia, oedema, nephrotic-range proteinuria).
- Haematuria is characterised by dysmorphic RBCs and formation of RBC casts that are best seen in freshly prepared urine sediments.
- Anaemia, hyperglycaemia (if diabetic), hyperlipidaemia (nephrotic picture), and hypoalbuminaemia (nephrotic picture) may also be evident from the FBC, and from metabolic and lipid profiles.

If urinalysis indicates GN, subsequent tests are ordered to determine the aetiology and hence to guide the treatment. Specific serological testing for systemic causes include ESR, complement, ANA, RF, anti-double-stranded DNA, antineutrophil cytoplasmic antibodies, anti-glomerular basement membrane antibodies, monoclonal protein on serum or urine electrophoresis, antistreptococcal antibodies (antistreptolysin O antibody, anti-DNase B, and antihyaluronidase), circulating cryoglobulin, HIV serology, hepatitis B virus serology, hepatitis C virus serology, and drug toxicology screen.

Imaging

Ultrasound is useful to assess kidney size and eliminate other causes of decreased renal function, such as obstruction.

CXR is required in rapidly progressive GN to evaluate for pulmonary haemorrhage or granulomas and in nephrotic syndrome to assess for carcinoma or lymphoma.

Renal biopsy

Patients are referred to a specialist for the decision to biopsy or not.

Renal biopsy (with light, immunofluorescence, and electron microscopy) remains the most sensitive and specific test for definitive diagnosis of GN for patients with nephrotic and nephritic syndromes and rapidly progressive GN.[Fig-2] [Fig-3] [Fig-4] [Fig-6] [Fig-5] [Fig-7] [Fig-8] However, a renal biopsy is not routinely performed for syndromes of haematuria, haematuria + proteinuria <2 g, and proteinuria <2 g. Some systemic diseases may not require a renal biopsy to establish the diagnosis: for example, post-infectious GN, mixed cryoglobulinaemia, or antiglomerular basement membrane disease. In some systemic diseases, biopsy of other sites (such as lung for Wegener's granulomatosis) can be performed.[31]

Glomerulonephritis	Site of renal injury	Clinical presentation	Serological markers	Treatment
Post-infectious glomerulonephritis	Endothelial cell injury	Nephritic syndrome	Antibodies to streptococcus, low complement	Antibiotics Rarely steroids
IgA nephropathy	Mesangial cell injury	Nephritic syndrome	None	Treatment of underlying cause
Anti GBM nephritis	Endothelial cell injury	Rapidly progressive GN	Anti-GBM, ANCA	Plasmapheresis, Pulse methylprednisone, cyclophosphamide
Vasculitis	Endothelial cell injury	Rapidly progressive GN	ANCA	Pulse methylprednisone, cyclophosphamide
Lupus nephritis, class I	Mesangial cell injury	Mild form of GN	Anti-DNA	No specific therapy
Lupus nephritis, class II	Mesangial cell injury	microscopic haematuria and/or proteinuria	Anti-DNA	No specific therapy
Lupus nephritis, class III, IV	Endothelial cell injury	Nephritic syndrome	Hypocomplementaemia and elevated anti-DNA levels	Pulse methylprednisone, cyclophosphamide
Lupus nephritis, class V	Epithelial cell injury	Nephrotic syndrome	Hypocomplementaemia and elevated anti-DNA levels	Pulse methylprednisone, cyclophosphamide if progressive
Minimal change disease	Epithelial cell injury	Nephrotic syndrome	None	Oral steroids
Focal and segmental glomerulosclerosis	Epithelial cell injury	Nephrotic syndrome	None	Treatment of underlying cause, antiproteinuric measures, oral steroids, immunosuppressants
Membranous nephropathy	Epithelial cell injury	Nephrotic syndrome with slow progression	Depends on underlying aetiology	Oral steroids and cyclophosphamide
Mesangioproliferative GN	Mesangial cell injury	Nephrotic syndrome with slow progression	Depends on underlying aetiology	Oral steroids

Presentation and treatment of GN. ANCA: anti-neutrophil cytoplasmic antibody; GBM: glomerular basement membrane

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DIAGNOSIS

Risk factors

Strong

group A beta-haemolytic Streptococcus

- Specific nephritogenic strains include M types 1, 2, 4, 12, 25, 49, 55, 57, and 60. The incidence of clinically detectable disease in children infected with pharyngitis is approximately 5% to 10%, and the inidence of skin infections during an epidemic is 25%.[19]

respiratory infections

- Associated with IgA nephropathy. May trigger recurrent episodes of gross haematuria, beginning 1 to 3 days post-infection.[20]

GI infections

- Associated with IgA nephropathy. May trigger recurrent episodes of gross haematuria, beginning 1 to 3 days post-infection.[20]

hepatitis B

- Can result in the deposition of circulating antigen-antibody complexes in the mesangium and subendothelial space (causing membranoproliferative GN), in the subepithelial space (causing membranous nephropathy and nephrotic syndrome), or in the vessels (causing polyarteritis nodosa).[21]

hepatitis C

- The most common patterns of renal involvement are membranoproliferative GN (with cryoglobulinaemia) and, frequently, membranous nephropathy. The pathogenesis appears to relate to deposition of immune complexes containing antibodies to the virus and viral RNA in the glomeruli.[22]

infective endocarditis

- Common organisms are *Staphylococcus aureus* and *Streptococcus viridans*. There is immune complex deposition in the subendothelium and subepithelium, as well as thickening of the capillary wall. Patients mostly present with membranoproliferative GN.[23]

HIV

- A collapsing form of focal glomerulosclerosis has been considered the primary form of HIV nephropathy, especially in black people. The mechanisms by which these changes occur are not well understood, but may be related to direct infection of the glomerulus by HIV.
- Proliferative GN, IgA nephropathy, and lupus-like GN have also been described. Other presentations due to co-infection with hepatitis B or C, concurrent IV drug use, and therapy-related GN may also occur.[24] [25]

SLE

- Renal involvement is common in idiopathic SLE, with the prevalence of clinically evident renal disease ranging from 40% to 75%. The time course for the development of lupus nephritis varies with gender, age, and ethnicity. It appears that males, younger patients, and non-white Americans are at increased risk of developing nephritis earlier in the course of the disease. The pattern and extent of glomerular injury is primarily related to the site of formation of the immune deposits and is accordingly classified into 6 different patterns or classes.[26]

systemic vasculitis

- Such as classic polyarteritis nodosa, Wegener's granulomatosis, microscopic polyarteritis, Churg-Strauss syndrome, and the hypersensitivity vasculitides (including Henoch-Schonlein purpura, mixed cryoglobulinaemia, and serum sickness).[27]

Hodgkin's lymphoma

- Minimal change disease mostly occurs at the time of initial presentation, whereas renal amyloidosis is generally a late event.[28]

lung cancer

- Solid tumours are associated with membranous nephropathy. The likely mechanism is deposition of tumour antigens within the glomeruli, followed by antibody deposition and complement activation.[29]

colorectal cancer

- Solid tumours are associated with membranous nephropathy. The likely mechanism is deposition of tumour antigens within the glomeruli, followed by antibody deposition and complement activation.[29]

non-Hodgkin's lymphoma

- Minimal change disease or focal glomerulosclerosis may occur in association with non-Hodgkin's lymphoma.[29]

leukaemia

- Minimal change disease, focal glomerulosclerosis, or membranoproliferative GN may occur in association with leukaemia.[30]

thymoma

- Minimal change disease or focal glomerulosclerosis may occur in association with thymoma.[29]

haemolytic uraemic syndrome

- Has been associated with membranoproliferative GN.[29]

drugs

- Well-studied offending agents include penicillamine, gold sodium thiomalate, NSAIDs, captopril, heroin, mitomycin C, and ciclosporin.

History & examination factors

Key diagnostic factors

presence of risk factors (common)

- Risk factors include infections (group A beta-haemolotyic streptococci, hepatitis B and C, respiratory and GI infections, infective endocarditis, HIV), connective tissue diseases (SLE, systemic vasculitides), malignancy (Hodgkin's lymphoma, lung cancer, colorectal cancer, non-Hodgkin's lymphoma, leukaemia, thymoma), haemolytic uraemic syndrome, and drugs.

haematuria (common)

- Microscopic haematuria is common; haematuria that is visible to the patient has variable frequency depending on the type of GN.

oedema (common)

- Generalised. More specific to nephrotic syndrome.[Fig-10] [Fig-9]

hypertension (common)

- Reduced GFR together with salt and water retention results in systemic HTN.

Other diagnostic factors

oliguria (common)

- Early presentation if renal failure develops rapidly, otherwise a late feature.

anorexia (common)

- Part of a generalised vasculitic picture.

nausea (common)

- Part of a generalised vasculitic picture.

malaise (common)

- Part of a generalised vasculitic picture.

weight loss (common)

- May indicate systemic disease.

fever (common)

- May occur with infectious aetiology, for example, post-streptococcal GN.

skin rash (common)

- In vasculitic aetiology.[Fig-12]

arthralgia (common)

- In vasculitic aetiology.

haemoptysis (common)

- In anti-glomerular basement membrane disease and Wegener's granulomatosis.

abdominal pain (common)

- In post-streptococcal GN and Henoch-Schonlein purpura.

sore throat (common)

- Preceding renal symptoms by 1 to 2 weeks in post-streptococcal GN and at the same time in IgA nephropathy.

hypervolaemia (uncommon)

- Symptoms of fluid overload due to reduced urinary output, such as shortness of breath and oedema.

Diagnostic tests

1st test to order

Test	Result
FBC • Anaemia is a feature of several systemic diseases that are associated with GN.	**normocytic normochromic anaemia**
comprehensive metabolic profile • Elevated creatinine (indicates severe or advanced disease). • Elevated liver enzymes may be seen if aetiology is related to hepatitis C virus or hepatitis B virus. • Patients with nephrotic syndrome have hypoalbuminaemia.	**renal failure, elevated liver enzymes, hypoalbuminaemia**
urinalysis • Dysmorphic RBCs, sub-nephrotic proteinuria, and active sediment points to the presence of GN. • This is reasonably sensitive and specific.	**haematuria, proteinuria, dysmorphic RBCs, leukocytes, and RBC casts**
GFR • Determined by mathematical equations such as the Cockcroft-Gault Calculator or the Modification of Diet in Renal Disease Formula, the GFR gives an indication of the severity and stage of chronic kidney disease. [National Kidney Foundation: MDRD GFR calculator] • More accurate than serum creatinine alone.	**normal or reduced**
lipid profile • May reveal hyperlipidaemia.	**hyperlipidaemia or normal**

Test	Result
24-hour urine collection • Quantifies proteinuria and is generally ordered as a follow-up to urinalysis showing proteinuria.	**proteinuria is generally <3.5 g/day**
ultrasound of kidneys • Thinning of the cortico-medullary junction and shrunken kidneys indicate a chronic process, thereby reducing the chances of treatment success. • Helps differentiate from other causes of acute renal failure such as obstructive uropathy.	**small kidneys or normal**

Other tests to consider

Test	Result
ESR • Non-specific test; an elevated ESR indicates vasculitis.	**elevated or normal**
complement levels • Differentiates pauci-immune from immune complex GN.	**low or normal C3**
rheumatoid factor • Positive result indicates rheumatoid arthritis.	**positive or normal**
anti-neutrophil cytoplasmic antibody (ANCA) • Positive result indicates pauci-immune or antiglomerulobasement disease. It is fairly specific but not very sensitive.	**positive or normal**
anti-glomerular basement membrane (GBM) antibody • Positive result indicates anti-GBM disease or Goodpasture's syndrome.	**positive or normal**
antistreptolysin O antibody • high or rising titres indicate post-streptococcal GN.	**high or rising titres, or normal**
antihyaluronidase • high or rising titres indicate post-streptococcal GN.	**high or rising titres, or normal**
anti-DNase • Positive result indicates post-streptococcal GN.	**positive or normal**
anti-double-stranded DNA • Positive result indicates SLE.	**positive or normal**
ANA • High titres indicate SLE.	**high titres, or normal**
cryoglobulins • Positive result indicates cryoglobulinaemia.	**positive or normal**
hepatitis C virus and hepatitis B serology • Positive result indicates acute or chronic hepatitis C virus/hepatitis B virus infection.	**positive or normal**
HIV serology • Presence of antibody ndicates HIV infection. Note that the test is highly sensitive for detecting HIV but not GN.	**antibody to HIV, or normal**

Test	Result
electrophoresis • Raised gamma-globulin associated with number of conditions including lymphoma, amyloidosis, and SLE.	**polyclonal gammopathy or normal**
drug screen • May be useful if suspected drug or medication toxicity.	**positive or normal**
renal biopsy • Core-needle biopsy remains the most sensitive and specific test for diagnosis. Light and electron microscopy will reveal pattern of cellular proliferation and number of glomeruli involved.[Fig-2] [Fig-3] [Fig-4] [Fig-8] [Fig-11] Immunofluorescence microscopy may show patterns of immune complex deposition.[Fig-6] [Fig-5]	**characteristic findings on light and immunofluorescence microscopy**

Differential diagnosis

Condition	Differentiating signs / symptoms	Differentiating tests
Nephrolithiasis	• Patients usually have severe pain in addition to haematuria. The site and radiation of pain depend on the position of the stone.	• Urinalysis shows haematuria, but no dysmorphic RBCs or casts. IV pyelogram or renal ultrasound reveals the stone.
Bladder cancer	• Important cause of painless haematuria. Patients are older and mostly have a history of smoking.	• Urinalysis shows haematuria, but no dysmorphic RBCs or casts. Diagnosis is made by cystoscopy and biopsy of the lesion.
Renal cancer	• A triad of flank pain, fever, and haematuria is typical. Many cases are detected incidentally when a CT is done for other purposes.	• Urinalysis shows haematuria, but no dysmorphic RBCs or casts. Imaging by CT would reveal a renal mass.
Pre- or post-renal failure	• Patients present with vague generalised symptoms (fatigue, loss of appetite, and nausea) besides those of the underlying aetiology.	• Urinalysis does not reveal dysmorphic RBCs or casts. Fractional excretion of sodium is <1% in azotaemia (abnormal levels of nitrogen-containing compounds in the blood) due to pre-renal causes. • Renal imaging (ultrasound or CT) shows obstructive uropathy.

Diagnostic criteria

Simplified clinical severity classification

- Mild: asymptomatic isolated haematuria or proteinuria <2 g.

- Moderate to severe: symptomatic proteinuria, haematuria, and reduced GFR (nephrotic and nephritic syndromes and rapidly progressive GN).

Step-by-step treatment approach

The goal of specific therapy for GN is to reverse the renal damage or to preserve the renal function; it is monitored by checking renal function and the degree of proteinuria. Most of the specific treatment (especially plasmapheresis, corticosteroid therapy, and immunosuppression) is managed with the help of a specialist.

Complications such as HTN and hyperlipidaemia should be managed appropriately to counteract cardiovascular events, as well as to delay progression of renal pathology.

Treatment is patient specific and directed towards the underlying aetiology and managing the complications.

Mild disease

In general, patients who present with isolated haematuria, minimal or no proteinuria, and a normal GFR have a better outcome and may not need specific therapies other than treating the systemic cause (e.g., antibiotics, antivirals, withdrawal of the causative drug).

Moderate to severe disease

Patients with haematuria, proteinuria, and reduced GFR are managed with:

- Specific therapies targeted at reversing the underlying aetiology: for example, antibiotics in acute nephritic post-streptococcal GN
- Non-specific pharmacological measures that reduce proteinuria and are also first-line considerations for controlling hypertension, including:
    - Angiotensin-converting enzyme (ACE) inhibitors, which have been demonstrated to be beneficial in patients with proteinuria >1 g/day and are the most commonly used strategy
    - Angiotensin-II receptor antagonists, which can be used in place of, or in addition to, ACE inhibitors. The European Medicines Agency's Pharmacovigilance Risk Assessment Committee has advised that combining drugs that act on the renin-angiotensin system should only be considered if absolutely necessary, and should be carried out under strict specialist supervision with close monitoring.[32]

Severe disease presenting as nephrotic syndrome (e.g., minimal change disease, focal and segmental glomerulosclerosis, membranous nephropathy, and mesangioproliferative GN) is usually treated with corticosteroids and immunosuppressants. A review of the literature suggests that a shorter course of oral corticosteroids (2 or 3 months) may be just as beneficial as a prolonged duration of treatment in children with nephrotic syndrome.[33] Patients should be referred to a specialist for advice on immunosuppressant therapy.

Complications such as proteinuria are managed with the addition of ACE inhibitors or angiotensin-II receptor antagonists.

In addition, HTN may develop as a result of volume expansion and salt retention. Uncontrolled HTN will hasten renal damage and have cardiovascular complications, and requires aggressive management.

Rapidly progressive glomerulonephritis

Categorised into the following:

- Anti-glomerular basement membrane (linear type)
- Immune-complex mediated (granular type): causes include post-infectious causes, connective tissue disease, IgA nephropathy, and membranoproliferative GN
- Pauci-immune: causes include Wegener's granulomatosis and polyarteritis nodosa.

Corticosteroids and immunosuppressant therapy with or without plasmapheresis (depending on the aetiology) are the mainstay of treatment for severe and progressive disease presenting acutely with massive proteinuria and acute renal failure.[34] [35] [36] [37] The choice of corticosteroid depends on the aetiology of GN.

Glomerulonephritis	Site of renal injury	Clinical presentation	Serological markers	Treatment
Post-infectious glomerulonephritis	Endothelial cell injury	Nephritic syndrome	Antibodies to streptococcus, low complement	Antibiotics Rarely steroids
IgA nephropathy	Mesangial cell injury	Nephritic syndrome	None	Treatment of underlying cause
Anti GBM nephritis	Endothelial cell injury	Rapidly progressive GN	Anti-GBM, ANCA	Plasmapheresis, Pulse methylprednisone, cyclophosphamide
Vasculitis	Endothelial cell injury	Rapidly progressive GN	ANCA	Pulse methylprednisone, cyclophosphamide
Lupus nephritis, class I	Mesangial cell injury	Mild form of GN	Anti-DNA	No specific therapy
Lupus nephritis, class II	Mesangial cell injury	microscopic haematuria and/or proteinuria	Anti-DNA	No specific therapy
Lupus nephritis, class III, IV	Endothelial cell injury	Nephritic syndrome	Hypocomplementaemia and elevated anti-DNA levels	Pulse methylprednisone, cyclophosphamide
Lupus nephritis, class V	Epithelial cell injury	Nephrotic syndrome	Hypocomplementaemia and elevated anti-DNA levels	Pulse methylprednisone, cyclophosphamide if progressive
Minimal change disease	Epithelial cell injury	Nephrotic syndrome	None	Oral steroids
Focal and segmental glomerulosclerosis	Epithelial cell injury	Nephrotic syndrome	None	Treatment of underlying cause, antiproteinuric measures, oral steroids, immunosuppressants
Membranous nephropathy	Epithelial cell injury	Nephrotic syndrome with slow progression	Depends on underlying aetiology	Oral steroids and cyclophosphamide
Mesangioproliferative GN	Mesangial cell injury	Nephrotic syndrome with slow progression	Depends on underlying aetiology	Oral steroids

Presentation and treatment of GN. ANCA: anti-neutrophil cytoplasmic antibody; GBM: glomerular basement membrane

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Treatment details overview

Consult your local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing. (see Disclaimer)

Acute (summary)

Patient group	Tx line	Treatment
mild disease	**1st**	**treatment of underlying cause + supportive measures**
	adjunct	**antibiotic therapy**

TREATMENT

Acute (summary)

moderate-severe disease	1st	ACE inhibitors and/or angiotensin-II receptor antagonists
	adjunct	antibiotic therapy
	adjunct	furosemide
with nephrotic syndrome	adjunct	prednisolone + immunosuppressant
rapidly progressive		
anti-GBM	1st	plasmapheresis + pulse methylprednisolone + immunosuppressants
	adjunct	antibiotic therapy
immune complex	1st	corticosteroids
	adjunct	antibiotic therapy
pauci-immune or severe lupus nephritis	1st	corticosteroids + immunosuppressants
	adjunct	antibiotic therapy

Ongoing (summary)

Patient group	Tx line	Treatment
persistent haematuria, proteinuria, or reduced GFR	1st	ACE inhibitors and/or angiotensin-II receptor antagonists
	adjunct	furosemide

Treatment options

Acute

Patient group	Tx line	Treatment
mild disease	**1st**	**treatment of underlying cause + supportive measures** » In general, patients who present with mild disease (isolated hematuria, minimal or no proteinuria, and a normal GFR) do not need specific therapies other than treating the systemic cause (e.g., antibiotics, antivirals, withdrawal of the causative drug). Dietary intake of salt and water may need to be restricted.
	adjunct	**antibiotic therapy** » Most patients with poststrepotoccal GN can be treated with outpatient oral antibiotics. Benzathine benzylpenicillin can be given intramuscularly as a single dose where compliance is an issue. » Azithromycin and clarithromycin are reserved for patients with penicillin allergies. **Primary options** » phenoxymethylpenicillin: 250-500 mg orally every 6 hours for 10 days **OR** » benzylpenicillin: 2400 to 4800 mg intramuscularly/intravenously every 6 hours for 10 days **OR** » amoxicillin: 500 mg orally twice daily for 10 days **OR** » amoxicillin/clavulanate: 875 mg orally twice daily for 10 days Dose refers to amoxicillin component. **OR** » cefalexin: 500 mg orally twice daily for 10 days **OR** » cefuroxime: 250 mg orally twice daily for 10 days **OR** » azithromycin: 500 mg orally once daily for 5 days **OR**

TREATMENT

Acute

Patient group	Tx line	Treatment
		» clarithromycin: 250-500 mg orally twice daily for 7-10 days; or 1000 mg orally (extended-release) once daily for 7-14 days
moderate-severe disease	**1st**	**ACE inhibitors and/or angiotensin-II receptor antagonists** » Patients who present with haematuria, proteinuria, and reduced GFR are considered to have moderate to severe disease. ACE inhibitors or angiotensin-II receptor antagonists may be used to decrease proteinuria. However, the European Medicines Agency's Pharmacovigilance Risk Assessment Committee has advised that combining drugs that act on the renin-angiotensin system should only be considered if absolutely necessary, and should be carried out under strict specialist supervision with close monitoring.[32] **Primary options** » captopril: 12.5 mg orally twice daily **-or-** » enalapril: 5 mg orally once daily **-or-** » lisinopril: 10 mg orally once daily **--AND/OR--** » losartan: 50 mg orally once daily **-or-** » candesartan: 8-16 mg orally once daily **-or-** » irbesartan: 150 mg orally once daily
	adjunct	**antibiotic therapy** » Patients with poststrepotoccal GN are generally treated with oral antibiotics. Benzathine benzylpenicillin can be given intramuscularly as a single dose where compliance is an issue. » Azithromycin and clarithromycin are reserved for patients with penicillin allergies. **Primary options** » phenoxymethylpenicillin: 250-500 mg orally every 6 hours for 10 days **OR** » benzylpenicillin: 2400 to 4800 mg intramuscularly/intravenously every 6 hours for 10 days **OR**

Acute

Patient group	Tx line	Treatment
		» amoxicillin: 500 mg orally twice daily for 10 days **OR** » amoxicillin/clavulanate: 875 mg orally twice daily for 10 days Dose refers to amoxicillin component. **OR** » cefalexin: 500 mg orally twice daily for 10 days **OR** » cefuroxime: 250 mg orally twice daily for 10 days **OR** » azithromycin: 500 mg orally once daily for 5 days **OR** » clarithromycin: 250-500 mg orally twice daily for 7-10 days; or 1000 mg orally (extended-release) once daily for 7-14 days
	adjunct	**furosemide** » Hypertension, which may develop as a result of volume expansion and salt retention, will hasten renal damage and have cardiovascular complications, and requires aggressive management. Patients who remain hypertensive despite therapy with ACE inhibitors or angiotensin-II receptor antagonists may have added diuretic therapy. **Primary options** » furosemide: 10-40 mg orally once daily
with nephrotic syndrome	adjunct	**prednisolone + immunosuppressant** » Patients who have nephrotic syndrome, including those who relapse after apparent remission, should receive oral corticosteroids. » Severe disease presenting as nephrotic syndrome (e.g., minimal change disease, focal and segmental glomerulosclerosis, membranous nephropathy, and mesangioproliferative GN) is usually treated with a corticosteroid plus an immunosuppressant. A review of the literature suggests that a shorter course of oral corticosteroids (2 or 3 months) may be just as beneficial as a prolonged duration of treatment in children with nephrotic syndrome.[33] Patients should be referred to a specialist for advice on immunosuppressant therapy.

Acute

Patient group	Tx line	Treatment
		Primary options » prednisolone: 1 mg/kg/day orally, taper dose gradually once remission is induced **--AND--** » cyclophosphamide: 750 mg/square metre of body surface area intravenously once monthly; switch to 2 mg/kg/day orally once patient is stable **-or-** » azathioprine: 1-2 mg/kg/day orally **-or-** » mycophenolate mofetil: 1 g orally twice daily
rapidly progressive		
anti-GBM	**1st**	**plasmapheresis + pulse methylprednisolone + immunosuppressants** » Significant proteinuria and altered renal function indicates severe or progressive disease. Corticosteroids, immunosuppressants, and plasmapheresis should be implemented on diagnosis.[34] [38] [39] » Pulse methylprednisolone is recommended first-line treatment. Once patients are stable, defined by renal function and level of proteinuria, oral prednisolone can replace pulse methylprednisolone. » Monitoring is done with serial assessment of anti-GBM titres and clinical status. The decision to stop plasmapheresis depends on renal function and level of proteinuria, and also on serial assessment of anti-GBM titres and clinical status. If the patient still has haemoptysis or positive anti-GBM titres at the end of the 2- to 3-week regimen, then plasmapheresis is continued until haemoptysis resolves and anti-GBM titres are markedly suppressed or negative.[38] [39] **Primary options** » plasmapheresis: daily or alternate day, 4 L exchanges (with albumin given as the replacement fluid) are done for 2-3 weeks **--AND--** » methylprednisolone: 1 g intravenously once daily for 3 days, then switch to prednisolone 1 mg/kg/day orally, taper gradually once remission is induced **--AND--** » cyclophosphamide: 750 mg/square metre of body surface area intravenously once monthly; switch to 2 mg/kg/day orally once patient is stable

Acute

Patient group	Tx line	Treatment
		-or- » azathioprine: 1-2 mg/kg/day orally **-or-** » mycophenolate mofetil: 1 g orally twice daily
	adjunct	**antibiotic therapy** » Patients with poststrepotoccal GN are generally treated with oral antibiotics. Benzathine benzylpenicillin can be given intramuscularly as a single dose where compliance is an issue. » Azithromycin and clarithromycin are reserved for patients with penicillin allergies. **Primary options** » phenoxymethylpenicillin: 250-500 mg orally every 6 hours for 10 days **OR** » benzylpenicillin: 2400 to 4800 mg intramuscularly/intravenously every 6 hours for 10 days **OR** » amoxicillin: 500 mg orally twice daily for 10 days **OR** » amoxicillin/clavulanate: 875 mg orally twice daily for 10 days Dose refers to amoxicillin component. **OR** » cefalexin: 500 mg orally twice daily for 10 days **OR** » cefuroxime: 250 mg orally twice daily for 10 days **OR** » azithromycin: 500 mg orally once daily for 5 days **OR** » clarithromycin: 250-500 mg orally twice daily for 7-10 days; or 1000 mg orally (extended-release) once daily for 7-14 days
immune complex	1st	**corticosteroids** » Significant proteinuria and altered renal function indicates severe or progressive disease. In this group

Acute

Patient group	Tx line	Treatment
		of patients corticosteroids should be implemented on diagnosis.[35] [38] [39]
		Primary options
		» methylprednisolone: 1 g intravenously once daily for 3 days, then switch to oral prednisolone
		OR
		» prednisolone: 1 mg/kg/day orally, taper gradually once remission is induced
	adjunct	**antibiotic therapy**
		» Patients with poststrepotoccal GN are generally treated with oral antibiotics. Benzathine benzylpenicillin can be given intramuscularly as a single dose where compliance is an issue.
		» Azithromycin and clarithromycin are reserved for patients with penicillin allergies.
		Primary options
		» phenoxymethylpenicillin: 250-500 mg orally every 6 hours for 10 days
		OR
		» benzylpenicillin: 2400 to 4800 mg intramuscularly/intravenously every 6 hours for 10 days
		OR
		» amoxicillin: 500 mg orally twice daily for 10 days
		OR
		» amoxicillin/clavulanate: 875 mg orally twice daily for 10 days Dose refers to amoxicillin component.
		OR
		» cefalexin: 500 mg orally twice daily for 10 days
		OR
		» cefuroxime: 250 mg orally twice daily for 10 days
		OR
		» azithromycin: 500 mg orally once daily for 5 days
		OR

Acute

Patient group	Tx line	Treatment
		» clarithromycin: 250-500 mg orally twice daily for 7-10 days; or 1000 mg orally (extended-release) once daily for 7-14 days
pauci-immune or severe lupus nephritis	**1st**	**corticosteroids + immunosuppressants** » Significant proteinuria and altered renal function indicates severe or progressive disease. Corticosteroids and immunosuppressants should be implemented on diagnosis.[35] [38] [39] » Pulse methylprednisolone is recommended first line. Once patients are stable, defined by renal function and level of proteinuria, oral prednisolone can replace pulse methylprednisolone. » Pulse IV cyclophosphamide is given in combination and should be switched to oral dosing as soon as possible. **Primary options** » methylprednisolone: 1 g intravenously once daily for 3 days, then switch to prednisolone 1 mg/kg/day orally, taper gradually once remission is induced **--AND--** » cyclophosphamide: 750 mg/square metre of body surface area intravenously once monthly; switch to 2 mg/kg/day orally once patient is stable **-or-** » azathioprine: 1-2 mg/kg/day orally **-or-** » mycophenolate mofetil: 1 g twice daily orally
	adjunct	**antibiotic therapy** » Patients with poststrepotoccal GN are generally treated with oral antibiotics. Benzathine benzylpenicillin can be given intramuscularly as a single dose where compliance is an issue. » Azithromycin and clarithromycin are reserved for patients with penicillin allergies. **Primary options** » phenoxymethylpenicillin: 250-500 mg orally every 6 hours for 10 days **OR** » benzylpenicillin: 2400 to 4800 mg intramuscularly/intravenously every 6 hours for 10 days

TREATMENT

Acute

Patient group	Tx line	Treatment
		OR » amoxicillin: 500 mg orally twice daily for 10 days **OR** » amoxicillin/clavulanate: 875 mg orally twice daily for 10 days Dose refers to amoxicillin component. **OR** » cefalexin: 500 mg orally twice daily for 10 days **OR** » cefuroxime: 250 mg orally twice daily for 10 days **OR** » azithromycin: 500 mg orally once daily for 5 days **OR** » clarithromycin: 250-500 mg orally twice daily for 7-10 days; or 1000 mg orally (extended-release) once daily for 7-14 days

Ongoing

Patient group	Tx line	Treatment
persistent haematuria, proteinuria, or reduced GFR	**1st**	**ACE inhibitors and/or angiotensin-II receptor antagonists** » ACE inhibitors and angiotensin-II receptor antagonists by themselves are demonstrated to preserve renal function by reducing proteinuria.[40] » ACE inhibitors are commonly prescribed first line; if patients are intolerant, angiotensin-II receptor antagonists can be used instead of, or in combination with ACE inhibitors. However, the European Medicines Agency's Pharmacovigilance Risk Assessment Committee has advised that combining drugs that act on the renin-angiotensin system should only be considered if absolutely necessary, and should be carried out under strict specialist supervision with close monitoring.[32] » Therapy with these drugs is lifelong. Frequent follow-up for proteinuria, renal function, lipid profile, and BP management is required to effectively slow or prevent chronic renal failure. **Primary options**

Ongoing

Patient group	Tx line	Treatment
		» captopril: 12.5 mg orally twice daily **-or-** » enalapril: 5 mg orally once daily **-or-** » lisinopril: 10 mg orally once daily **--AND/OR--** » losartan: 50 mg orally once daily **-or-** » candesartan: 8-16 mg orally once daily **-or-** » irbesartan: 150 mg orally once daily
	adjunct	**furosemide** » Hypertension should be treated aggressively. If a patient remains hypertensive despite therapy with ACE inhibitors or angiotensin-II receptor antagonists, a diuretic may be added.[40]

Primary options

» furosemide: 10-40 mg orally once daily

Emerging

Immunoadsorption

This is an investigational therapy for anti-GBM antibody disease.[41]

CD28-B7 blockade

Investigational therapy for anti-glomerular basement membrane antibody disease. CD28-B7 is a co-stimulatory pathway for T-cell activation, thereby reducing the immune response.[42]

Rituximab

This is an anti-CD 20 antibody that depletes B lymphocytes, used in the treatment of B-cell lymphoma and in a variety of autoimmune disorders. Treatment with rituximab has been suggested for lupus nephritis resistant to conventional therapies. There is increasing evidence for its potential use in frequent relapsing and corticosteroid-dependent nephrotic syndrome. More studies need to be conducted to prove efficacy.[43] [44] [45]

Statins

Lipid-lowering agents, particularly statins, are used for hyperlipidaemia that is more common with nephritic syndromes. Their role in slowing renal progression is under evaluation.[46]

Recommendations

Monitoring

The major parameters that are serially monitored are urine sediment, protein excretion (usually estimated from the protein-to-creatinine ratio), and the serum creatinine concentration. These should be obtained at 2- to 4-week intervals during the initial therapy and then at 1- to 2-month intervals once drug therapy is stabilised and/or is being tapered. Disease activity for individual aetiologies can be monitored by their specific antibody titres every 1 to 2 weeks during the initial therapy and then at 1- to 2-month intervals, or whenever there are signs suggestive of recurrence.[38]

Patient instructions

Patients should adhere strictly to diet and medication regimens to avoid long-term consequences of this disorder. Diet should be low in salt, water, and fat. Protein restriction, if advised, should be done cautiously to avoid malnutrition. Frequent follow-ups will be required to achieve aggressive BP goals and to monitor disease progression by protein in urine and renal functions. If patients receive corticosteroids or immunosuppressive treatments, additional medications to avoid infections and osteoporosis may be prescribed.

Complications

Complications	Timeframe	Likelihood
acute renal failure	**short term**	**medium**
Acute kidney failure is more likely to occur with acute GN (e.g., diffuse nephritic). Early diagnosis and treatment of diffuse and rapidly progressive disease is important. Some forms will result in progressive renal injury despite therapy, ultimately requiring renal replacement (dialysis, transplant).		
hypervolaemia	**short term**	**medium**
This reflects a severe decrease in GFR resulting in generalised oedema. Diuretics are the mainstay of therapy.		
hypercholesterolaemia	**short term**	**medium**
Seen more in nephrotic syndrome. It is probably the consequence of increased hepatic lipoprotein synthesis and loss of lipid-regulating proteins in urine. An increase in low-density lipoproteins and cholesterol is the commonest pattern. Lowering lipids may not necessarily be renoprotective but does prevent cardiovascular death. Initial treatment is with diet and exercise, followed by drug therapy with statins, bile-acid sequestrants, fibric acid derivatives, and nicotinic acid.		
hypertriglyceridaemia	**short term**	**medium**
Seen more in nephrotic syndrome. It is likely the consequence of increased hepatic lipoprotein synthesis and loss of lipid-regulating proteins in urine. An increase in low-density lipoproteins and cholesterol is the commonest pattern. Lowering lipids may not necessarily be renoprotective but does prevent cardiovascular death. Initial treatment is with diet and exercise, followed by drug therapy with statins, bile-acid sequestrants, fibric acid derivatives, and nicotinic acid.		

Complications	Timeframe	Likelihood
hypercoagulability	**short term**	**medium**
Associated with lupus (antiphospholipid antibody) and nephrotic syndrome (urinary loss of antithrombin III, altered levels of protein C and S, increased platelet aggregability). Anticoagulation with heparin and warfarin may be required.		
susceptibility to infection	**short term**	**medium**
Related to increased urinary loss and catabolism of IgG, or may be related to treatment with corticosteroids and immunosuppressants. Prophylaxis for *Pneumocystis* pneumonia for patients receiving cyclophosphamide and thrush for patients receiving corticosteroids is recommended. Other infections are treated as they develop.		
hypertension	**long term**	**high**
Most patients with GN will have hypertension as a result of impaired GFR and increased reabsorption of salt and water. If uncontrolled, this would predispose to cardiovascular disease. A low-salt diet and exercise can be attempted initially. Treatment with diuretics, ACE inhibitors, or an angiotensin-II receptor antagonist is preferred because of their effects on fluid retention and proteinuria. Multidrug therapy will often be needed.		
cardiovascular disease	**long term**	**high**
A higher predisposition may be related to the HTN, hypervolaemia, and hyperlipidaemia, or the underlying disease may affect the coronary arteries independently.		
chronic renal failure	**variable**	**medium**
Patients with post-streptococcal GN and IgA nephropathy have a low incidence of developing chronic kidney disease as long as the underlying disease is treated. For other glomerular diseases, the long-term prognosis tends to be better in patients who present with asymptomatic haematuria and proteinuria and who have focal, rather than diffuse, glomerular involvement on renal biopsy. Principal determinants of a relatively poor renal outcome include more severe renal dysfunction at presentation, more severe proteinuria, lack of response to initial treatment, and an enhanced amount of fibrotic changes, such as interstitial fibrosis and glomerulosclerosis on initial renal biopsy. End-stage renal disease eventually occurs in up to 50% to 60% of untreated patients with membranoproliferative disease within 10 to 15 years[47] and in approximately 20% to 25% of patients with Wegener's granulomatosis.[48]		

Prognosis

Patients with post-streptococcal GN and IgA nephropathy have a low incidence of developing chronic kidney disease as long as the underlying disease is treated. Most patients, particularly children, eventually have complete clinical recovery from the initial episode.

For other glomerular diseases, the long-term prognosis tends to be better in patients who present with asymptomatic haematuria and proteinuria and who have focal, rather than diffuse, glomerular involvement on renal biopsy. Principal determinants of a relatively poor renal outcome include more severe renal dysfunction at presentation, more severe

FOLLOW UP

proteinuria, lack of response to initial treatment, and an enhanced amount of fibrotic changes, such as interstitial fibrosis and glomerulosclerosis on initial renal biopsy.

End-stage renal disease eventually occurs in up to 50% to 60% of untreated patients with membranoproliferative disease within 10 to 15 years,[47] and in approximately 20% to 25% of patients with Wegener's granulomatosis.[48]

Diagnostic guidelines

Europe

Clinical practice guidelines: acute kidney injury

Published by: UK Renal Association **Last published:** 2011

Asia

Evidence-based clinical practice guidelines for rapidly progressive glomerulonephritis 2014

Published by: Japanese Society of Nephrology; Ministry of Health and Labour and Welfare (Japan) **Last published:** 2016

Summary: Details signs and symptoms indicative of rapidly progressive glomerulonephritis.

Treatment guidelines

Europe

Clinical practice guidelines: acute kidney injury

Published by: UK Renal Association **Last published:** 2011

International

KDIGO clinical practice guideline for glomerulonephritis

Published by: Kidney Disease: Improving Global Outcomes (KDIGO) Glomerulonephritis Work Group **Last published:** 2012

Summary: Provides comprehensive evidence-based recommendations for the management of glomerulonephritis.

Asia

Evidence-based clinical practice guidelines for rapidly progressive glomerulonephritis 2014

Published by: Japanese Society of Nephrology; Ministry of Health and Labour and Welfare (Japan) **Last published:** 2016

Summary: Includes a treatment algorithm for the management of rapidly progressive glomerulonephritis.

Online resources

1. National Kidney Foundation: MDRD GFR calculator *(external link)*

Key articles

- Couser WG. Glomerulonephritis. Lancet. 1999;353:1509-1515. Abstract
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- Hahn D, Hodson EM, Willis NS, et al. Corticosteroid therapy for nephrotic syndrome in children. Cochrane Database Syst Rev. 2015;(3):CD001533. Full text Abstract
- Kidney Disease: Improving Global Outcomes (KDIGO) Glomerulonephritis Work Group. KDIGO clinical practice guideline for glomerulonephritis. Kidney Int. 2012;2(suppl 2):139-274. Full text
- Arimura Y, Muso E, Fujimoto S, et al. Evidence-based clinical practice guidelines for rapidly progressive glomerulonephritis 2014. Clin Exp Nephrol. 2016;20:322-341. Full text Abstract

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Images

Glomerulonephritis	Site of renal injury	Clinical presentation	Serological markers	Treatment
Post-infectious glomerulonephritis	Endothelial cell injury	Nephritic syndrome	Antibodies to streptococcus, low complement	Antibiotics Rarely steroids
IgA nephropathy	Mesangial cell injury	Nephritic syndrome	None	Treatment of underlying cause
Anti GBM nephritis	Endothelial cell injury	Rapidly progressive GN	Anti-GBM, ANCA	Plasmapheresis, Pulse methylprednisone, cyclophosphamide
Vasculitis	Endothelial cell injury	Rapidly progressive GN	ANCA	Pulse methylprednisone, cyclophosphamide
Lupus nephritis, class I	Mesangial cell injury	Mild form of GN	Anti-DNA	No specific therapy
Lupus nephritis, class II	Mesangial cell injury	microscopic haematuria and/or proteinuria	Anti-DNA	No specific therapy
Lupus nephritis, class III, IV	Endothelial cell injury	Nephritic syndrome	Hypocomplementaemia and elevated anti-DNA levels	Pulse methylprednisone, cyclophosphamide
Lupus nephritis, class V	Epithelial cell injury	Nephrotic syndrome	Hypocomplementaemia and elevated anti-DNA levels	Pulse methylprednisone, cyclophosphamide if progressive
Minimal change disease	Epithelial cell injury	Nephrotic syndrome	None	Oral steroids
Focal and segmental glomerulosclerosis	Epithelial cell injury	Nephrotic syndrome	None	Treatment of underlying cause, antiproteinuric measures, oral steroids, immunosuppressants
Membranous nephropathy	Epithelial cell injury	Nephrotic syndrome with slow progression	Depends on underlying aetiology	Oral steroids and cyclophosphamide
Mesangioproliferative GN	Mesangial cell injury	Nephrotic syndrome with slow progression	Depends on underlying aetiology	Oral steroids

Figure 1: Presentation and treatment of GN. ANCA: anti-neutrophil cytoplasmic antibody; GBM: glomerular basement membrane

Created by Priyanka Sharma, MD, and used with permission

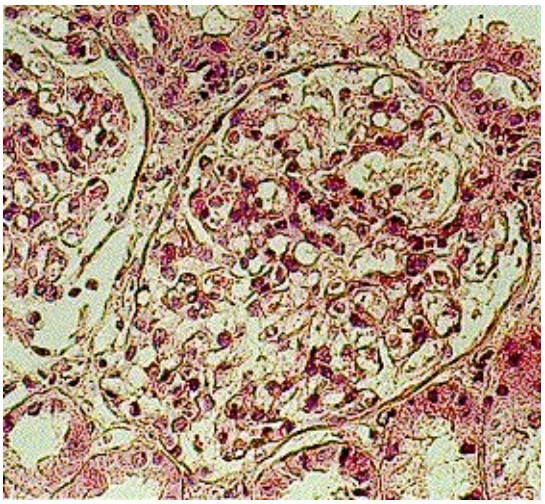

Figure 2: Minimal change nephropathy: the glomerulus has a normal appearance

From: Mason PD, Musey CD. BMJ. 1994;309:1557-1563

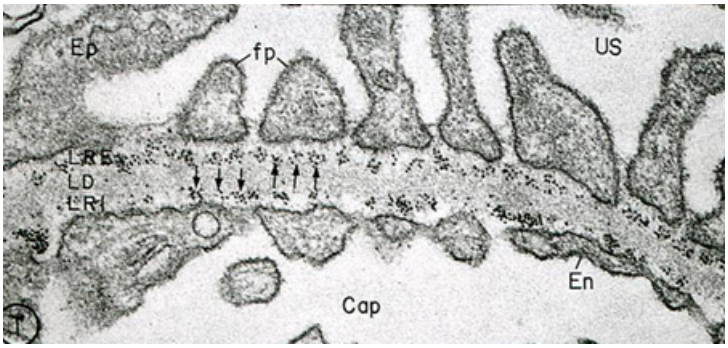

Figure 3: Normal glomerular basement membrane on electron microscopy

From the collection of Dr Mehul Dixit

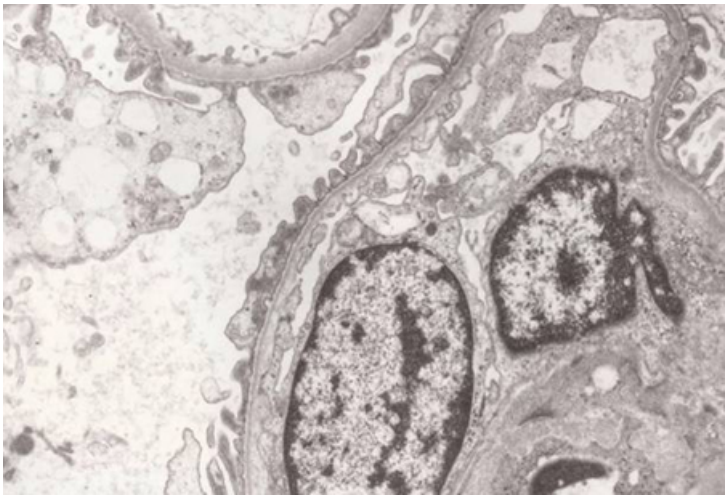

Figure 4: Minimal change nephropathy: podocyte effacement on electron microscopy

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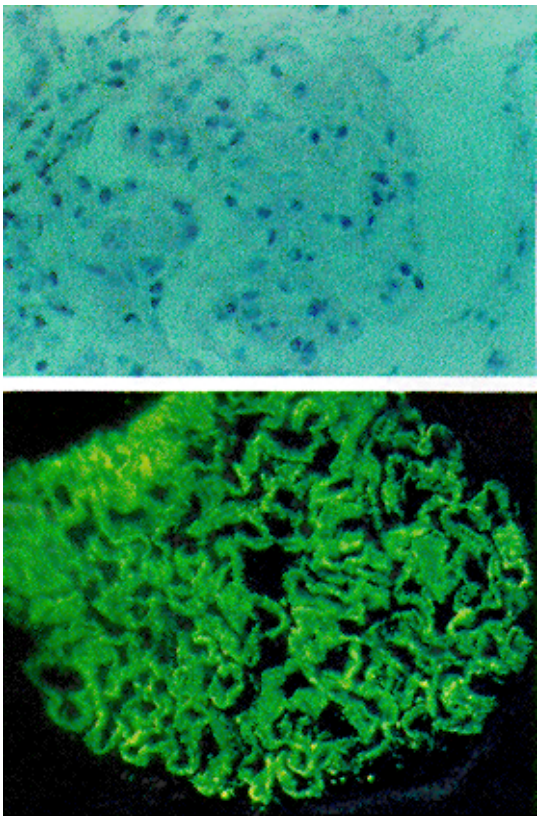

Figure 5: Membranous nephropathy showing (above) thickened basement membrane with normal cellularity (light microscopy; stains: haematoxylin and eosin) and (below) fine granular immunofluorescent staining of IgG along basement membrane

From: Mason PD, Musey CD. BMJ. 1994;309:1557-1563

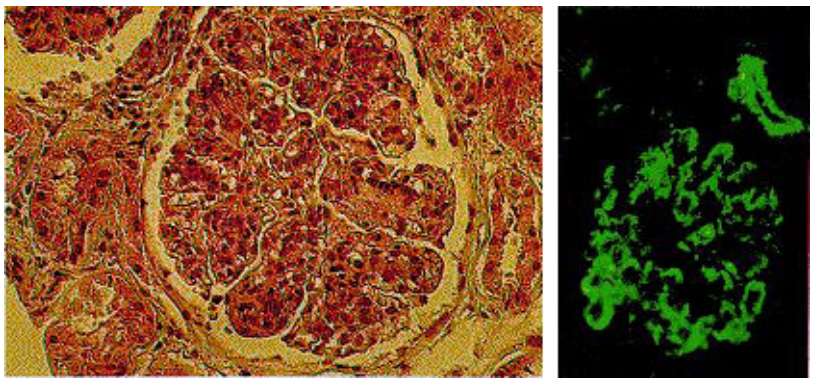

Figure 6: Mesangiocapillary glomerulonephritis showing (left) thickened capillary loops with diffuse cellular proliferation, giving characteristic 'lobular' appearance (light microscopy; stains: haematoxylin and eosin) and (right) coarse patchy granular immunofluorescent staining of IgM along capillary loops

From: Mason PD, Musey CD. BMJ. 1994;309:1557-1563

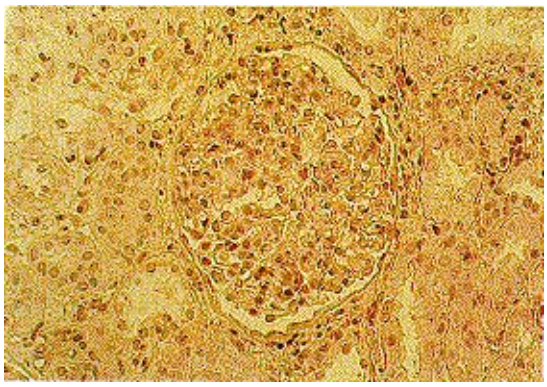

Figure 7: Diffuse proliferative glomerulonephritis as seen in poststreptococcal glomerulonephritis

From: Mason PD, Musey CD. BMJ. 1994;309:1557-1563

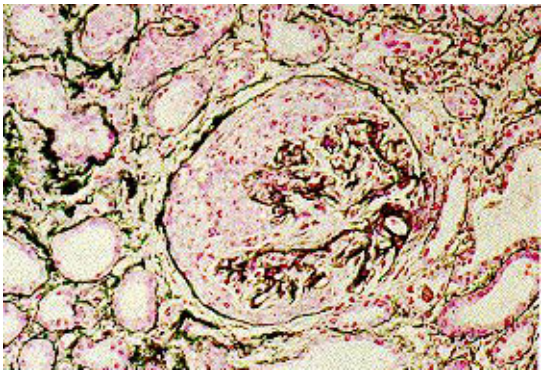

Figure 8: Crescentic glomerulonephritis with cellular crescent occupying large portion Bowman's capsule and compressing glomerular tuft

From: Mason PD, Musey CD. BMJ. 1994;309:1557-1563

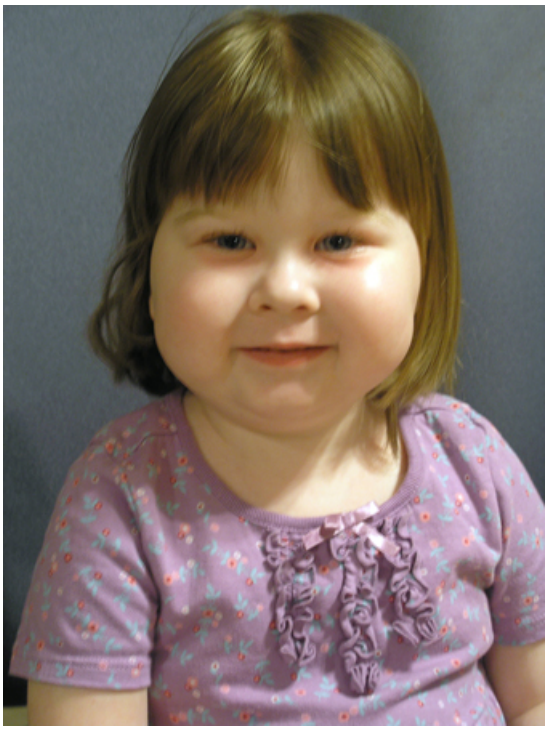

Figure 9: Facial oedema demonstrated in a child presenting in relapse of minimal change nephropathy

From the collection of Dr Mehul Dixit; photo used with parental consent

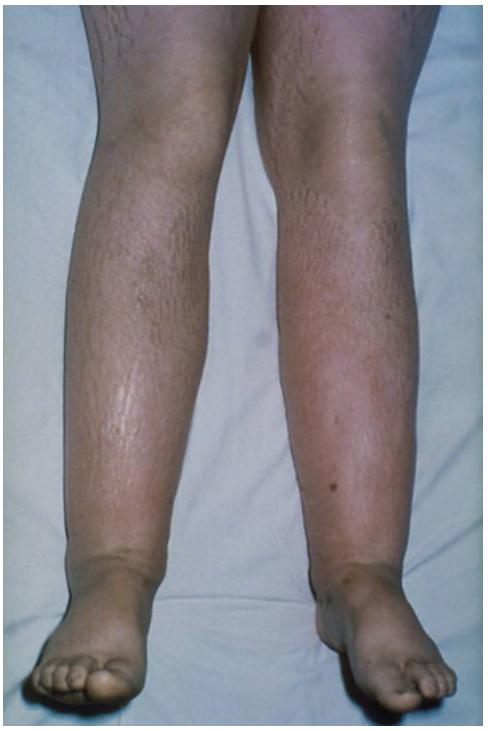

Figure 10: Oedema of the legs

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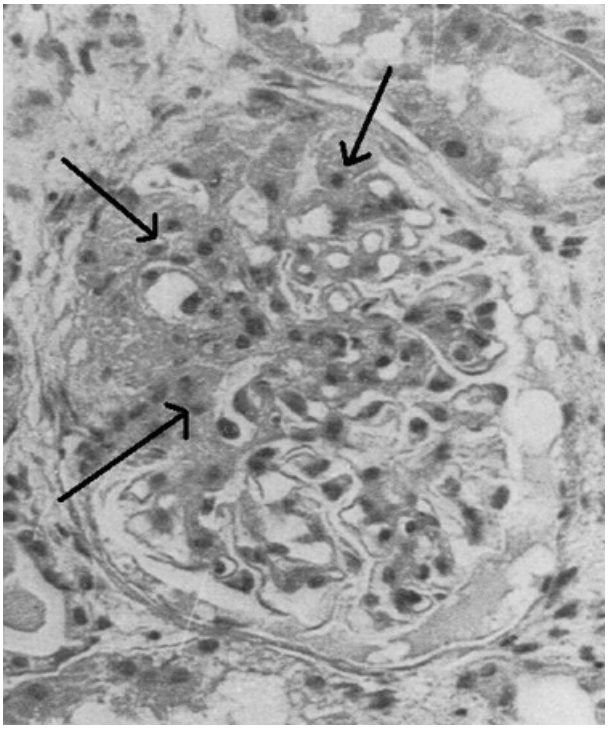

Figure 11: Light microscopy of renal biopsy showing typical lesions of focal segmental glomerulosclerosis (arrows)

Adapted from Nagi AH, Alexander F, Lannigan R. J Clin Pathol. 1971;24:846-850

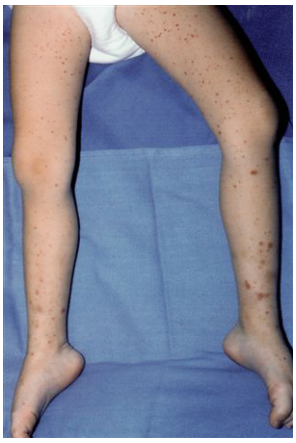

Figure 12: Palpable purpura on the lower extremities of a child with Henoch-Schonlein purpura

From the collection of Dr Paul F. Roberts

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Contributors:

// Authors:

Padmanabhan Premkumar, MD

Assistant Director
Site Director, Internal Medicine Residency , University of Connecticut, Hartford Hospital , Department of Medicine , Hartford , CT
DISCLOSURES: PP declares that he has no competing interests.

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// Peer Reviewers:

Martin Schreiber, MD

Department Chairman
Nephrology and Hypertension, Cleveland Clinic Foundation, Cleveland, OH
DISCLOSURES: MS declares that he has no competing interests.

Patrick Naish, MB, FRCP

Teaching Fellow
Keele University Medical School, Keele, UK
DISCLOSURES: PN declares that he has no competing interests.

Richard Banks, MBBS, FRCP, MD

Consultant Nephrologist
Gloucestershire Royal Hospital, Gloucester, UK
DISCLOSURES: RB declares that he has no competing interests.