Fortnightly Review

Glomerulonephritis: diagnosis and treatment

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The term "glomerulonephritis" is often used loosely to cover all types of glomerular disease, although not all are associated with inflammation of the glomerulus (see below). It is perhaps more accurate to refer to non-proliferative glomerular disease as glomerulopathy or nephropathy. Furthermore, many of the "glomerulonephritides" are associated with interstitial in addition to glomerular inflammation. Although immunological processes are implicated in the pathogenesis of most forms of glomerular disease, the precise mechanisms are understood in only a few. Early referral for evaluation and diagnosis is important as timely treatment, when indicated, may slow or prevent progression to end stage renal failure.

Presentation and diagnosis of glomerulonephritis

Glomerulonephritis may present in many different ways (box 1) and, although certain histological types of glomerular disease often present with a characteristic clinical picture, it is not possible to predict the histological diagnosis accurately so renal biopsy is often indicated. Many patients are first diagnosed in the absence of symptoms after incidental detection of haematuria or proteinuria. Referral is indicated for patients with proteinuria, once infection has been excluded, and for those with impaired renal function. The assessment of haematuria is more difficult, but patients under 50 years with isolated asymptomatic haematuria should generally be referred to a nephrologist, whereas those over 50 years are more likely to have a urological cause and should initially be referred to a urologist.

There is a spectrum of disease, from such asymptomatic urinary abnormalities to the nephritic and nephrotic syndromes and indeed some patients have features of both. The nephritic syndrome is the abrupt onset of haematuria (often with red blood cell casts), proteinuria (usually moderate), reduced renal function, and salt and water retention causing oedema and hypertension. The nephrotic syndrome is heavy proteinuria (> 3.5 g/24 h) associated with hypoprotein-

Summary points

- Glomerulonephritis presents in many different ways and an accurate diagnosis cannot be made clinically
- Dipstick testing of urine is a sensitive way of detecting occult glomerulonephritis once infection has been excluded
- Early referral of patients for assessment and renal biopsy is essential to detect treatable conditions
- Early treatment is more likely to result in preservation of or improvement in renal function
- Patients with glomerular disease of whatever type and severity require long term follow up while urinary abnormalities persist
- Assiduous blood pressure control (aiming for < 145/90 mm Hg) is vital to minimise the rate of progression of renal failure
- Consider antithrombotic and anti-infection prophylaxis in patients with severe and refractory nephrotic syndrome
- Specific treatment may be indicated depending on the disease

aemia, distinct oedema, and often hypercholesterolaemia. Although the history, examination, urine analysis, and blood investigations (box 2) may suggest a likely cause, definitive diagnosis requires a renal biopsy. Underlying glomerulonephritis is also considered to be the cause of end stage renal failure in about a quarter of patients accepted on to dialysis programmes. As the progression of glomerulonephritis may be insidious some patients present in chronic renal failure with small smooth kidneys. By this time renal biopsy is more hazardous and less likely to be informative so the precise diagnosis is often more difficult to confirm. Despite the attraction of making a tissue diagnosis the risk of a biopsy must always be weighed against the benefits. Although the incidence of severe complications is low, the findings, especially in patients with mild disease, may be non-specific and of little prognostic value. Many nephrologists therefore carry out a biopsy only in patients in whom specific treatment is likely to be indicated or when assessment of prognosis is important.¹ Mild haematuria and low level proteinuria (less than 2 g/day) in the absence of renal impairment or hypertension are associated with a good long term prognosis. Such patients can be safely managed with regular monitoring. An increase in

Box 1—Manifestations of glomerular disease

- Asymptomatic proteinuria
- Asymptomatic haematuria
- The nephrotic syndrome
- The nephritic syndrome
- Acute/rapidly progressive renal failure
- End stage chronic renal failure
- Hypertension

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Box 2—Useful blood tests in investigation of glomerular disease

TEST	INTERPRETATION
<i>Non-specific</i>	
Full blood count	High white blood cell count in vasculitis, infection
Electrolytes, urea, and creatinine	Severity of renal impairment
Albumin	Low in those with the nephrotic syndrome, chronic infection
Immunoglobulins	High in vasculitis, systemic lupus erythematosus, postinfectious glomerulonephritis
	IgA raised in about 50% of IgA nephropathy and Henoch-Schönlein purpura
Complement	IgM paraprotein in mixed essential cryoglobulinaemia
	Low C4 $\pm$ C3, in mixed essential cryoglobulinaemia, systemic lupus erythematosus, postinfectious glomerulonephritis, and mesangiocapillary glomerulonephritis type I
	Low C3, normal C4 in mesangiocapillary glomerulonephritis type II and sometimes systemic lupus erythematosus
	High C3, C4 in systemic vasculitis
<i>Specific</i>	
Antiglomerular basement membrane antibody	Goodpasture's disease
Antineutrophil cytoplasmic antibodies	Systemic vasculitis
Anti-dsDNA antibody	Systemic lupus erythematosus
Cryoglobulins	Mixed essential cryoglobulinaemia (low levels in systemic lupus erythematosus and postinfectious glomerulonephritis)
C3 nephritic factor	Mesangiocapillary glomerulonephritis type II and occasionally systemic lupus erythematosus

proteinuria, the development of hypertension, or deterioration of renal function would then be indications for renal biopsy.

Classification of glomerulonephritis

Ideally glomerular disease should be classified according to the underlying immunopathological process, but this is possible in only a few conditions.² Currently the most satisfactory classification depends on the histological appearances, which divide the glomerulonephritides into proliferative and non-proliferative types. The former may then be subdivided dependent on the proliferating cell types and qualified by the pattern of involvement. The terms "diffuse" or "focal" refer to the proportion of glomeruli affected, while "segmental" implies the involvement of only a segment of each affected glomerulus. Extra glomerular proliferation is the accumulation of cells within Bowman's capsule. If this is extensive, occupying more than one half of Bowman's space, it is referred to as a "crescent"—hence the term crescentic nephritis. In addition the pattern, distribution, and nature of immune deposits as determined by immunostaining and electron microscopy may aid diagnosis. Box 3 gives a brief classification of the primary glomerulonephritides. Secondary glomerular disease may be associated with multisystem disorders including mixed cryoglobulinaemia, systemic vasculitis, and systemic lupus erythematosus, and with infection, malignancy, and drugs.

General aspects of management

Glomerular diseases, particularly the proliferative types, are often associated with hypertension.

Vigorous control of blood pressure is important at every stage of management, and there is a strong impression that effective control slows the rate of progression of renal failure irrespective of the underlying cause.³ Nephrotic patients should be prescribed a low salt, normal protein diet. Control of oedema may be accomplished with diuretics, but care must be taken to avoid hypovolaemia which may precipitate renal failure. Angiotensin conversion enzyme inhibitors may considerably reduce proteinuria and are often useful especially when an antihypertensive effect is also necessary. Non-steroidal anti-inflammatory drugs also reduce proteinuria and act synergistically with angiotensin conversion enzyme inhibition. Although non-steroidal anti-inflammatory drugs are useful in selected patients, care must be taken as they may also cause a large fall in glomerular filtration rate and diminish the effectiveness of diuretics. Severely nephrotic patients may need prophylactic anticoagulants and antibiotics.⁴ If the underlying cause cannot be cured treatment of the hypercholesterolaemia should also be considered. The management of progressive chronic renal failure is beyond the scope of this article. Low protein diets have been recommended,⁵ but it is now apparent that protein restriction is of little value in most patients.⁶

Specific treatment of glomerulonephritides

Although a similar range of immunosuppressive agents has been used in most types of glomerulonephritis, the treatment regimens and results of treatment vary considerably. We shall therefore discuss the diagnosis and management of the common histological types separately.

MINIMAL CHANGE NEPHROPATHY

Minimal change nephropathy is responsible for 90% of the nephrotic syndrome in children and about 20% in adults. Clinical onset is usually abrupt, and the glomeruli are normal on light microscopy (fig 1) with fusion of epithelial foot processes on electron microscopy. Before treatment is started, underlying causes of minimal change nephropathy should be considered (box 4).

Children are treated with prednisolone 1 mg/kg/day (or 2 mg/kg alternate days) for eight to 12 weeks or for one week after induction of remission. Half the

Box 3—Classification of glomerular disease

<i>Non-proliferative</i>	<i>Proliferative</i>
Minimal change nephropathy	Mesangial proliferative (IgA) nephropathy
Focal segmental glomerulosclerosis	Mesangiocapillary glomerulonephritis
Membranous nephropathy	Diffuse proliferative glomerulonephritis
	Focal segmental glomerulonephritis
	Crescentic glomerulonephritis

FIG 1—Minimal change nephropathy; glomerulus has normal appearance (light microscopy; stains: haematoxylin and eosin)

induction dose is then given for up to one month with a subsequent tapering over several months. More than 90% of children respond within eight weeks (80% within four weeks). The risk of relapse is higher if treatment is stopped after four weeks (81% at 12 months) rather than 12 weeks (36% at 12 months).⁷ About 30% of responders never have a relapse, another 10-20% are cured after one to four episodes responsive to steroids, while the remainder are frequent relapsers or become dependent on steroids. Such patients may be managed by a gradual tapering of the steroids after remission to the "threshold" at which previous relapses occurred, with continuation of this dose for six to 12 months. Although often successful, the safety of this regimen depends on the dose of steroids required. The question of using alkylating agents in children with steroid responsive disease is controversial, and the risks have to be weighed against those of steroid toxicity or the nephrotic syndrome. Children who require a dose of steroids likely to interfere with growth (>0.5 mg/kg on alternate days) probably need alternative treatment.⁸ Cyclophosphamide (2-2.5

mg/kg/day) for eight weeks is effective at inducing longer lasting remissions, and there is some evidence that 12 weeks' treatment results in fewer relapses.⁹ Frequently relapsing children are more likely to have a permanent remission than those who are dependent on steroids. Chlorambucil (0.2 mg/kg/day) for two months seems to have a similar effect to cyclophosphamide. Cyclosporin (up to 150 mg/m²/day) is usually effective in children with the nephrotic syndrome who are dependent on steroids or frequently relapse.¹⁰ Relapse is almost invariable, however, within three months of stopping treatment, and there is a risk of cyclosporin nephrotoxicity. Consequently, cyclosporin is usually reserved for patients who have failed to respond to other treatments and who require doses of steroids likely to result in long term toxicity. Levamisole has also been used successfully, but most patients relapse within three months after the course of treatment.

Adults are treated initially with steroids (1 mg/kg/day) but respond more slowly and a quarter fail to respond within three to four months. They tend to relapse less often than children (30-50%). Patients who frequently relapse or are dependent on steroids should be treated with cyclophosphamide, which induces a permanent remission more often than in children (75% at two years). Some adults develop transient non-nephrotic relapses, and further treatment should await development of the nephrotic syndrome. Cyclosporin (3-6 mg/kg/day) is also effective but, as in children, relapse usually follows reduction of the dose or withdrawal. It may be worth considering as a short to medium term management strategy as there is evidence that remission eventually occurs in 50-75% patients even without treatment.¹¹ Care is required, however, as nephrotoxicity is common after more than one year's treatment.¹²

FOCAL SEGMENTAL GLOMERULOSCLEROSIS

The aetiology of this fairly common type of glomerular disease, which causes up to 15% of the cases of the nephrotic syndrome, is unknown. The characteristic pathological features are of focal and segmental glomerular scars containing IgM and C3 on immunostaining. Figure 2 shows the features on light microscopy. Most cases are idiopathic, but there are several reported associations (box 4), although the pathogenesis in these circumstances may be different.

Traditionally focal segmental glomerulosclerosis, especially in nephrotic patients, has been thought to have a poor prognosis with a low rate of response to treatment and a high rate of progression to end stage renal failure (50% in 10 years). It is now recognised, however, that up to 40% of patients (adults and children alike) respond to steroids with complete remission, and in those who respond the five year actuarial renal survival exceeds 95%. Even in those

Box 4—Secondary causes or associations of glomerulonephritis

Minimal change

Drugs, especially non-steroidal anti-inflammatory drugs
Hodgkin's disease

Focal segmental glomerulosclerosis

Intravenous drug abuse
HIV infection
Malignancy
After focal segmental glomerulonephritis
Lithium treatment

IgA nephropathy

Hepatic cirrhosis
Coeliac disease/dermatitis herpetiformis
Seronegative arthritis
Tuberculosis

Membranous nephropathy

Tumours—15% of cases, proportion increasing with age
Drugs—especially gold and penicillamine
Infections—hepatitis B, syphilis, quartan malaria
Systemic lupus erythematosus
Sickle cell disease

Mesangiocapillary glomerulonephritis

Tumours and chronic lymphatic leukaemia
Infections—endocarditis, hepatitis B, schistosomiasis
Mixed essential cryoglobulinaemia
Systemic lupus erythematosus

FIG 2—Focal segmental glomerulosclerosis showing segmental scar and preserved capillary loops within single glomerulus (light microscopy; stains: haematoxylin and eosin)

patients who do not go into remission, the renal survival is 55% at five years.¹³

Patients should therefore be treated initially with steroids as for minimal change nephropathy. It is worth treating those who respond but subsequently relapse with cyclophosphamide as a proportion can expect a sustained remission.¹⁴ Patients who are unresponsive to steroids, however, are unlikely to respond to cyclophosphamide, and the decision to treat should be carefully considered for each individual patient. Cyclosporin is sometimes effective and may have a role in patients with the refractory nephrotic syndrome.

IgA NEPHROPATHY

This is the commonest form of glomerulonephritis and is characterised histologically by mesangial hypercellularity and matrix expansion, with mesangial deposits of IgA, IgG, and complement (fig 3). Typically presentation is with recurrent episodes of macroscopic haematuria in young men five to 10 days after an upper respiratory tract infection. It may also present, however, with persistent microscopic haematuria or proteinuria and occasionally with the nephrotic syndrome or rapidly progressive nephritis. Associated diseases are described in box 4.

Although IgA nephropathy was originally thought to follow a benign course, it is now clear that the risk of end stage renal failure is considerable (about 15% at 10 years and 20% or more at 20 years), with rapid deterioration in some patients. Poor prognostic indicators include hypertension, the nephrotic syndrome, and persistent heavy haematuria or proteinuria. Few controlled trials of treatment have been performed, and those that have are generally insufficiently "powerful" to answer the question of whether treatment is effective. Steroids, cyclophosphamide, dipyridamole, and warfarin have all been tried but with little convincing evidence of efficacy, and no specific treatment is currently recommended, at least for patients with low levels of proteinuria.¹⁵ It may be reasonable to try prednisolone in patients with the severe nephrotic syndrome (affecting about 5%), although only those with mild histological lesions are likely to respond.^{15 16} The other subgroup potentially worth treating with steroids and cytotoxic drugs are patients with rapidly progressive disease and crescentic nephritis.

MEMBRANOUS NEPHROPATHY

Membranous nephropathy is the commonest cause of the nephrotic syndrome in adults. Pathologically it is characterised by relatively normal glomerular cellularity but a thickened basement membrane (fig 4a). Fine granular peripheral deposits of immunoglobulin and complement are seen on immunostaining (fig 4b), with subepithelial deposits on electron microscopy. Several underlying causes and associations are known (box 4).

A substantial proportion (20-30%) of patients with primary membranous nephropathy have a spontaneous remission, up to 40% have a partial remission or remain stable, and only a minority (15-30%) develop progressive renal failure. A poor prognosis is more likely to be associated with male sex, age > 50 years, and heavy proteinuria, although impaired or deteriorating renal function is the best predictor of progressive disease.^{17 18}

Steroids alone may diminish proteinuria (by up to 30%) during treatment and a reduced rate of progression of renal failure was reported in one controlled trial, although this was not confirmed in two subsequent trials. Treatment with steroids and cytotoxic drugs, however, has been shown to increase the likelihood of remission and preservation of renal function in controlled trials.^{19 20} Patients were given

alternating months of steroids (0.5 mg/kg/day prednisolone after methylprednisolone 1g intravenously for the first three days) and chlorambucil, while the control groups received placebo¹⁹ or steroids alone.²⁰ This approach has become known as the "Ponticelli" regimen. Cyclophosphamide is generally better tolerated than chlorambucil and may be associated with a lower incidence of late malignancy. It has been used in various regimens with reported success but has not been subjected to adequate controlled trials.

Because of the natural course of the disorder and the potential toxicity of the Ponticelli regimen most nephrologists are unwilling to treat aggressively all patients with membranous nephropathy. Our current recommendation is not to treat non-nephrotic patients with normal renal function. Those with impaired renal function in whom other causes have been excluded (especially renal vein thrombosis, interstitial nephritis, and acute tubular necrosis) are offered the Ponticelli regimen. We are currently studying the effect of three months of cyclophosphamide followed by a change to azathioprine together with tapering steroids in an open trial. Such treatments are probably also indicated for severely nephrotic patients, even if their renal function is preserved, because of the inherent risks of the nephrotic syndrome.

MESANGIOCAPILLARY GLOMERULONEPHRITIS

There are two main types of mesangiocapillary (or membranoproliferative) glomerulonephritis classified by the findings on electron microscopy. Type I is characterised by subendothelial and mesangial immune deposits, while in type II ("dense deposit disease") linear electron dense deposits are found within the basement membrane. In both, there is proliferation of the mesangial cells giving the glomeruli a lobular appearance. In addition, the basement membrane characteristically has a double contour caused by immune deposits and interposition of

FIG 3—Mesangial IgA nephropathy showing mesangial deposits of IgA (immunofluorescence)

FIG 4—Membranous nephropathy showing (a) thickened basement membrane with normal cellularity (light microscopy; stains: haematoxylin and eosin) and (b) fine granular staining of IgG along basement membrane (immunofluorescence)

FIG 5—Mesangiocapillary glomerulonephritis showing (a) thickened capillary loops with diffuse cellular proliferation, giving characteristic "lobular" appearance (light microscopy; stains: haematoxylin and eosin) and (b) coarse patchy granular staining of IgM along capillary loops (immunofluorescence)

mesangial cells. Figure 5A and B shows the appearances on light microscopy and immunofluorescence. Both types may present with asymptomatic proteinuria or haematuria, or both; the nephrotic syndrome; or acute or chronic renal failure. Hypertension is common, and up to 30% of patients present with rapidly deteriorating renal function with crescents on renal biopsy.

Type I mesangiocapillary glomerulonephritis is usually associated with depletion of complement through the classic pathway (low C4 and C3), possibly initiated by immune complexes. Type II is often associated with C3 nephritic factor, which causes alternative pathway complement activation (low C3 with normal C4). A proportion of these patients also have partial lipodystrophy. A number of secondary causes are recognised (box 4).

In patients with no apparent underlying cause, the probability of developing end stage renal failure is about 50% and 90% at 10 and 20 years, respectively. Spontaneous remission rates of up to 20%, however, have been reported, making interpretation of uncontrolled trials difficult. Furthermore, most data relate to type I since type II is rare. A wide variety of treatments have been tried, mostly in uncontrolled settings, including steroids, cytotoxic drugs, anticoagulants, antiplatelet drugs, and cyclosporin.²¹ The rationale for giving steroids is their anti-inflammatory effect, but there is little evidence of efficacy. In children, one controlled trial reported a modest reduction in the incidence of renal failure²² but with a high morbidity from the side effects of steroids. There have been no controlled trials of steroids in adults with mesangiocapillary glomerulonephritis but even retrospective studies have failed to provide support for their role.^{23, 24} There is similarly little evidence for a beneficial effect

Box 5—Main forms of crescentic glomerulonephritis

- Antiglomerular basement membrane disease
- Primary systemic vasculitis—microscopic polyarteritis, Wegener's granulomatosis, the Churg-Strauss syndrome
- Systemic disorders—systemic lupus erythematosus, essential mixed cryoglobulinaemia, Henoch-Schönlein purpura, Behçet's syndrome, rheumatoid disease
- Primary glomerulonephritis—mesangiocapillary glomerulonephritis, mesangial IgA nephropathy, membranous nephropathy
- Infection associated—postinfectious glomerulonephritis, endocarditis
- Malignancy—carcinoma, lymphoma
- Drugs—hydralazine, penicillamine

of cytotoxic drugs and antiplatelet and anticoagulant agents (tried since platelet abnormalities are detectable).

A recent review of the published data from controlled trials of treatment failed to support claims for any form of specific treatment.²⁵ Therefore we do not generally recommend specific treatment of such patients. Patients with a rapidly progressive course and crescentic nephritis (a subgroup in which controlled trials are unlikely to be organised), however, are often given a trial of prednisolone and cyclophosphamide, with variable results.

DIFFUSE PROLIFERATIVE GLOMERULONEPHRITIS

Post-streptococcal glomerulonephritis is the archetypal example of this form of nephritis (fig 6), but it is also seen after a variety of other bacterial, viral, and parasitic infections. Although globally post-streptococcal nephritis remains a common cause, it is now relatively rare in the West.

FIG 6—Diffuse proliferative glomerulonephritis as seen in post-streptococcal glomerulonephritis (light microscopy; stains: haematoxylin and eosin)

Patients typically present with the nephritic syndrome one to three weeks after an infection. The creatinine concentration is usually increased, hypocomplementaemia (especially a low C3) is present in 90% of patients, and rheumatoid factor and cryoglobulins are commonly found. When related to streptococcal infection, the titre of antistreptolysin-O is raised in three quarters of patients with upper respiratory tract infection but in only 40% of those with skin infection.

Although diffuse proliferative glomerulonephritis almost certainly becomes apparent after eradication of the infecting organism, penicillin is usually recommended. Specific treatment directed against the immunological underlying process is not indicated, although control of hypertension and fluid retention is necessary. The prognosis remains somewhat controversial with a reported long term incidence of renal abnormalities ranging from <5% to 60%, although the latter figure is probably biased by more severely affected patients and possibly by inclusion of some with mesangiocapillary glomerulonephritis.²⁵ The prognosis seems to be worse in adults and those nephrotic at presentation, but overall less than 2% of patients develop end stage renal failure after 20 years. None the less, long term follow up of these patients is recommended.

CRESCENTIC GLOMERULONEPHRITIS

The clinical features and diagnostic criteria depend on the underlying cause of the condition²⁶ (box 5). Figure 7 shows the classic appearance of a cellular crescent on light microscopy. The rate of deterioration is variable, but loss of renal function may occur over days, weeks, or months.

FIG 7—Crescentic glomerulonephritis with cellular crescent occupying large portion Bowman's capsule and compressing glomerular tuft (light microscopy; stain: silver stain)

ANTIGLOMERULAR BASEMENT (OR GOODPASTURE'S) DISEASE

This condition presents with rapidly progressive glomerulonephritis, often accompanied by lung haemorrhage, and is due to autoantibodies against the glomerular basement membrane. The antibodies cross react with lung basement membrane, leading to pulmonary haemorrhage especially in patients who smoke. The histological picture is of a crescentic nephritis, affecting a large proportion of glomeruli, usually at a similar stage of evolution. Immunofluorescence shows linear staining of the glomerular basement membrane with immunoglobulins and sometimes complement (fig 8), and circulating antibodies to the glomerular basement membrane can be detected.

Untreated, all patients die rapidly from pulmonary haemorrhage or renal failure. The prognosis has improved since the introduction of plasma exchange and immunosuppression. Plasma exchange is used to remove antiglomerular basement membrane antibodies, and combined with steroids and cyclophosphamide to treat the glomerular inflammation and prevent resynthesis of antibody.²⁷ Most patients treated early (creatinine concentration <600 $\mu\text{mol/l}$) recover renal function, but oligoanuric patients or patients dependent on dialysis are unlikely to respond. For this reason, the risks of treatment in advanced cases should be assessed for each individual patient. The presence of lung haemorrhage is a separate indication for aggressive treatment.

PRIMARY SYSTEMIC VASCULITIS

Although the primary systemic vasculitides are uncommon, they comprise an important and treatable cause of rapidly progressive renal failure. A detailed description of these conditions is beyond the scope of this article.²⁸ Renal disease is a particular feature of the small vessel vasculitides, Wegener's granulomatosis, and microscopic polyarteritis. So called idiopathic crescentic nephritis probably represents a form of small vessel vasculitis limited to the kidneys. Anti-neutrophil cytoplasmic antibodies are present in around 90% of cases of active vasculitis. There are two principal patterns of these antibodies on indirect immunofluorescence: cytoplasmic and perinuclear. Most patients with Wegener's have the cytoplasmic form, whereas the perinuclear form predominates in microscopic polyarteritis and idiopathic rapidly progressive glomerulonephritis. The renal lesion is characteristically a focal segmental necrotising glomerulonephritis, often with crescents, but with few or no deposits on immunostaining.

The standard treatment for vasculitis is a combination of steroids and an alkylating agent. Our regimen consists of prednisolone 60 mg/day, tapering rapidly to 20 mg/day, and oral cyclophosphamide (2-3 mg/kg/day, or 2 mg/kg/day if >55 years) for three months.

Patients with advanced renal failure or life threatening vasculitis of other organs are managed by the addition of either plasma exchange or pulse methylprednisolone. After three months, cyclophosphamide is switched to azathioprine (at an equivalent dose) and the prednisolone is gradually tapered. Treatment is continued for at least a year after remission because of the tendency to relapse. Relapse may be preceded by reappearance or rising titres of antineutrophil cytoplasmic antibodies, but treatment should be determined by clinical features.

SYSTEMIC LUPUS ERYTHEMATOSUS

Lupus nephritis takes many forms and a detailed description is beyond the scope of this article.²⁹ There is controversy regarding the value of renal biopsy, but we believe that it is essential in patients who have substantial renal involvement to define the pathology and plan treatment. Because of the heterogeneity of lupus nephritis, trials are difficult to design and interpret and controlled data are lacking, although few dispute that treatment of diffuse proliferative disease with cytotoxic drugs and steroids greatly reduces the incidence of renal failure.³⁰ Management needs to be considered in the different clinical settings of acute, severe disease and more chronic indolent nephritis.

Acute severe disease with impaired or deteriorating renal function and a diffuse proliferative nephritis with or without crescents may be treated with oral prednisolone (1 mg/kg/day) and cyclophosphamide (2 mg/kg/day) for about 12 weeks, followed by a change to azathioprine, while the prednisolone dose is tapered, although monthly pulses of cyclophosphamide is an alternative approach.³⁰ Fulminant disease is often managed with plasma exchange or pulse methylprednisolone, although the latter may be associated with severe hypertension.

There are few helpful data from the literature concerning maintenance treatment. Some nephrologists would never stop azathioprine and low dose steroids, but we believe that it is reasonable to withdraw these drugs except in patients who have suffered several relapses of disease. Patients with indolent disease or recurrent relapse are currently managed with pulse cyclophosphamide. After one year most such patients are converted to azathioprine and managed as above.

Few data are available regarding treatment of mild focal proliferative glomerulonephritis and depending on its severity, prednisolone alone or prednisolone and azathioprine may be recommended. Membranous nephropathy generally responds poorly to steroids, azathioprine, and cyclophosphamide, although some patients respond to a four to eight week course of prednisolone 45-60 mg/day. Cyclosporin A may be effective, but reduction in dose usually results in relapse, and long term use requires careful consideration of potential risks.

FIG 8—Antiglomerular basement membrane disease showing linear staining of IgG along basement membrane with compression of glomerular tuft by crescent (immunofluorescence)

- 1 Madio MP. Renal biopsy. *Kidney Int* 1990;38:529-43.
- 2 Williams DG, Peters DK. Glomerulonephritis and renal manifestations of systemic disease. In: Weatherall DJ, Ledingham JGG, Warrell DA, eds. *Oxford textbook of medicine*. Oxford: Oxford University Press, 1987; 18:36-51.
- 3 Klahr S. Chronic renal failure: management. *Lancet* 1991;338:423-7.
- 4 Bernard DB. Extrarenal complications of the nephrotic syndrome. *Kidney Int* 1988;33:1184.
- 5 Fouque D, Laville M, Boiseel JP, Chiffet R, Labeeuw M, Zech PY. Controlled low protein diets in chronic renal insufficiency: meta-analysis. *BMJ* 1992;304:216-20.
- 6 Klahr S, Levey AS, Beck GJ, Caggiula AW, Hunsicker L, Kusek JW, et al. The effect of dietary protein restriction and blood pressure control on the progression of chronic renal disease. *N Engl J Med* 1994;330:877-84.
- 7 Arbeitsgemeinschaft für Pädiatrische Nephrologie. Short versus standard prednisolone therapy for initial treatment of idiopathic nephrotic syndrome in children. *Lancet* 1988;ii:380.
- 8 Trompeter RS. Minimal change nephrotic syndrome and cyclophosphamide. *Arch Dis Child* 1986;61:727-9.
- 9 Arbeitsgemeinschaft für Pädiatrische Nephrologie. Cyclophosphamide treatment of steroid-dependent nephrotic syndrome: comparison of eight weeks with 12 weeks course. *Arch Dis Child* 1987;62:1102-6.

- 10 Niaudet D, Broyer M, Habib R. Treatment of idiopathic nephrotic syndrome with cyclosporin A in children. *Clin Nephrol* 1991;35:831-6.
- 11 Nolasco F, Cameron JS, Heywood EF, Hicks J, Ogg C, Williams DG. Adult-onset minimal change nephrotic syndrome: a long term follow-up. *Kidney Int* 1986;29:1215-23.
- 12 Melocoton TL, Vanni ES, Cohen AS, Fine RN. Long-term cyclosporin A treatment of steroid-resistant nephrotic and steroid-dependent nephrotic syndrome. *Am J Kidney Dis* 1991;18:583.
- 13 Pei Y, Cattiran D, Delmore T, Katz A, Lang A, Rance P. Evidence suggesting undertreatment in adults with idiopathic focal segmental glomerulosclerosis. Regional glomerulonephritis registry study. *Am J Med* 1987;82:938-44.
- 14 Siegal NJ, Gaudio KM, Krassner LS, McDonald BM, Anderson FP, Kashgarian M. Steroid-dependent nephrotic syndrome in children: histopathology and relapses after cyclophosphamide treatment. *Kidney Int* 1981;19:454-9.
- 15 Schena FP, Montenegro M, and Scivattaro, V. Meta-analysis of randomised controlled trials in patients with primary IgA nephropathy (Berger's disease). *Nephrol Dial Transplant* 1990;suppl 1:47-52.
- 16 Mustonen J, Pasternack A, Rantala A. The nephrotic syndrome in IgA glomerulonephritis: response to corticosteroid therapy. *Clin Nephrol* 1983;20:172-6.
- 17 Donadio JV Jr, Torres VE, Velosa JA, Wagoner RD, Holley KE, Okamura M, et al. Idiopathic membranous nephropathy: the natural history of untreated patients. *Kidney Int* 1988;33:708-15.
- 18 Schieppati A, Mosconi L, Perna A, Mecca G, Bertani T, Garattini S, et al. Prognosis of untreated patients with idiopathic membranous nephropathy. *N Engl J Med* 1993;329:85-9.
- 19 Ponticelli C, Zucchelli P, Imbasciati E, Cagnoli L, Cesana B, Pozzi C, et al. A controlled trial of methylprednisolone and chlorambucil in idiopathic membranous nephropathy. *N Engl J Med* 1984;310:946-50.
- 20 Ponticelli C, Zucchelli P, Imbasciati E, Cagnoli L, Pozzi C, Passerini P, et al. A randomized trial of methylprednisolone and chlorambucil in idiopathic membranous nephropathy. *N Engl J Med* 1989;320:8.
- 21 D'Amico G. Influence of clinical and histological features on actuarial renal survival in adult patients with idiopathic IgA nephropathy, membranous nephropathy and membranoproliferative glomerulonephritis: survey of the recent literature. *Am J Kidney Dis* 1992;20:315-23.
- 22 Tarshish P, Berstein J, Tobin J, Edelman C. Treatment of mesangiocapillary glomerulonephritis with alternate-day prednisolone: a report of the international study of kidney disease in children. *Pediatr Nephrol* 1992;6:123.
- 23 Donadio JV Jr, Offord KP. Reassessment of treatment results in membranoproliferative glomerulonephritis, with emphasis on life-table analysis. *Am J Kidney Dis* 1989;14:445.
- 24 Schena FP, Cameron JS. Treatment of proteinuric glomerulonephritides in adults. *Am J Med* 1988;85:315.
- 25 Tejani A, Ingulli E. Poststreptococcal glomerulonephritis. Current clinical and pathologic concepts. *Nephron* 1990;55:1.
- 26 Rees AJ, Cameron JS. Crescentic glomerulonephritis. In: Cameron JS, Davison AM, Grünfeld J-P, Kerr DNS, Ritz E, eds. *Oxford textbook of clinical nephrology*. Vol 1. Oxford: Oxford University Press, 1992:318-38.
- 27 Turner AN, Rees AJ. Antiglomerular basement membrane disease. In: Cameron JS, Davison AM, Grünfeld J-P, Kerr DNS, Ritz E, eds. *Oxford textbook of clinical nephrology*. Vol 1. Oxford: Oxford University Press, 1992:438-56.
- 28 Gaskin G, Pusey CD. Systemic vasculitis. In: Cameron JS, Davison AM, Grünfeld J-P, Kerr DNS, Ritz E, eds. *Oxford textbook of clinical nephrology*. Vol 1. Oxford: Oxford University Press, 1992:612-36.
- 29 Glasscock RJ, Cohen AH, Adler SG, Ward HJ. Secondary glomerular disease: systemic lupus erythematosus. In: Brenner BM, Rector FC, eds. *The kidney*. 4th ed. Philadelphia: WB Saunders, 1991:1280-98.
- 30 Austin HA III, Klippel JH, Balow JB, le Riche NG, Steinberg AD, Plotz PH, et al. Therapy of lupus nephritis: controlled trial of prednisolone and cytotoxic drugs. *N Engl J Med* 1986;314:614-24.

Management for Doctors

Getting started as a medical manager

J F Riordan, Jenny Simpson

This is the second in a series of articles dealing with issues arising as clinical practitioners increasingly take on managerial roles. The series is edited by Jenny Simpson

Case study

Three years after his appointment as a consultant physician, Dr B was persuaded by his colleagues to become chairman of the cogwheel division of medicine, all the other physicians having taken their turn. He coped easily with running the monthly divisional meeting, found some satisfaction in juggling the junior medical rotas, and saw his most challenging role as resisting the attempts of the surgeons to "protect" their beds.

After a year in post a keen new general manager was appointed to take the hospital into trust status; he selected Dr B with several other consultants, not all of whom were divisional chairs, to form a management board. Dr B became the first clinical director of medicine. Initially he found this difficult as his colleagues continued to run the old divisional structure in parallel with the new arrangements. Also the senior nurses in medicine were suspicious of medical involvement in their management.

After some months of regular meetings with the nurse manager, along with several training and team building sessions, Dr B found that by working as part of a team he could influence the functioning of the medical service and achieved a number of successes. These included improving the process of case note retrieval; rearranging the appointments procedure; and developing a number of enthusiastic teams to take on specific projects within the directorate. After a few months the atmosphere and communication within the directorate had improved considerably, with staff of all grades beginning to contribute their ideas and support for the new systems. On the strength of this, Dr B managed to persuade his consultant colleagues to disband the cogwheel division and set up a

full directorate structure with a number of subdirectorates. To his surprise he found that he enjoyed working with some of the newly recruited, bright, and keen business managers and took the opportunity to learn and develop new skills in negotiation, information management, time management, and financial monitoring and planning.

Now, with Dr B's three year fixed term of directorship coming to an end and the hospital well established as a trust, he has to give up his post—just when he feels he is beginning to make the most valuable contribution. Having invested time and effort into organising the directorate and understanding its functioning, Dr B is determined that it should succeed. Fortunately, a capable deputy to Dr B had been appointed and trained over the past year, and Dr B has the satisfaction of knowing that she will continue the good work.

However, Dr B's interest in management has been stimulated and he is at present discussing with the chief executive his wish to take on further management responsibility. He will probably take a lead role in coordinating management development within the trust, which has declared as one of its objectives the decentralisation of clinical management down to subunit level. The chief executive has also asked him to become the trust's medical director. Other possibilities include involvement with a region wide training scheme for medical management, helping the medical school to develop an undergraduate course on management, and making a contribution to medical management at national level within the British Association of Medical Managers.

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We live in times of constant change. There are increasing pressures for the NHS to be more efficient, more effective, and more responsive, and these are now accepted throughout the NHS.

The old approach of administering a relatively fixed and unchanged system has given way to the introduction of the techniques of general management which allow organisations to respond appropriately to

change. The introduction of general management began with the Griffiths report of 1983 and has been continued since with the introduction of resource management, followed by the white paper *Working for Patients*, with its separation of the purchaser and provider functions. Inherent in all these changes has been the idea that doctors should have a pivotal role in managing health service resources.