Classification of Glomerulonephropathies

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Introduction

A number of classifications may be proposed according to whether one desires to define a glomerulopathy by its morphology, clinical presentation, aetiology or pathogenesis. The use of renal biopsy in the study of glomerular diseases has amply demonstrated that from a practical point of view a glomerulonephritis (GN) is now best defined according to the morphological criteria, since this is the only way in which prognosis can be evaluated (Habib, 1970, 1973a). However, for the pathologist who is faced with the problem of a renal biopsy performed in a patient presenting all the signs of a glomerulopathy four main situations may be distinguished.

1. The lesions revealed by renal biopsy are pathognomonic of the causative disease, ie histological examination by itself allows with certainty the diagnosis of a precise aetiology.

2. Whether the nephropathy has an acute onset or is a chance discovery, the symptoms (proteinuria with or without nephrotic syndrome, haematuria, hypertension, azotaemia) occur in a previously healthy person with non-antecedent illness. This could be called a primary glomerulopathy.

3. The nephropathy is discovered in the course of a specific disease and often associated with extra-renal signs. This could be called a secondary glomerulopathy.

4. The nephropathy occurs in a family where other members are affected. There are few hereditary disorders where there is a glomerular involvement, but they deserve a special chapter although some of the glomerular lesions are not specific.

We propose, therefore, a classification based essentially on morphology as well as on the aetiological circumstances in which the glomerulopathy is discovered. (Table I)

I. PATHOGNOMONIC GLOMERULAR LESIONS

Most of the glomerular lesions observed by light microscopy are non-pathognomonic
TABLE I. Classification of Glomerular Lesions (GL)

I. Pathognomonic Glomerular Lesions
   Thrombotic Microangiopathy
   Amyloidosis
   Diabetic Glomerulosclerosis
   Tropical 'Membranous' GN
   Lupus Nephritis (with hematoxyphil bodies)

II. GL in Primary Glomerular Diseases
   Minimal GL
   Focal GL  \{ segmental and focal proliferative GN
   \{ focal glomerular sclerosis
   Diffuse GL \{ extramembranous GN
   \{ proliferative GN

III. GL in Specific Diseases
   Acute Post-infectious GN
   Septicaemia \{ sub-acute endocarditis
   \{ shunt nephritis
   \{ Schönlein-Henoch
   Systemic Diseases \{ SLE
   \{ periarteritis nodosa and necrotizing arteritis
   Mixed Essential LG-LM Cryo-globulinaemia
   Anti-GBM Nephritis and Goodpasture's Syndrome

IV. GL in Hereditary Nephropathies
   Alport's Syndrome
   Nail-patella Syndrome
   Infantile Diffuse Mesangial Sclerosis
   Familial NS
   Partial Lipodystrophy
   Amyloidosis of FMF
   Storage Diseases (Fabry, etc)

V. Unclassified

of the causative disease. The only pathognomonic glomerular lesions are thrombotic microangiopathy which is always associated with the haemolytic-uraemic syndrome (Royer et al, 1960; Habib, 1969), diabetic glomerulosclerosis when the pattern described by Kimmelstiel and Wilson is observed, amyloidosis, and lupus nephritis when haematoxyphil bodies are present in the capillary lumens. Apart from these few exceptions a pathologist should never diagnose a specific disorder from the observation of a particular lesion.

II. PRIMARY GLOMERULOPATHIES (Table II)

In this group, the main aim of a morphological study of the renal parenchyma is to determine the precise diagnosis of the lesion responsible for the symptoms. Three main categories of glomerular lesions may be separated on the basis of their
TABLE II. Glomerular Lesions in Primary Glomerular Diseases

1. **Minimal Glomerular Lesions**
   - idiopathic NS
   - asymptomatic proteinuria and/or haematuria
   - recurrent macroscopic haematuria (mesangial IgA nephritis)

2. **Focal Glomerular Lesions**
   - Segmental and Focal Proliferative GN
   - Focal Glomerular Sclerosis
     - focal and segmental hyalinosis
     - focal and global sclerosis

3. **Diffuse Glomerular Lesions**
   - Extra-membranous GN
   - Proliferative GN
     - (a) pure mesangial GN
     - acute post-infectious GN
     - idiopathic nephrotic syndrome
     - 1. with focal crescents
     - 2. with diffuse crescents
     - with sub-endothelial deposits
     - with dense intramembranous deposits
     - (b) endo- and extracapillary GN
     - (c) membrano-proliferative GN

appearance by light microscopy: 'minimal' glomerular lesions indicates that the glomeruli are normal or only slightly modified; 'focal' glomerular lesions mean that, by light microscopy, a limited number of glomeruli are affected and the remainder are normal; and 'diffuse' glomerular lesions describes generalized glomerular involvement which may, however, not be uniform either in degree or type.

**Minimal Glomerular Lesions**

This term describes glomeruli which are normal by light microscopy as well as those with minor changes such as widening of the mesangium, slight increase in mesangial matrix or mild and focal hypercellularity. This pattern is frequent in children with the nephrotic syndrome, with proteinuria sometimes associated with haematuria and with recurrent macroscopic haematuria.

The identification of minimal glomerular lesions generally permits the clinician to predict a favourable prognosis and to eliminate all other types of glomerular abnormalities which may be associated with a less optimal outcome, but clinicopathologic correlations differ depending on which of these clinical findings are present. For example, patients with the nephrotic syndrome are likely to respond to steroids and pursue a favourable course. However, some patients with minimal glomerular lesions may be unresponsive to steroid therapy and may develop focal glomerular sclerosis (Habib and Kleinknecht, 1971).

Examination by electron and immunofluorescent microscopy of renal biopsy tissue which demonstrates minimal glomerular lesions by light microscopy is of invaluable help. Details which are inconspicuous or undetectable by light microscopy can be demonstrated, eg fusion of the foot processes of the glomerular epithelial cells in 'minimal lesion' nephrotic syndrome as seen by electron
microscopy or immunofluorescent staining of anti-sera to IgA deposited in the mesangial areas of patients with recurrent macroscopic haematuria (Berger, 1969; Levy et al, 1973).

Focal Glomerular Lesions

Focal and Segmental Proliferative Glomerulonephritis

Criteria for the diagnosis of segmental and focal glomerulonephritis require that by light microscopy only segments of the tuft are affected with some uninvolved capillary loops and that normal glomeruli are also present. In this type of glomerulonephritis, the segmental lesion is characterized at an early stage by proliferation of both endocapillary (mainly mesangial) and epithelial glomerular cells. Fibrinoid material may sometimes be found among the proliferated cells. At a later stage, collagenous fibres are intermingled with the proliferated cells and a portion of the glomerular tuft is replaced by a fibrous triangle which is adherent to Bowman’s capsule. Electron microscopy demonstrates that lesions are more diffuse than they appear since there are electron-dense deposits in the mesangial areas of all the glomeruli and in most cases immunofluorescent staining reveals mesangial deposits which are mainly composed of IgA in all glomeruli (Levy et al, 1973).

The usual clinical manifestation of this type of nephropathy is proteinuria with haematuria which is often recurrent and macroscopic. Nephrotic syndrome in this setting is rare, mild, usually transient and always accompanied by haematuria. Asymptomatic haematuria is very rarely the only manifestation of renal involvement.

Short-term prognosis often depends on the number of glomeruli affected by the segmental proliferative lesion. Patients usually recover. Some have persistent proteinuria, with or without haematuria, which may lead to chronic renal failure only after several years.

Focal Glomerular Sclerosis (FGS)

The focal lesion may be either complete sclerosis or a segmental hyalinosis and/or sclerosis of some glomeruli. In the segments affected the lesions consist of shrinkage of capillary loops with hyaline deposition or increased mesangial fibrillar material but without any cellular proliferation. Sub-endothelial fibrinoid deposits and foamy endothelial capillary cells may be present in the middle of the hyalinized segments. These changes result in sticking together of some capillary loops in an irregular distribution so that parts of the tuft directly adhere to Bowman’s capsule. Epithelial crescents are almost always absent. (Habib and Gubler, 1971)

Electron microscopy shows the presence of segmental sub-endothelial electron-dense deposits which occlude some capillary lumens, and of diffuse mesangial deposits.
With immunofluorescent microscopy it is usual to detect IgM and C₃ within the areas of hyalinosis but unaffected glomeruli do not demonstrate any fixation of anti-sera.

Most patients with FGS appear without an antecedent illness and present with a nephrotic syndrome, with or without haematuria. They may however have only persistent proteinuria (> 1 g/day) with or without haematuria.

Patients with the nephrotic syndrome who have FGS on renal biopsy are often corticosteroid resistant and they are likely to develop chronic renal failure. In our experience the 50% statistical mortality is around the sixteenth year. Complete more-or-less-prolonged remissions, however, may occur but are followed in most instances by relapses (Habib and Gubler, 1971; Habib, 1973b).

**Diffuse Glomerular Lesions**

Two main categories of diffuse glomerular lesions can be distinguished on the basis of absence or presence of mesangial proliferation.

**Extra-membranous Glomerulonephritis (EMGN) (membranous nephropathy)**

By light microscopy, the glomerular lesion is characterized by a diffuse and homogeneous thickening of the capillary walls without or with mild mesangial hypercellularity. In most cases, the trichrome stain reveals fibrinoid or hyaline deposits all along the epithelial side of the basement membrane. These deposits are not argentophilic with silver impregnation but the capillary walls have a comb-like, hatched appearance (Habib et al, 1973c).

Electron microscopy clearly demonstrates the presence of sub-epithelial deposits. With silver impregnation methods, spiky projections arising from the glomerular basement membrane which separate or surround the deposits are demonstrable.

Immunofluorescence findings in extra-membranous glomerulo-nephritis are very characteristic. There is a diffuse regular granular deposition of IgG and often of C₄ along all the capillary walls while C₁q and C₃ are almost always absent.

In this group of patients proteinuria is often discovered on routine urine analysis. A nephrotic syndrome (persistent or transient) almost always occurs during the course of disease but its presence is not invariable. In most instances, microscopic haematuria is associated with proteinuria.

Extra-membranous glomerulonephritis has a relatively benign course in children. In our experience (Habib et al, 1973c) with an average follow-up of four years, only 10% of affected children progressed to terminal renal failure. Half of the group underwent remissions which were sometimes followed by relapses but which were long enough in others to suggest a complete recovery.

In adults the mean rate of remissions is 16% and the mortality rate is higher: eight to 50% according to the various series published.
Diffuse Proliferative Glomerulonephritis

This category may be subdivided into three groups: pure mesangial proliferative (endothelial capillary glomerulonephritis), mesangial proliferative with epithelial crescents (endo- and extracapillary glomerulonephritis) and membranoproliferative glomerulonephritis.

(a) Endocapillary glomerulonephritis (mesangial proliferative GN) The glomerular lesion is characterized by a proliferation of mesangial cells and an increase in mesangial matrix but without thickening of the capillary walls. If numerous polymorphonuclear cells are seen in the lumens of the capillary tuft along with scattered fibrinoid sub-epithelial deposits, called ‘humps’, the diagnosis of acute glomerulonephritis is almost certain even if a streptococcal infection has not been demonstrated. As a rule ‘humps’ are stained by anti-sera against C₃, often IgG and rarely fibrin. During the resolving phase, when the polymorphonuclear cells and ‘humps’ have disappeared, hyperplastic mesangial cells are grouped together in the mesangial stalks.

When this pattern is associated with an acute nephritic syndrome patients present with proteinuria, haematuria and, in some instances, with a mild and transient nephrotic syndrome.

Azotemia and hypertension are frequent early in the disease, and usually rapidly resolve. The prognosis of an acute nephritic syndrome associated with endocapillary glomerulonephritis is excellent; all affected children recover within three months to one year (Royer et al, 1973). According to several published series the prognosis may be less good in adults.

When this pattern is associated with an idiopathic nephrotic syndrome, the latter is severe and, in some instances, is accompanied by haematuria. These patients are often corticosteroid resistant and may develop chronic renal failure within a few years. Immunofluorescent staining is negative. In some cases repeat biopsies have shown lesions of focal and segmental hyalinosis associated or not with mesangial hypercellularity (Habib, 1973b).

(b) Endo- and extracapillary glomerulonephritis The characteristic feature of this lesion is the presence of more or less diffuse proliferation of epithelial cells (extracapillary) which are seen along with varying degrees of mesangial proliferation. In our experience, only those patients whose biopsies reveal crescent formation involving 80 to 100% of the glomeruli have developed a rapidly progressive course. Accordingly two sub-groups of endo- and extracapillary glomerulonephritis must be distinguished.

(1) With focal crescents (less than 80%): In all glomeruli, proliferation of mesangial cells is present. In addition, in some glomeruli a segment of tuft is severely affected by sub-endothelial deposits, necrosis and/or sclerosis and proliferated epithelial cells cause this segment of the tuft to adhere to the adjacent Bowman’s capsule. Immunofluorescent studies show various patterns according to aetiology.
Most patients present with proteinuria, haematuria (often macroscopic), azotemia and hypertension. Azotemia and hypertension, if present at the time of onset, tend to resolve within a few days or weeks. A mild and usually transient nephrotic syndrome may also occur. The prognosis is variable and depends mainly on the number of glomeruli affected by crescent formation. Complete recovery is possible.

(2) With diffuse crescents (more than 80%): The characteristic morphologic feature of this type of glomerulonephritis is the presence of epithelial of fibroepithelial crescent is formations which surround the glomerular tufts of 80 to 100% of the glomeruli. Fibrin deposits may be seen by light microscopy among proliferated epithelial cells in early lesions. The glomerular tuft is frequently so severely altered by sclerosis and proliferation that light microscopic analysis of the lesions is almost impossible. In some instances, a huge epithelial crescent surrounds apparently normal capillary loops, or humps may be seen on the epithelial side of the basement membrane. In other instances, crescents may be found along with a typical membrano-proliferative glomerulonephritis. The results of immunofluorescent staining vary according to aetiology and to the type of glomerular tuft involvement.

The common clinical denominator for this group of patients is the severe course of the nephropathy. Most patients present with a nephrotic syndrome with haematuria and with renal insufficiency associated with oligo-anuria. These findings may be present from the onset or develop after a few weeks. These patients do not recover; they develop fatal renal insufficiency within several weeks or months but death may not occur until two or three years later.

(c) Membranoproliferative glomerulonephritis (MPGN) (mesangiocapillary GN)
This type of glomerulonephritis is characterized by diffuse mesangial cell proliferation, increased mesangial matrix and irregular thickening of the capillary walls. The changes in the capillary walls may be due to:

(1) an interposition of mesangial cell matrix between the capillary basement membrane and the endothelium which gives the capillary wall an appearance of splitting or ‘double contour’. By electron microscopy, sub-endothelial deposits are usually found. The modifications of the capillary walls lead to progressive narrowing of the capillary lumen.

(2) the presence within the basement membrane of dense deposits which in fact replace the lamina densa and give to the capillary walls a ‘ribbon-like’ appearance. Such deposits are also present within the tubular basement membranes and within Bowman’s capsule.

Whatever the type of thickening of the capillary basement is, two patterns are observed:

(a) Mesangial proliferation and diffuse thickening of the capillary walls (classical MPGN).
(b) Marked increase in mesangial matrix which gives a lobulated appearance to the glomerular tuft (lobular GN or MPGN with a lobular pattern). In addition, epithelial crescents which may be diffuse can be seen with either of the above patterns (a) or (b).

Immunofluorescent microscopy demonstrates different staining patterns according to the type of capillary wall involvement.

In MPGN with sub-endothelial deposits irregular granular deposits of IgG and C3 are found along the capillary walls sometimes accompanied by IgM, IgA or fibrin. In some cases, however, there is only a fixation of sera against C3.

In MPGN with dense deposits there is always a strong fixation of anti-C3 serum in granules in the mesangium and a weak pseudo-linear fixation on the capillary walls with the same serum.

Patients with MPGN usually have low levels of serum C3 which, in some patients, may become normal. In other patients, however, the C3 level is never low. We have shown that persistently low levels of C3 are mainly seen in MPGN with dense deposits (Habib et al, 1973d).

Most patients present with a nephrotic syndrome and haematuria although some may have persistent proteinuria as their only clinical finding. Azotaemia and hypertension may occur at the onset in some cases but usually resolve within a few weeks. Complete remissions, generally of short duration, may occur during the course of the disease.

In most patients, however, the nephropathy has a chronic course for several years with or without episodes of nephrotic syndrome but the prognosis of MPGN is severe since the mean annual mortality rate is approximately 6.4% during the first 10 years and the 50% statistical mortality occurs during the 11th year. Indicators of a poor prognosis include nephrotic syndrome (especially if it is persistent), renal insufficiency developing early in the course, and demonstration by renal biopsy of epithelial crescents in addition to the membranoproliferative pattern.

III. SECONDARY GLOMERULOPATHIES (Table III)

A nephropathy arising in a particular disease process may show various types of glomerular lesions. These are in many ways similar to most of the lesions seen in primary glomerular diseases but may have different patterns by immunofluorescence and a different prognosis. Renal biopsy in this group is therefore performed in order to evaluate the type and intensity of the glomerular involvement.

(1) Acute Post-streptococcal GN

When renal biopsy is performed early in the course of the disease, it reveals quite a uniform picture: diffuse mesangial proliferation with large numbers of
### TABLE III. Glomerular Lesions in Specific Diseases

1. *Acute Post-infectious GN* (streptococcal, etc)
   - Diffuse Mesangial Proliferative GN
   - Endo- and Extracapillary GN
   - Membranoproliferative GN

2. *Septicaemia* (sub-acute endocarditis, shunt nephritis, etc)
   - Segmental and Focal Proliferative GN
   - Endo- and Extracapillary GN
   - Membranoproliferative GN

3. *Systemic Diseases*
   - (a) Schönlein–Henoch
     - Segmental and Focal Proliferative GN
     - Diffuse Mesangial Proliferative GN
     - Endo- and Extracapillary GN
     - Membranoproliferative GN
   - (b) SLE
     - Segmental and Focal Proliferative GN
     - Extramembranous GN
     - Endo- and Extracapillary GN
     - Membranoproliferative GN
     - Lupus Nephritis (with hematoxyphil bodies)
   - (c) Periarteritis Nodosa
     - Segmental and Focal Proliferative GN
     - Endo- and Extracapillary GN
     - Membranoproliferative GN

4. *Mixed Essential IgG—IgM Cryoglobulinaemia*
   - Diffusive Endocapillary GN with Occlusive Thrombi

5. *Anti-GBM Nephritis and Goodpasture’s Syndrome*
   - Segmental and Focal Proliferative GN
   - Endo- and Extracapillary GN

Polymorphonuclear cells in the capillary lumens as well as ‘humps’ (small, scattered sub-epithelial deposits fixing anti-IgG and anti-C₃ sera). During the second month the polymorphonuclear cells and the humps disappear and only the mesangial proliferation remains. Subsequently, proliferation disappears and the histologic appearance returns to normal after an interval varying from two months to two years. However, a rapidly progressive course as well as progression to chronic disease may be observed in patients whose initial presentation is similar to that of the curable form. The histopathological patterns revealed by renal biopsy in these situations are then different: there may be either mesangial proliferation with focal or diffuse epithelial crescents (endo- and extracapillary GN) or membranoproliferative GN (with sub-endothelial or dense intra-membranous deposits. (Royer et al, 1973).
(2) Septicaemia

In sub-acute endocarditis, as well as in nephritis associated with infected ventriculo-atrial shunt, renal involvement may be very variable. The most common patterns observed by light microscopy are: segmental and focal GN, diffuse mesangial proliferative GN, endo- and extracapillary GN with a variable number of glomeruli affected with crescent formations and membranoproliferative GN. Immunofluorescent studies demonstrate the presence of immunoglobulins (predominantly IgM) and C₃ as well as C₁₉ and C₄ in two main localizations: peripheral along the capillary walls, and/or mesangial.


(3) Systemic Diseases

(a) Schönlein—Henoch syndrome Histologic study of renal biopsy material reveals that a great variety of glomerular lesions can occur in this syndrome. The main patterns observed by light microscopy are: segmental and focal proliferative GN, diffuse mesangial proliferative and endo- and extracapillary GN with variable glomerular involvement by crescent formations. Each type of glomerular involvement indicates a different clinical course. The pattern by immunofluorescence microscopy is quite uniform: there are always intense mesangial deposits of IgA and less often of IgG, C₃ and fibrinogen (Habib and Levy, 1972).

(b) Systemic lupus erythematosus (SLE) A great variety of patterns of glomerular involvement is revealed by light microscopy: extra-membranous GN, segmental and focal proliferative GN, endo- and extracapillary GN, and membranoproliferative GN. As already mentioned, in rare cases, there may be haematoxyphil bodies in the capillary lumens. This feature is pathognomonic for SLE. Karyorrhexis, wire-loops, foci and fibrinoid necrosis in the zones of hypercellularity and intraluminal thrombi are only suggestive of the diagnosis. Immunofluorescent studies reveal the nearly constant presence of immunoglobulin (predominantly IgG) and of C₃ as well as C₁₉ and C₄ in two main patterns: peripheral along the capillary walls, or mesangial. Granules of IgG, C₃ and C₁₉ are also found around the tubules. In this disease as well, each type of glomerular involvement indicates a different clinical course (Royer et al, 1973) although there may be transformation of the lesions with or without treatment.

(c) Periarteritis nodosa and necrotizing arteritis The patterns of glomerular involvement in the microscopic forms of PAN are not different from those observed in the other systemic diseases or in primary glomerulopathies and the clinical course usually correlates with the type of glomerular lesion revealed by renal biopsy. Segmental and focal GN, endo- and extracapillary GN membranoproliferative are the more common patterns observed. The presence of necrotizing arteriolar lesions
with a perivascular granuloma as well as the absence of IgG by immunofluorescence microscopy are highly suggestive of the diagnosis (Royer et al, 1973).

(4) Mixed Essential IgG–IgM Cryo-globulinemia and Monoclonal gammopathies

The lesions are characterized by proliferation of endocapillary cells accompanied by an infiltration of the glomeruli by numerous polymorphonuclear cells and by the presence of numerous large amorphous eosinophilic thrombi located on the endothelial side of the GBM. Their number varies from one glomerulus to another and even from one loop to another.

However, in some instances the patterns are less characteristic, and segmental and focal proliferative GN, or membranoproliferative GN may be observed. In all these cases, immunofluorescent studies demonstrate the presence of IgG and IgM in mixed cryo-globulinemia and either IgG and IgA in monoclonal gammopathies, associated with C3, as well as C1q and C4.

(5) Anti-GBM Nephritis and Goodpasture’s Syndrome

By light microscopy, the glomerular lesions are undistinguishable from the ones observed in primary glomerulopathies. Endo- and extracapillary GN is the more commonly observed pattern, but segmental and focal proliferative GN may also be revealed by renal biopsy. Anti-GBM nephritis can only be diagnosed by immunofluorescent microscopy which reveals linear deposits mainly composed of IgG along all the capillary walls (Wilson and Dixon, 1973) and by the detection of anti-GBM antibodies in the serum which may be revealed by indirect immunofluorescence applied to a normal kidney.

IV. HEREDITARY NEPHROPATHIES

Several hereditary disorders may be associated with glomerular involvement. The main ones are listed below.

(1) Alport’s syndrome In early stages glomeruli are almost normal by light microscopy. In later stages, the nephropathy is characterized by mild proliferative and sclerosing glomerular lesions very difficult to classify by light microscopy but in which electron microscopy has demonstrated specific lesions of the basement membrane: reduplication of the lamina densa with electron-dense round particules in the clear zones of the basement membrane (Hinglais et al, 1972).

(2) In Nail-Patella syndrome there is an irregular thickening of the glomerular basement membranes and electron microscope studies show the presence of collagen fibres in the thickened basement membrane as well as in the mesangial stalks (Ben Bassat et al, 1971).
(3) **Infantile diffuse mesangial sclerosis** is a lesion characterized by an increase in mesangial matrix in the absence of proliferation of mesangial cells, observed in some cases of congenital and infantile nephrotic syndrome (Habib and Bois, 1973).

(4) **Familial nephrotic syndrome** The glomerular lesions observed in this condition are identical to the ones observed in non-familial nephrosis: minimal lesion NS, or focal glomerular sclerosis. The patients however seem to be more often corticosteroid resistant than in the non-familial cases (Moncrieff et al, 1973).

(5) **Partial lipodystrophy** It seems to have been demonstrated that most cases of partial lipodystrophy with glomerular involvement have the same type of glomerulopathy, i.e. membranoproliferative GN with dense intramembranous deposits. These patients have always a persistently low C₃ even in the absence of glomerulonephritis (Hamza et al, 1970; Peters and Williams, 1974).

(6) **Amyloidosis of familial Mediterranean fever (FMF)** Familial Mediterranean fever is a disease commonly found in Sephardic Jews and among Mediterranean populations. Main cause of death is chronic renal failure due to amyloidosis. This is in no way different from primary amyloidosis.

(7) **Storage diseases** Glomerular involvement, with the presence of an abnormal metabolite in the epithelial cells of the tuft and convoluted proximal tubules which show a foamy cytoplasm, is frequent in storage diseases. The one best known to nephrologists is Fabry’s disease, where the metabolite is a ceramide trihexoside (Rosenmann and Aviram, 1973).

**Conclusion**

The concepts of acute, sub-acute and chronic glomerulonephritis, terms which should be used only by clinicians and exclusively to designate a type of evolution and not a type of glomerular involvement, have been replaced by new concepts based on clinico-pathologic entities and using descriptive terms.

The natural history of these entities should be well-known to all nephrologists not only in order to enable them to interpret the results of the renal biopsies performed in their patients but, above all, in order to enable them to take appropriate decisions about eventual therapies. The fact that most of these glomerular lesions may recur in the grafted kidney is one more reason for identifying the underlying disease.

**References**

Ben Bassat, M., Cohen, L and Rosenfeld, J (1971) *Archives of Pathology*, 92, 350
Open Discussion

M MALECK (Los Angeles) Would you please tell us what happens to the long-term follow-up of those 20% patients with focal glomerulosclerosis who are steroid sensitive.

HABIB In Kidney International, December 1973, I wrote an editorial, and the only Table that I included showed the difference between the sensitive and the resistant because it was so very striking. All the deaths and all children who developed chronic renal failure were in the steroid resistant group. Till now none of the steroid sensitives has developed chronic renal failure.

MALECK Yes, but my concern is that these patients may lapse.

HABIB Oh yes, they do lapse. But only three patients who had been steroid sensitive became steroid resistant later and even when they became steroid resistant, we were able to induce remissions with cyclophosphamide. So even when they become steroid resistant, they remained ‘good cases’.

R R SIEGEL (Kentucky) I wonder if you have seen anything of a type of mem-

branous glomerulonephritis with classical histology and classical immunofluorescence in which there is a rather rapid progression towards renal failure, perhaps in under five years. Our radiologists think some have renal vein thrombosis, and yet it may well be just slow renal blood flow.

HABIB Well, we have seen in fact two cases, but they were very special in that in one we found antitubular basement membrane antibody in his serum. By immunofluorescence deposits were found along the tubules. A similar case
occurred many years ago with much cellular infiltration in the interstitium. I know of two other cases, not children, who developed crescents around a typical membranous nephropathy. In our group we have never demonstrated renal vein thrombosis associated with membranous glomerulonephritis.

A KENNEDY (Glasgow) May I seek a little guidance about a matter which is of very great clinical importance to a nephrologist. The situation is the patient who has severe renal failure of recent onset, the biopsy shows extensive cellular proliferation with diffused crescents more than 80%. The prognosis is bad. You said that the prognosis is usually very bad, implying that it is not invariably very bad. Can you guide us as to which biopsies indicate possible recovery of function and which suggest the opposite.

HABIB That is a very naughty question because I think that we have not enough material by now to be sure of that, and I'll tell you why. I think that maybe we could have discussed that after Judy Whitworth's paper. I think that what appeared to be a very homogenous anatomico-clinical entity with more than 80% crescents on light microscopy and a rapidly progressive course, appeared later, with immunofluorescence, to be a very mixed group of diseases. In a typical membrane proliferative glomerulonephritis there is anti-GBM, there are humps and a lot of other pathologies. I don't think the prognosis is the same for all these patients. Perhaps what is important is not so much the crescent formation. In our experience, of the two patients we thought were going to die, one recovered and the other has a stable renal function, but both these children had 'humps'. Perhaps the presence of humps might indicate a good prognosis, but I am not sure about this yet.