Virchows Arch. A Path. Anat. and Histol. 362, 265—282 (1974)

Focal and Segmental Sclerosing Glomerulopathy (-nephritis)

A Pathomorphological Study

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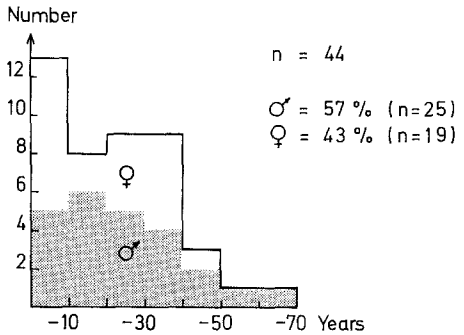
Received December 29, 1973

Summary. 10 out of 44 renal biopsy specimens obtained from patients with focal and segmental sclerosing glomerulopathy (-nephritis) (focal sclerosing lesion, sclerose s. hyalinose segmentaire et focale) were examined with the electron microscope and 11 by immunofluorescence microscopy. Particularly ultrastructural alterations are described in detail. A nephrotic syndrome was observed in 33 (75%), proteinuria in 11 (25%), and erythrocyturia in 21 (48%) patients. As the characteristic glomerular lesion a progressive increase in mesangial matrix material (sclerosis) is found which in the beginning concerns only few glomeruli and within these only a portion of the capillary tuft. The remaining glomeruli histologically show minimal changes. Electron microscopy, however, reveals these glomeruli as pathologically altered, too, indicating that the underlying mechanism is a diffuse one. Progression of sclerosing processes finally results in complete sclerosis of more and more capillary loops and glomeruli, respectively. Lightmicroscopically identifiable PAS-positive hyaline deposits were present in about 80%, thus representing an important diagnostic tool. Electron dense deposits, identical with typical immune deposits, are a regular finding in sclerosing areas and very rarely occur in minimally changed glomeruli, too. Immunofluorescence microscopy reveals a corresponding segmental deposition pattern of mostly IgM and C3 globulins. These findings are discussed with regard to an immune pathogenesis of the focal and segmental lesion.

Recently among the various types of glomerulonephritis particular interest was focussed on a special focal pattern of glomerular lesion which was referred to by various different terms ["focal sclerosing glomerulonephritis" (McGovern, 1964a, b), "focal sclerosing lesion" (Churg *et al.*, 1970), "focal glomerular sclerosis" (Duffy *et al.*, 1970), "hyalinose segmentaire et focale" (Habib, 1970), "segmental and focal hyalinosis" (Kincaid-Smith and Hobbs, 1972), "fokal-sklerosierende Glomerulopathie (-nephritis)" (Rumpelt and Thoenes, 1972, 1973; Thoenes, 1973), "focal sclerosing glomerulopathy with segmental hyalinosis" (Hyman and Burkholder, 1973)] all of them describing a focal and segmental type of sclerosing alteration (notice in the older literature: see Fahr, 1925). Clinically many cases are complicated by a steroid resistant nephrotic syndrome (Churg *et al.*, 1970). The course is slowly progressive and on an average 8 years after onset had proceeded to renal insufficiency (Hyman and Burkholder, 1973). Pathohistological, particularly electron microscopical and some supplementary immunofluorescence microscopical examinations were undertaken for elucidation of following problems: Which are the characteristic pathohistological and ultrastructural features of focal and segmental sclerosing glomerulopathy (-nephritis) (f.s.s.g.), are there indications for participation of minimally changed glomeruli in the underlying processes, and are there indications concerning pathogenesis.



nephrotic syndrome (proteinuria > 1 g/m²/die)	75% ($n=33$)
proteinuria (< 1 g/m²/die)	25% ($n=11$)
erythrocyturia	48% ($n=21$)
in nephrotic syndrome	49% ($n=16$)
in proteinuria	45% ($n=5$)

Fig. 1. Age and sex distribution at time of biopsy. Some clinical data are added

Materials and Methods

10 out of 44 percutaneously obtained renal biopsies[1] from patients affected with f.s.s.g. were studied with the electron microscope and 11 by immunofluorescence microscopy (by courtesy of Priv.-Doz. Dr. Seelig, Heidelberg; Dr. G. H. Thoenes, München; Prof. Dr. Bläker, Hamburg; and Dr. Schulte-Wissermann, Mainz). The diagnosis was stated when light microscopical examination of paraffin sections revealed a distinctly segmental sclerosis in at least one glomerulus. The age- and sex distribution of all patients as well as some important clinical data are summarized in Fig. 1.

Light microscopy: Biopsy specimens were fixed in 4% formalin solution and embedded in paraffin. Stains: H.-E., PAS, Pearse, Goldner's trichrome, Jones-chromotrop R (Ehrenreich and Espinosa, 1971).

Electron microscopy: Small tissue blocks were fixed in phosphate buffered (pH 7,2) 3% glutaraldehyde solution and embedded in Epon 812. Ultrathin sections were stained with uranyl acetate and lead citrate and examined with a Philips 300 electron microscope.

Terminology

The terms focal and segmental are used to designate the distribution of glomerular lesions: *focal* refers to those lesions which affect only some glomeruli within the total glomerular population; *segmental* refers to those lesions which affect only a portion of a single glomerulus. The terms sclerosis and hyaline deposits are used to designate the nature of a special glomerular lesion: *sclerosis* is used when a predominant increase in mesangial matrix material (PAS-positive, argyrophilic) is diagnosed. Defined depositions of homogenous, PAS-positive but argyrophobic material visible with the light microscope are denoted as *hyaline deposits* (synonyma: hyalinosis, fibrinoid deposits, insudative lesion).

1 For placing biopsy specimens and clinical data to our disposal we owe many thanks to Prof. Dr. Bläker (Universitäts-Kinderklinik Hamburg), Priv. Doz. Dr. Gekle (Universitäts-Kinderklinik Würzburg), Prof. Dr. Geßler, Dr. Schulz (4. Medizinische Klinik Nürnberg), Prof. Dr. Klaus (Medizinische Poliklinik der Universität Marburg), Prof. Dr. Olbing (Kinderklinik Klinikum Essen), Priv. Doz. Dr. Ritz, Priv. Doz. Dr. Andrassy (Ludolf-Krehl-Klinik Heidelberg), Prof. Dr. Schärer (Universitäts-Kinderklinik Heidelberg), Prof. Dr. Straub, Dr. Schulte-Wissermann (Universitäts-Kinderklinik Mainz).

Results

Light Microscopy

The pathohistological picture in f.s.s.g. is characterized by the direct juxtaposition of minimally changed and segmentally as well as totally sclerosed glomeruli (Fig. 2a). Tubular and interstitial alterations, which additionally develop, are of no diagnostic significance.

Segmentally sclerosed glomeruli are shown in Fig. 2c–e. Only a portion of the capillary tuft is affected, while the remaining loops show minimal changes. Some mesangial regions are strongly thickened and contain large amounts of PAS-positive, argyrophilic substances, which progressing accumulation leads to a compression of the adhering capillary loops until they disappear, clearing the way for large masses of mesangial material. Initially, sclerosing areas contain moderate numbers of cells, later they become distinctly hypocellular.

Another important phenomenon in f.s.s.g. which attracks attention is the presence of hyaline deposits. These occur in about 80% of all cases and seem to be more frequent when a nephrotic syndrome has established (85%) than in cases with mere proteinuria (64%). Hyaline deposits (Figs. 2d, e; 9) stain with PAS, but in contrary to sclerosing areas do not accept silver salts.

Most hyaline deposits are situated in the sclerosing areas itself, or in associated capillaries. Here crescent-shaped and globular forms occur compressing or obliterating the lumina. Outside the glomerular tufts identical deposits may develop in Bowman's capsules (Fig. 10a) and in the walls of arterioles, too.

Right from the beginning on sclerosing loops tend to adhere to Bowman's capsule forming local crescents with defined capsular fibrosis (Fig. 2c).

Previously intraglomerular foam cells were described to be a frequent finding in f.s.s.g. by Hyman and Burkholder (1973). In our biopsy material, however, these cells were completely absent.

When progression of sclerosing alterations finally results in a complete obliteration, i.e. a total sclerosis of a glomerulus, the attached tubular apparatus becomes atrophic (Fig. 2a). Some other obliterated glomeruli may be seen to be in the fibrosed condition, their capillary tufts are atrophic and their urinary spaces filled with densely arranged fibers.

In two cases, obviously initial stages of disease we happened to find only one typically altered glomerulus, each situated near the renal medulla, though 10 and 12 glomeruli were obtained, respectively.

In minimally changed glomeruli with slightly broadened mesangial regions (Fig. 2b), here and there in a minor part of a lobule a limited accumulation of sclerotic material may be noticed, the loop may then already be adherent to the capsule (Fig. 2c). Seldom single capillary loops are found to be obturated by hyaline masses lightmicroscopically identical with hyaline deposits.

Besides minimally changed and segmentally sclerosing glomeruli, glomeruli can be found which show a more generalized but still moderate mesangial thickening. The number of mesangial cells in these glomeruli is roughly not or only slightly increased. Glomeruli of normal histological appearance are a rather seldom finding.

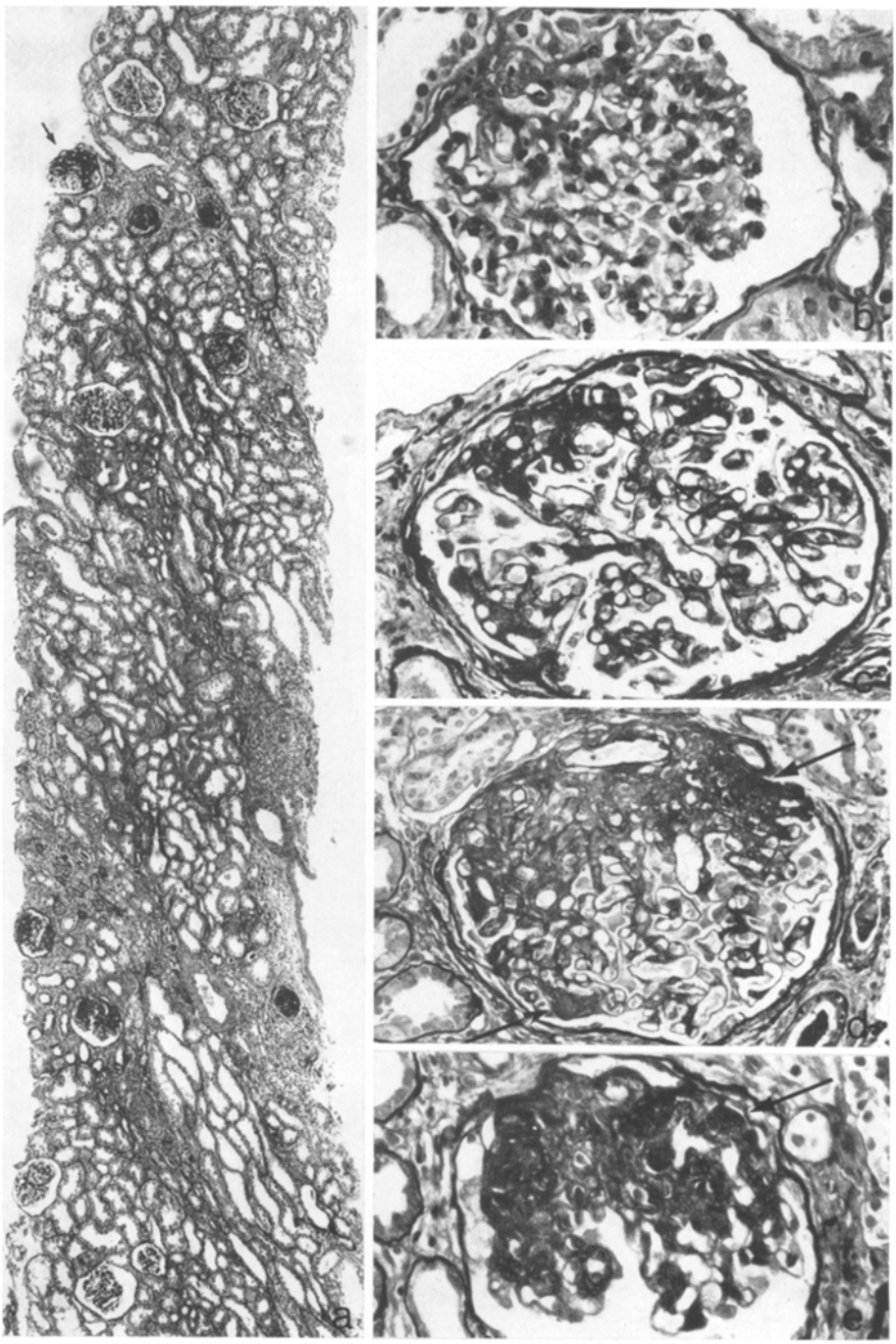


Fig. 2a—e

Electron Microscopy

In *minimally changed glomeruli* the foot processes of epithelial cells are usually transformed into large cytoplasmic plates (Fig. 3a, b). In other cases, presumably depending on the degree of actual proteinuria, they may be partly preserved. An epithelial microvillus formation as pronounced as in Fig. 2a was present in three cases, only, usually it was less marked.

High power electron micrographs reveal that large segments of the basement membranes are distinctly altered, too. The lamina densa, in fact, seems to be essentially normal in thickness (150–300 nm) and texture, but at its endothelial aspect loosely arranged "mesangial matrix-like" material is added in varying quantities (Fig. 3b). In favourable sections this material was observed to be in direct continuity with the similarly structured mesangium matrix (Fig. 3b).

The matrix substance, as usual enclosing filaments 50–80–100 Å in diameter (Fig. 3b), is slightly but distinctly increased in amount. The mesangial cells contain nuclei, the envelopes of which often show a deep indentation. The cytoplasm is rich in organelles, especially rough endoplasmic reticulum (RER) and free ribosomes are increased in amount. Mesangial cells possess short cytoplasmic branches which penetrate into the surrounding matrix.

Endothelial cells are similarly rich in organelles. Here RER and free ribosomes and particularly large Golgi apparatus are prominent. Distal sacculi as well as coated visicles bulging off from them contain electron dense grana (Fig. 4b). The endothelial cell plates covering the basement membranes, are fenestrated as usual. In three cases (Fig. 4a) they contained "tubular aggregates" (Baringer and Swoveland, 1972; Bariety *et al.*, 1973). Only rarely we happened to find subepithelial and subendothelial electron dense deposits (Figs. 5, 8c, d), the latter situated within the subendothelial "mesangium-matrix-like" material.

Sclerosing capillary loops (Figs. 5–8) are first of all characterized by an extensive accumulation of mesangial matrix substances. During early stages mesangial cells are voluminous, their RER is increased in amount and partly arranged in organized stacks (Fig. 4c), the cytoplasmic processes are long and ramified. When sclerosis has reached a more severe stage, myelin figures and lipid droplets occur in the cytoplasm. Cells, situated in the center of sclerosing areas finally become necrotic, thus large areas gain a hypocellular appearance. Additionally different types of fibers and various structures which presumably originate in debris material of perished mesangial cells are enclosed, indicating a possible qualitative alteration of the mesangial matrix, too.

Fig. 2a—e. Focal and segmental sclerosing glomerulopathy (-nephritis). Survey micrograph of cortex region of a renal biopsy specimen demonstrating the typical histological picture of f.s.s.g. Minimally changed as well as segmentally (←) and totally sclerosed glomeruli are present. Atrophic tubuli are enclosed in fibrotic areas which show dense infiltration with mononuclear cells. Pearse, × 55. (b) Minimally changed glomerulus (compare with Fig. 3a). Pearse, × 340. (c) Initial stage of glomerular sclerosis. Only two adjacent capillary loops are affected and already adherent to the capsule in an otherwise minimally changed glomerulus. Pearse, × 340. (d) Segmentally sclerosed glomerulus. Only few cells are visible within large amounts of PAS-positive matrix masses. Note the presence of hyaline deposits (←). PAS, × 330. (e) Largely sclerosed glomerulus with enclosed hyaline deposits (←). There are only few open capillary lumina left. Pearse, × 300

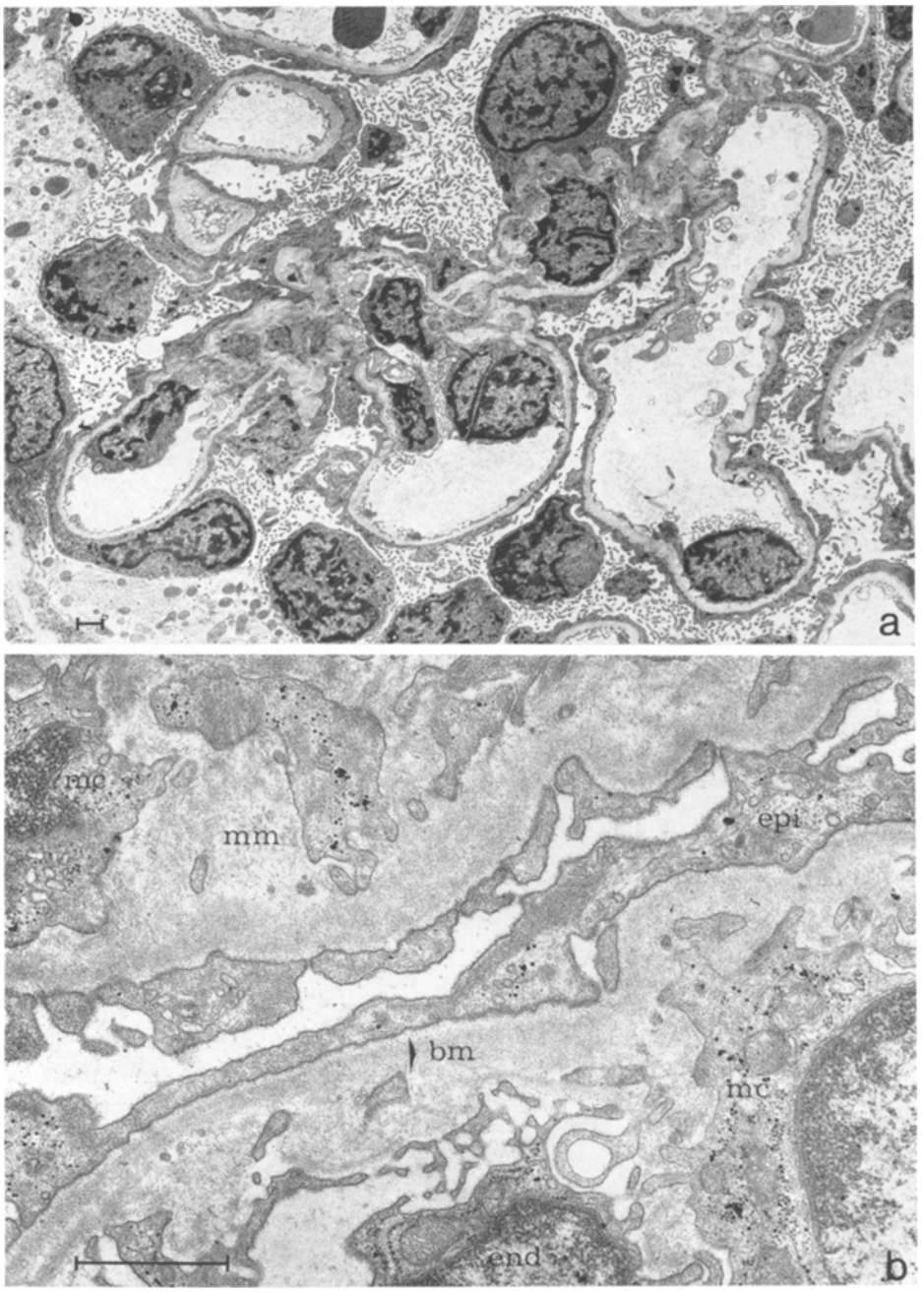


Fig. 3 a and b. Minimally changed glomeruli. (a) Low power electron micrograph showing the foot processes of podocytes replaced by large cytoplasmic plates (so-called "foot-process fusion"). Mesangial matrix is not visibly increased in this case. The urinary space is filled with numerous epithelial microvilli. × 3000. (b) Portion of a capillary wall showing finely filamentous material deposited between basement membrane and endothelial cell, which material is in direct connection with and ultrastructurally similar to mesangial matrix material. × 20500.
Abbreviations for all figures: *bm* basement membrane, *end* endothelial cell, *epi* epithelial cell, *mc* mesangial cell, *mm* mesangial matrix

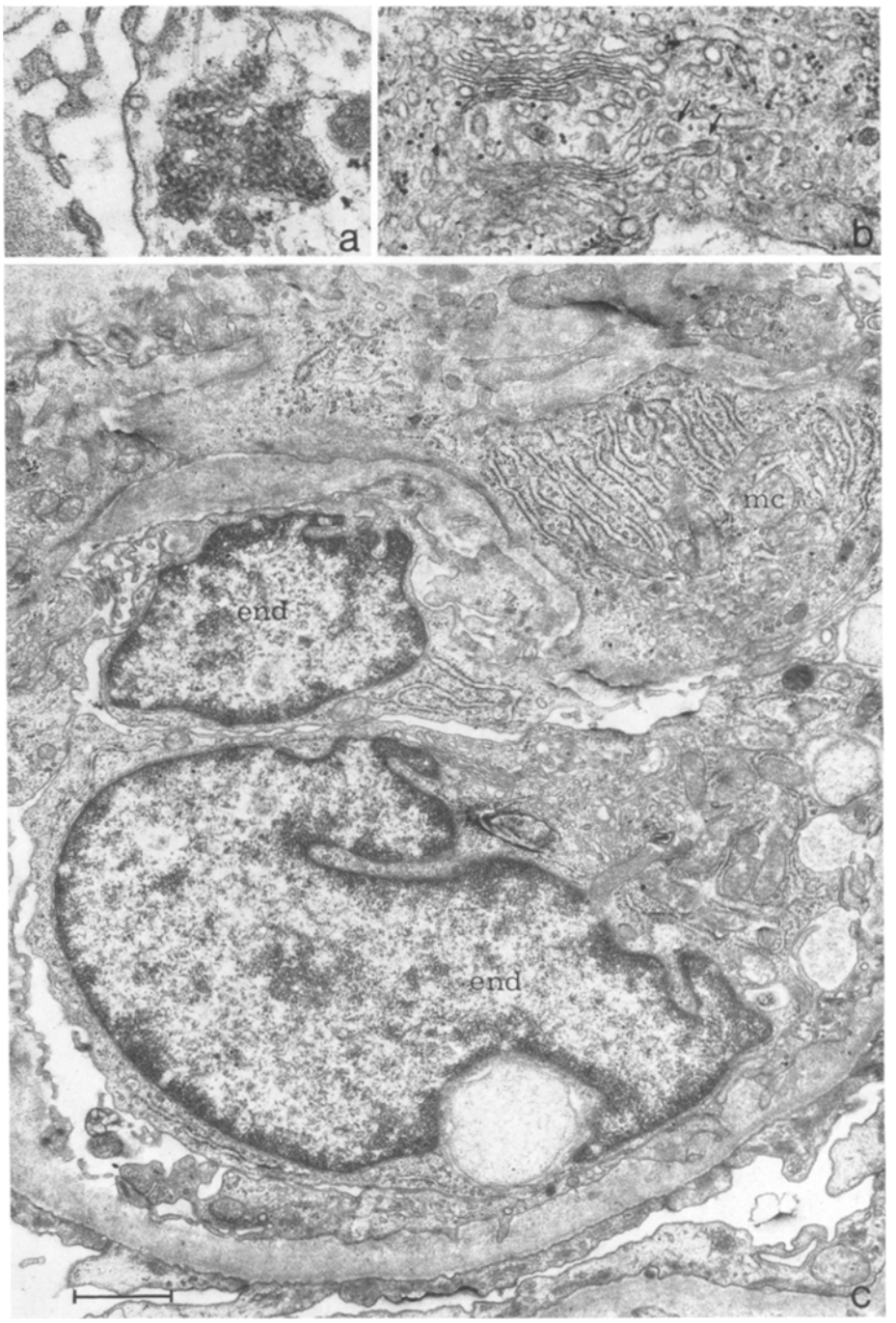


Fig. 4a—c. Segmentally sclerosed glomeruli. (a) Tubular aggregates within an endothelial cell. × 32000. (b) Portion of a Golgi apparatus of an endothelial cell containing grana of medium electron density in its distal sacculi and vesicles (←). × 37000. (c) Capillary loop adjacent to a sclerosing area. Voluminous endothelial cells narrow the lumen. Both endothelial as well as mesangial cells are strongly activated. Note the organized RER within the mesangial cell and the large Golgi apparatus in the endothelial cell. × 12800

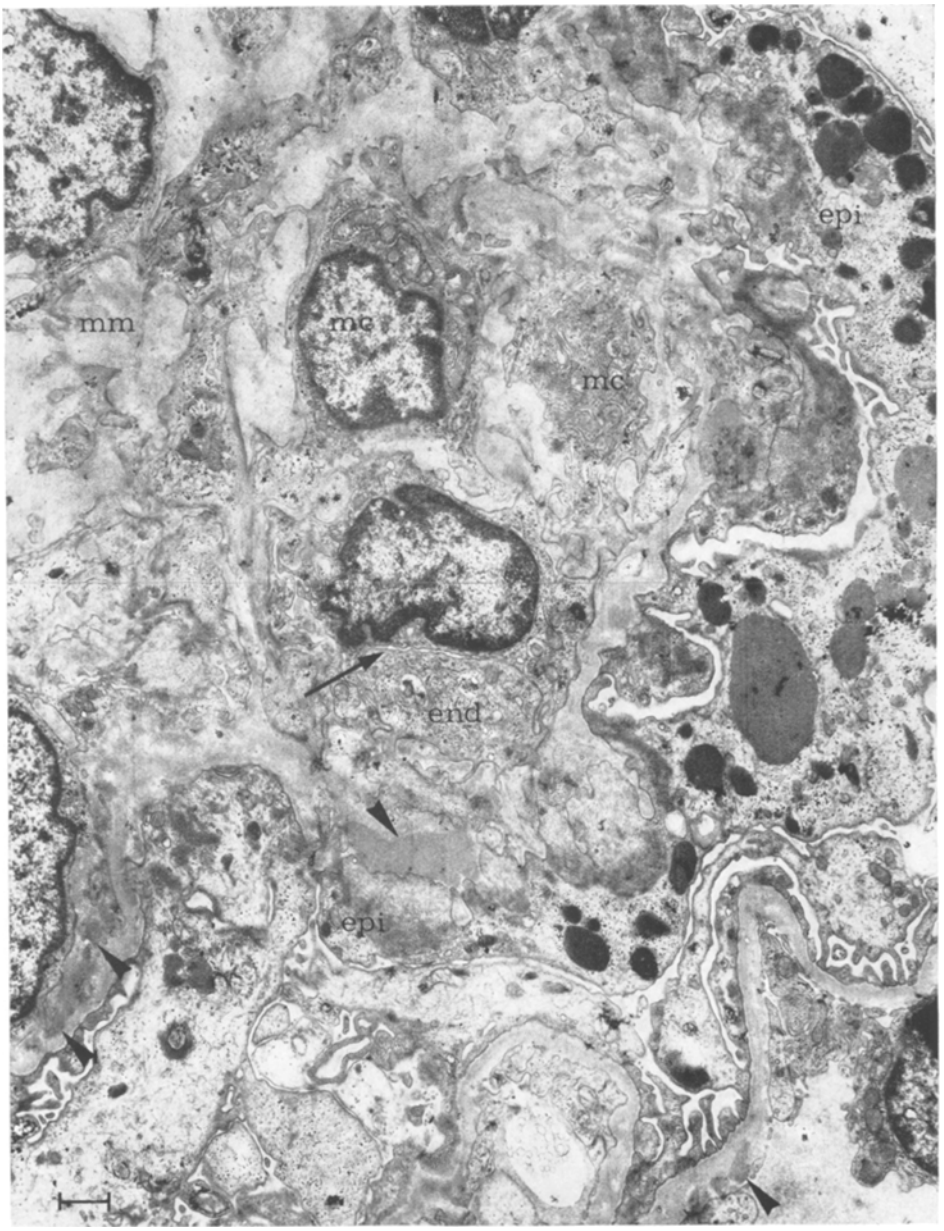


Fig. 5. Segmentally sclerosed glomerulus. Capillary loop adhering to a sclerosed area. Large mesangial matrix masses and mesangial cells have invaded the loop compressing the lumen to a cleft-shaped residual space (big arrow). The endocapillary (endothelial and mesangial) cells are rich in organelles. The epithelial cells contain electron dense proteinaceous droplets. Immediately adjacent the sclerosing loop a portion of a minimally changed loop can be seen. Electron dense deposits (arrow heads) are present in mesangial, subepithelial, and subendothelial positions. × 6600

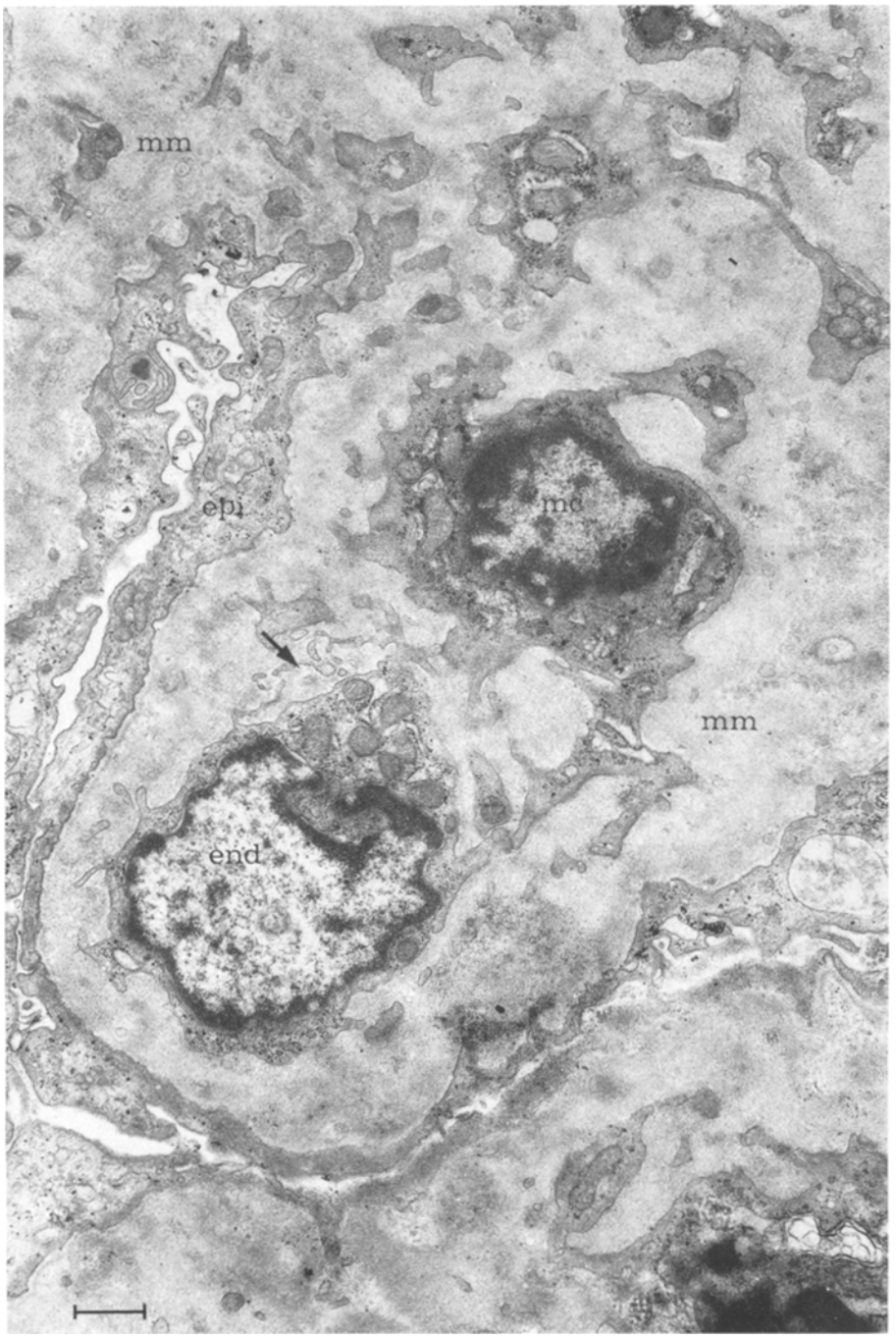


Fig. 6. Segmentally sclerosed glomerulus. Large amounts of mesangial matrix masses together with a mesangial cell have invaded the capillary loop, the lumen of which (←) is nearly completely vanished. Endothelial and mesangial cells are no longer in an activated condition. × 9500

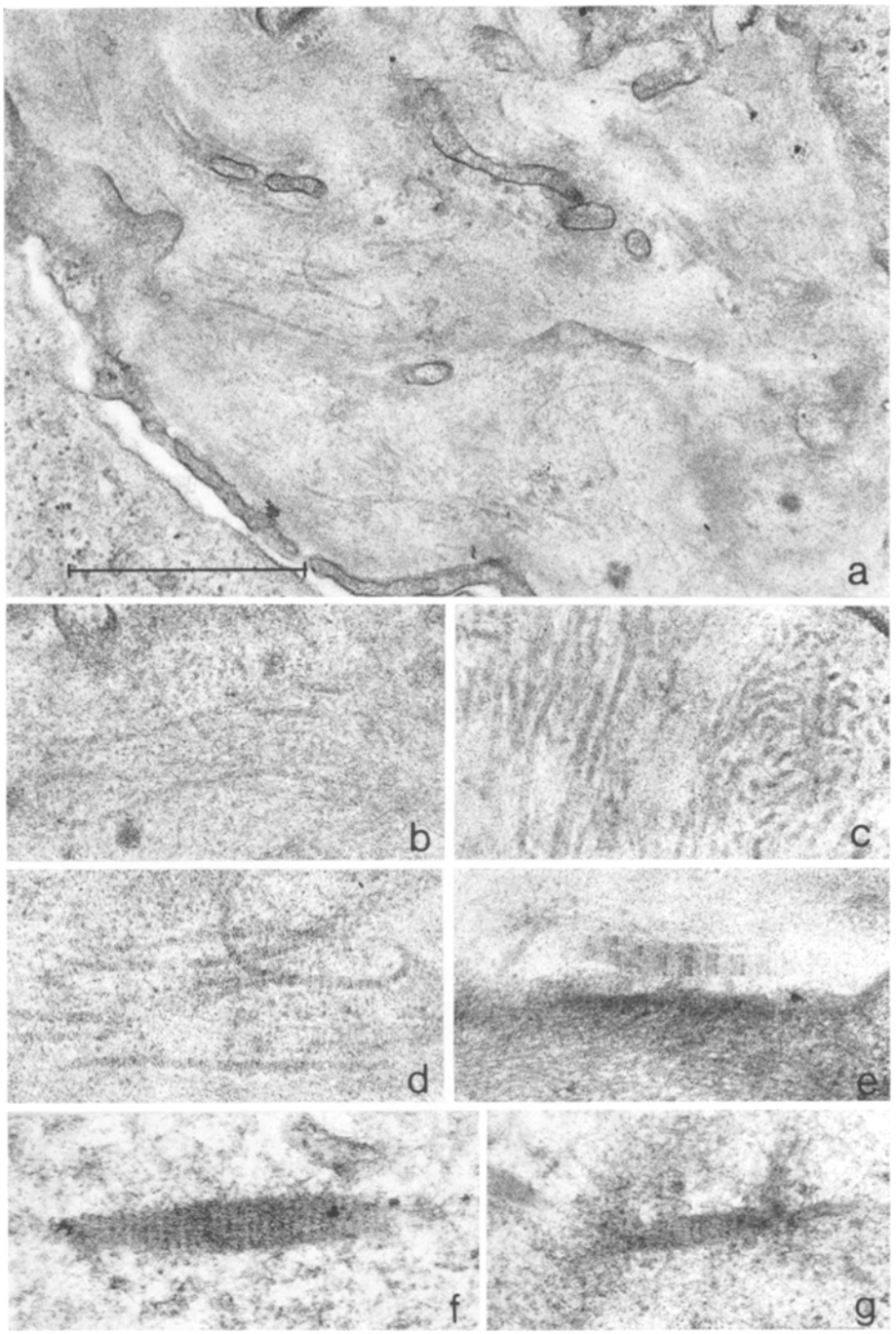


Fig. 7 a—g

In detail, besides those fibers already present in minimally changed glomeruli, fibers have developed about 140, 240, and 330 Å in diameter (Fig. 7). The latter ones as well as rarely detected fibers measuring 500 Å and up to 600 Å show periodic cross striations.

Preferentially in sites of low matrix density there were regularly found: a) Groups of roundish particles about 360 Å in diameter (see Bariety and Callard, 1972), b) Groups of vesicles 800 Å in diameter, with a central material condensation, c) Curious string-like structures resembling a railtrack pattern with cross striation and bordering lines (see Stekhoven and van Haelst, 1973). Sometimes lipid droplets were seen directly situated in the matrix substance.

Expanding mesangial masses invading the space between basement membrane and endothelial cell gradually compress the adhering capillaries, the endothelial cells of which subsequently loose large portions of their fenestrated cytoplasmic plates. The perinuclear cytoplasm develops short cytoplasmic branches which penetrate into the adjacent mesangial matrix. The former capillary lumen becomes cleff-shaped and finally vanishes. Thereafter it is no longer possible to differentiate endothelial from mesangial cells.

Epithelial cells, on the other hand, when enclosed by matrix masses become necrotic. Gusset-shaped electron lucent areas filled with cytoplasmic debris and fibers of various diameters mark their former sites.

Electron dense deposits (Fig. 8) were found in greater numbers nearly in each sclerosing (mesangial) area. They show a finely granular structure (Fig. 8b), are of variable size and shape and, when tightly arranged show a tendence to confluence. Similar deposits could rarely be found in minimally changed glomeruli, too, in subendothelial (Fig. 8c) and subepithelial (Fig. 8d) positions. Furthermore single capillary loops showed segments with linear deposition of electron dense material within the basement membrane itself (Fig. 8e).

Hyaline deposits (Fig. 9) are composed of a homogenous material of medium electron density which in higher magnifications appears to be more coarsely granular than the above mentioned electron dense deposits (Fig. 9b). Hyaline deposits often contain lipid droplets (Fig. 9a, d). Uncommon myelin-like membrane fragments were seen one time only (Fig. 9c). Hyaline deposits occur in the mesangial matrix, in Bowman's capsule, and in capillary loops, where they are situated between endothelium and basement membrane.

Intracapillary fibrin aggregates were found in one case (Fig. 7f), in another a basement membrane segment showed an infiltration with fibrin-like material (Fig. 7g).

Fig. 7a—g. Fiber formation within sclerosing mesangial matrix material. (a) Survey picture of a matrix area with relatively intense fiber formation. The matrix material shows an irregular electron density. × 32000. (b) Matrix fibers 160 Å in diameter. × 61500. (c) Matrix fibers 250 Å in diameter. × 61500. (d) Matrix fibers 320 Å in diameter showing cross striation. × 61500. (e) Matrix fiber 650 Å in diameter. Periodicity of cross striation 660 Å. × 61500. (f) Fibrin strand (periodicity 220 Å) within a capillary lumen. × 61500. (g) Fibrin-like strand within a glomerular basement membrane segment (periodicity 220 Å). × 61500

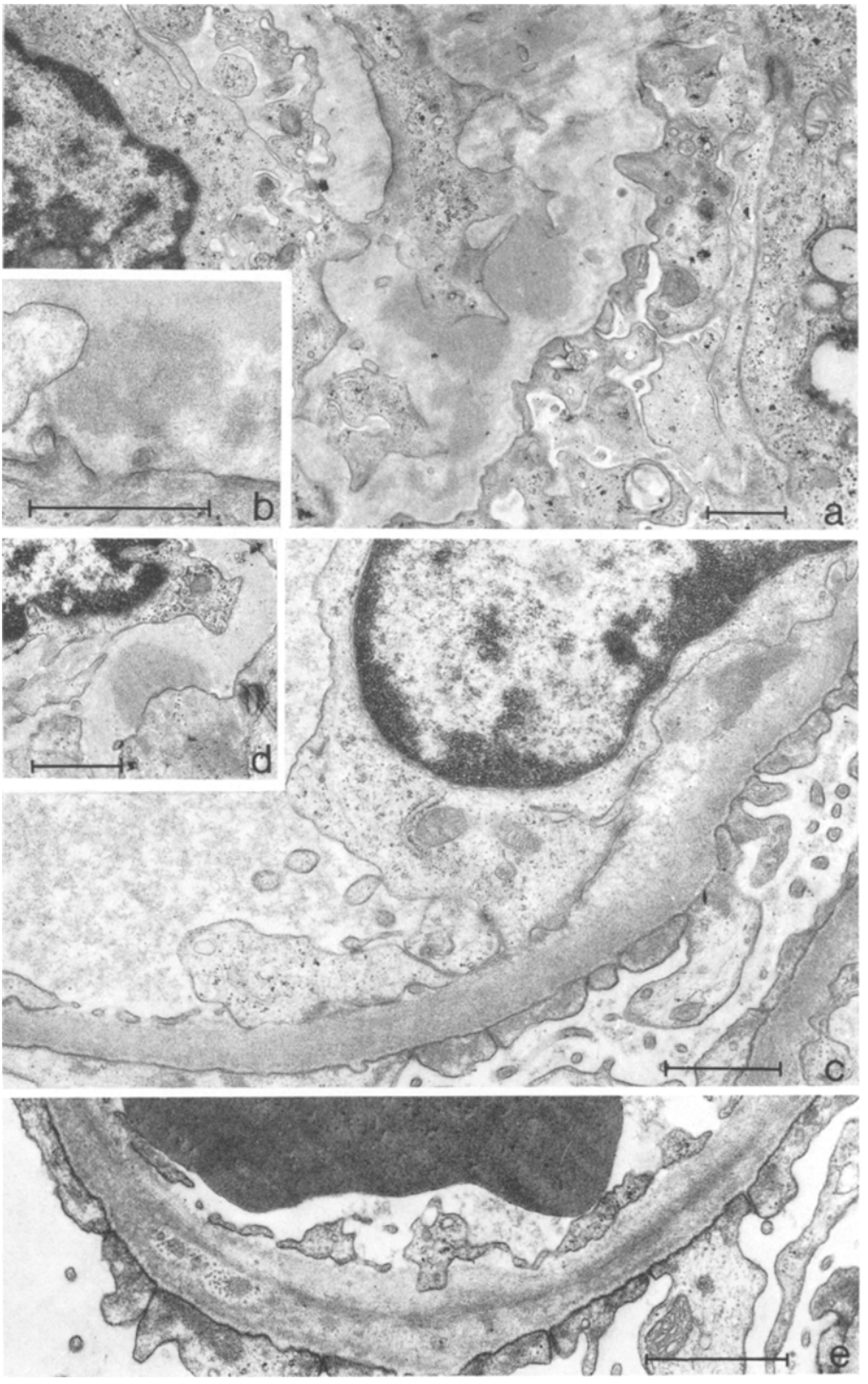


Fig. 8a—e

Completely sclerosed glomeruli in principle present the same alterations as sclerosing areas of advanced stages. Immense masses of mesangial matrix dominate the picture. Degenerating cells, some fibers, electron dense and hyaline deposits, and cell debris are the further compounds.

Immunofluorescence Microscopy

Immunofluorescence microscopical examinations were carried out in 11 cases [by courtesy of Priv.-Doz. Dr. Seelig (Heidelberg), Dr. G. H. Thoenes (München), Prof. Dr. Bläker (Hamburg), and Dr. Schulte-Wissermann (Mainz)]. While one case was completely lacking any immunoglobuline and complement deposition, in all the other 10 cases IgM could be demonstrated, mostly in a segmental, partly diffuse, partly granular pattern within the mesangial regions and along the basement membranes. IgG was additionally identified in 6, IgA in 2 cases. Complement factors (C3, C4) were present in all cases except one. One time fibrin was found to be positive.

Discussion

The pathohistological diagnosis of f.s.s.g. is based, first, on the characteristic focal and segmental pattern of glomerular lesion and, secondly, on the special nature of this lesion, i.e. the glomerular sclerosis. Referring to the definition given above the term glomerular sclerosis signifies an accumulation of mesangial matrix substances without or with only moderate mesangial cell proliferation. In stages of advanced sclerosis various types of fibers additionally appear in the matrix. The PAS-positive matrix is, in contrary to basement membrane material (Gekle and Merker, 1966; Kefalides, 1972), of unknown composition. The appearance of fibers, among them single collagen fibers, in sclerosing conditions, however, indicate, that collagen constituents, perhaps in form of tropocollagen molecules may be present in normal conditions, too. In sclerosis their increase or altered arrangement may induce fiber formation, which in f.s.s.g. however, never exceeds a slight extent.

Electron microscopical examination of minimally changed glomeruli reveals them as distinctly altered (Rumpelt and Thoenes, 1972). It therefore must be assumed that functional alterations causing nephrotic syndrome constellation (Churg *et al.*, 1970; Schärer *et al.*, 1973; Reichel *et al.*, 1973; Hyman and Burkholder, 1973) concern all, sclerosing as well as minimally changed glomeruli. The underlying process is obviously a diffuse one, causing a diffuse damage of the total glomerular apparatus. Sclerosing areas are therefore to interpret as sites of an accentuation of a diffuse process.

Fig. 8a—e. Electron dense deposits of the immune deposit type in f.s.s.g. (a) Numerous patch deposits of irregular size and shape within sclerosing mesangial area. × 11200. (b) Higher magnification of an electron dense mesangial deposit demonstrating its finely granular structure (compare with Fig. 9b). × 25000. (c, d) Minimally changed glomeruli c. Subendothelial deposit within the finely filamentous "mesangium matrix-like" material. d. Subepithelial deposit. × 11200. (e) Portion of a capillary loop out of a segmental sclerosed glomerulus. A streak of electron dense material is deposited within the basement membrane. × 20000

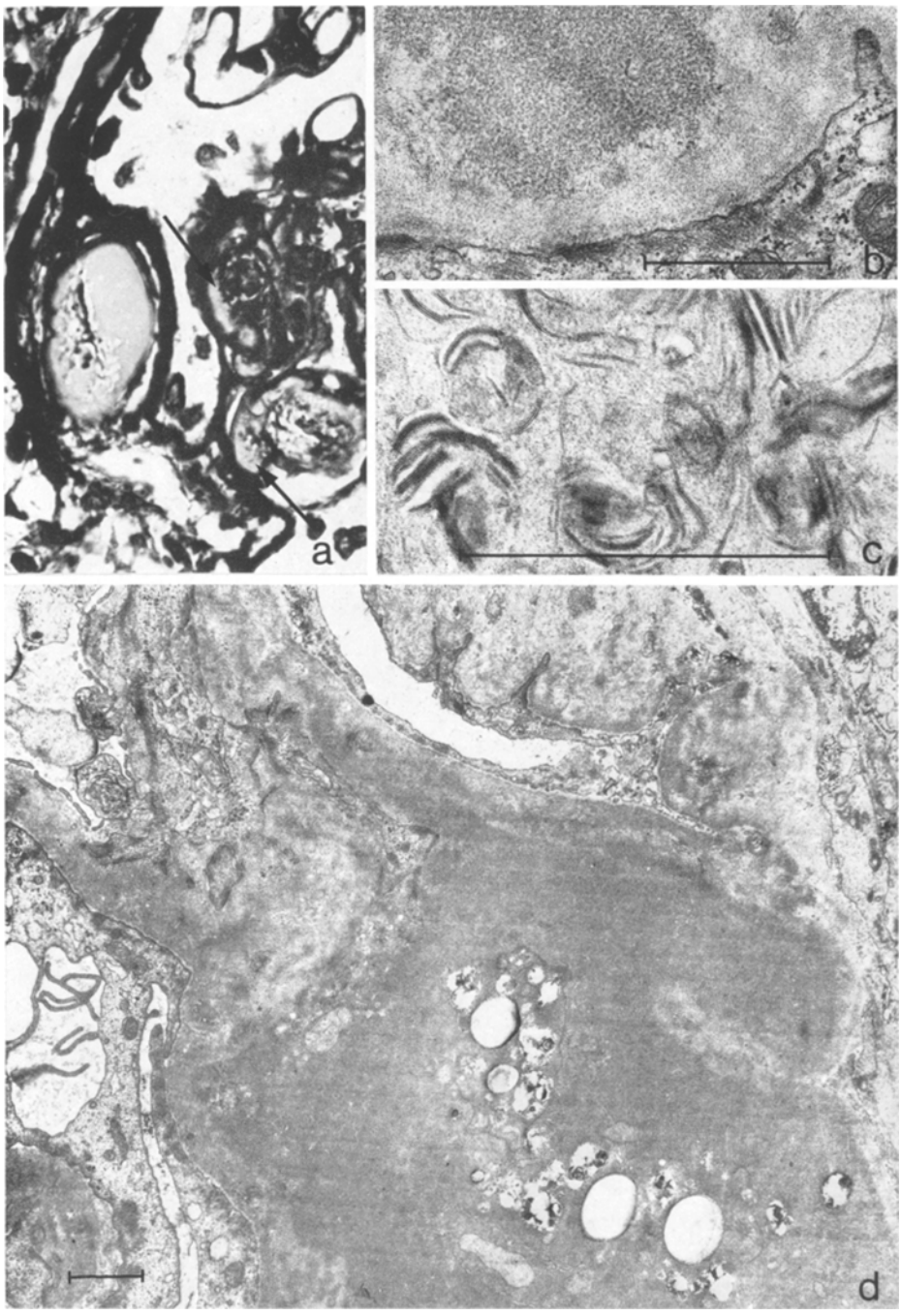


Fig. 9a—d

Both mesangial and endothelial cells are distinctly activated. Particularly those organelles involved in protein synthesis are increased in amount, in mesangial cells probably indicating a thorough matrix production. In endothelial cells the increased RER and the grana formation in the Golgi apparatus suggest a secretion activity, too, the product of which perhaps is represented in the subendothelial "mesangium matrix-like" material. Beyond that endothelial in contrast to epithelial cells are obviously capable to survive an enclosure by matrix masses for a long time. This may point to a relatively close cytogenetical relationship of these both endocapillary cell types suggesting that a secretion of matrix like substances might be not impossible for endothelial cells, too.

The presence of hyaline deposits in about 80% makes them a characteristic feature of diagnostic value. Habib and Gubler (1971) think hyaline deposits such an essential constituent of this special glomerular lesion that they prefer the term "hyalinose segmentaire et focale". Though identical intraglomerular hyaline deposits were reported to occur in diabetic glomerulosclerosis (Salinas-Madrigal *et al.*, 1970) and membranoproliferative glomerulonephritis (own observations) they certainly are of no specifity for f.s.s.g. As recently could be demonstrated with aid of immunofluorescence microscopy similar deposits in renal vein thrombosis in man (Cornog *et al.*, 1970) and in cortisone-induced renal lesions in rabbits (Moran *et al.*, 1962) contain fibrin/fibrinogen, complement factors and immunoglobulins. Habib and Kleinknecht (1971) describe them as "fibrinoid deposits". In our material among the 11 cases examined there was found one time only a granular deposition of fibrinogen along the basement membrane, all the other biopsies though containing hyaline deposits were fibrin/fibrinogen negative, on account of which we prefer the descriptive term "hyaline deposits" as far as this type of deposits is concerned in f.s.s.g.

In rabbits similar deposits were observed to develop during cortisone treatment (Bencosme *et al.*, 1958; Moran *et al.*, 1962; Wilson *et al.*, 1962; Bouissou *et al.*, 1966), because of which it must be taken into consideration that hyaline deposits in f.s.s.g. might represent an iatrogenically induced lesion. Hyaline deposits do, however, never occur in cortisone treated minimal changes lesion in man, thus cortisone application alone cannot be sufficient to produce the hyaline lesion.

Sometimes it may happen that in cases of actual f.s.s.g. exclusively minimally changed glomeruli were obtained. Then it may be difficult or even impossible not to pass the exact diagnosis. Minor lesions as for instance small sclerosing, adherent

Fig. 9a—d. Hyaline deposits in f.s.s.g. (a) Huge globular hyaline deposit within Bowman's capsule containing numerous vacuoles. Hyalin material is deposited at the inner side of two capillary walls, too (←). Jones-Chromotrop R, × 900. (b) Portion of a hyaline deposit demonstrating its coarsely granular ultrastructure (compare with Fig. 8b). × 25000. (c) Myelin-like membranous structures enclosed in a hyaline deposit. Periodicity 250 Å. × 50200. (d) Mesangial region with hyalin deposit enclosing electron-lucent (lipid?) vacuoles. × 9000

foci (Fig. 2c) may then indicate a f.s.s.g., particularly when connected with steroid resistance. According to Churg *et al.* (1970, 10 out of 12 cases), Habib and Gubler (1971, 63%), and Schärer *et al.* (1973, 23 out of 24 cases) steroid application in f.s.s.g. brings about no or only a partial effect on proteinuria. Steroid resistant cases with "minimal changes lesion" therefore are suspicious of an actual f.s.s.g.

Causal Pathogenesis

The finding of immunoglobulins, complement, and electron dense deposits in various glomerular diseases has been widely accepted as evidence that immune mechanisms may be operative in their pathogenesis (Dixon, 1968). This conception might prove right in f.s.s.g., too. Recent findings, however, cast some doubt on the general validity of such a statement (Hamburger *et al.*, 1973; Hoyer *et al.*, 1972). Therefore, it must be taken into account that at least in some cases a deposition of immunoglobulins occurs as a secondary step superimposing a lesion which primarily is a not immunological one. Thus it attracks attention that electron dense immune deposits (Churg and Grishman, 1972) which correspond to the immunofluorescence microscopical IgM/IgG pattern (compare also Habib et Gubler, 1971; Morel-Maroger *et al.*, 1972) were almost quantitatively found in already severely altered regions. Even when found in minimally changed glomeruli electron dense deposits were enclosed in the subendothelial "mesangial matrix-like" material. These observations seem to be compatible with the assumption, that circulating immunoglobulins/complexes are trapped in already altered matrix masses, where they then might cause a local stimulation and acceleration of the sclerosing process.

Because sclerosing alterations are already present in minimally changed glomeruli which in most cases show a negative immunofluorescence, sclerosis itself and not immunoglobulin deposition must be assumed to be the preceding lesion.

Finally it remains to explain why sclerosis starts in juxtamedullary glomeruli as formerly reported by Rich (1957) and Habib and Kleinknecht (1971) and now was confirmed by own observations. Nephrons in the outer and inner renal cortex are known to differ in structure, function (Horster and Thurau, 1968) and vascular supply (Barger and Herd, 1971). In the dog Thornburn *et al.* (1963) could demonstrate the blood flow rate in juxtamedullary cortex to reach only one third of that of the outer cortex. Perhaps it are these physiological differences which may facilitate a development of sclerosis and a preferential deposition of circulating immunoglobulins/complexes in juxtamedullary glomeruli.

This conception was advanced by Dr. K. Thurau on the 1. Symposion of Nephrology Hannover 1973.

The authors are greatly indebted to Mrs. B. Agricola and Miss L. Meyer for their excellent technical assistance.

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