Virchows Arch. Abt. A Path. Anat. 359, 185—200 (1973)

Glomerulonephritis Associated with (Infected) Ventriculo-Atrial Shunt*

Clinical and Morphological Findings

Werner Wegmann and Ernst P. Leumann

Department of Pathology, University Hospital
and Department of Pediatrics, University Children's Hospital
Zurich, Switzerland

Received October 11, 1972

Summary. Diffuse glomerulonephritis with the nephrotic syndrome was observed in two patients aged 3 years 8 months and 27 years, both of whom had ventriculo-atrial shunts. Removal of the shunts resulted in marked improvement in the first and complete recovery in the second patient. Serum β1C-globulin concentrations were initially low and returned to normal values. Cultures taken from cerebrospinal fluid and valve grew Staphylococcus albus in the pediatric patient and were negative in the adult patient. Initial renal biopsies obtained immediately before shunt removal showed diffuse intra- and extracapillary glomerulonephritis type III (crescent formation in over 90 percent of the glomeruli) in the first patient, and diffuse intracapillary proliferative and exudative glomerulonephritis in the second patient. Repeat biopsies were performed, on the first patient 22 months, and on the second patient 7 months after shunt removal. In the first patient, half of the glomeruli were sclerosed, and the others exhibited slight mesangial proliferation with some capsular adhesions. The repeat renal biopsy from the adult patient showed mesangial proliferation with lobulation. Immunofluorescence studies in both patients revealed positive staining in a coarsely granular pattern against IgG, IgM, and β1C globulin. On electron microscopy, subendothelial deposits were still visible in the second biopsies of both patients. Glomerulonephritis associated with infected ventriculo-atrial shunt is probably mediated by antigen-antibody complexes. Recovery is possible in spite of severe renal lesions since the antigen can be eliminated at once by removal of the shunt.

Zusammenfassung. Bei 2 Patienten im Alter von 3 8/12 bzw. 27 Jahren entwickelte sich nach Anlegen eines ventriculo-atrialen Shunt eine diffuse Glomerulonephritis mit nephrotischem Syndrom. Die Entfernung des Shunt führte beim ersten Patienten zu einer raschen Besserung und beim zweiten Patienten zu einer kompletten Heilung des Nierenleidens. Das anfänglich tiefe Serumkomplement (β1C) normalisierte sich. Bei dem Kinde konnte aus dem Liquor und vom Ventil Staphylococcus albus gezüchtet werden. Bei dem erwachsenen Patienten blieben die Kulturen steril. Beim ersten Patienten ergab die Nierenbiopsie vor Entfernung des Shunt eine diffuse intra- und extracapilläre Glomerulonephritis, Typ III (subakute Glomerulonephritis), beim zweiten eine diffuse intracapilläre proliferative und exsudative Glomerulonephritis. Bei beiden Patienten wurde 22, bzw. 7 Monate nach Entfernung des Shunt eine zweite Biopsie entnommen. Beim ersten Fall waren rund die Hälfte der Glomeruli hyalinisiert. Die übrigen zeigten mäßig ausgeprägte segmentäre Läsionen. Halbmonde waren keine mehr nachweisbar. Beim zweiten Patienten bestand nach 7 Monaten noch eine deutliche mesangiale Proliferation mit Lobulierung der Glomeruli. Immunfluorescenzmikroskopisch konnte in beiden Fällen in den Glomerulusschlingen IgG, IgM und β1C in grob granulärer Form nachgewiesen werden. Elektronenmikroskopisch fanden sich bei beiden Patienten auch in der zweiten Biopsie subendotheliale Ablagerungen.

Die nach einem infizierten ventriculo-atrialen Shunt auftretende Glomerulonephritis ist mit großer Wahrscheinlichkeit durch Immunkomplexe bedingt. Da durch Entfernung des

* Presented in part at the Second International Symposium of Pediatric Nephrology, Paris, August 25–28, 1971.

Shunt das Antigen sofort entfernt werden kann, ist selbst bei schweren Nierenläsionen eine weitgehende Besserung möglich.

Introduction

Black *et al.* (1965) described the occurrence of the nephrotic syndrome in two pediatric patients having an infection of a ventriculo-atrial shunt with Staphylococcus albus. Treatment by valve replacement and antibiotic therapy resulted in a transient improvement of renal disease in one patient. Microscopic examination of renal tissue showed proliferative glomerulonephritis with lobulation. Positive staining for IgG and complement could be demonstrated by immunofluorescence study in one case. The authors proposed an immunological mechanism as the cause of the renal disease. A limited number of similar observations have since been reported. The disease became better known in 1968 when Stickler *et al.* (1968) described six patients with infected ventriculo-atrial shunts and renal disease, four of which exhibited the nephrotic syndrome. The infecting organism in five cases had been a coagulase negative Staphylococcus and in the remaining one, Staphylococcus aureus. Renal disease improved in all patients after removal of the shunt. A causal relationship between infection of a ventriculo-atrial shunt and production of glomerulonephritis seems to be established. This condition offers a unique opportunity for studying glomerulonephritis in man since the presumably pathogenic agent can be immediately eliminated by removing the shunt.

The scarcity of detailed reports and the remarkable findings of repeated renal biopsies 7 and 22 months, respectively, following shunt removal, have prompted us to describe our two cases. The initial phase of the disease in patient K. A. has been the subject of earlier publications of Stauffer *et al.* (1970) and Molz and Doswald (1970).

Materials and Methods

Histopathology. Specimens of renal tissue were obtained by open (first biopsy, case K. A.) or percutaneous needle biopsy immediately before and 22 months (patient K. A.) and 7 months (patient G. G.), respectively, following shunt removal.

Light Microscopy. A portion of each specimen was fixed in Dubosq-Brazil solution, processed and embedded in paraffin. Sections cut at 3 μ were stained with hematoxylin-eosin (HE), Masson's trichrome stain, periodic acid Schiff (PAS), and periodic acid silver-methenamin.

Electron Microscopy. From case K. A. a portion of the second biopsy and from case G. G. a portion of both biopsies were cut into 1 mm fragments, fixed for 1–2 h or longer in 2.5 percent glutaraldehyde buffered with 0.1 M sodium phosphate, followed by fixation for 1 h in 1 percent osmium tetroxide, buffered with 2 M S-collidine and embedded in Epon 812. Ultrathin sections were cut on an LKB ultramicrotome and stained with uranyl acetate and lead citrate. The specimens were examined and photographed with a Zeiss EM 9.

Immunofluorescence Microscopy. Part of the tissue was rapidly frozen in a solution of isopentane cooled with liquid nitrogen and sectioned in a cryostat microtome.

The following sera were utilized in case K. A.: Goat antihuman IgG (Institute for Clinical Tumor Research, Berne), horse anti-human IgA and IgM (Dutch Red Cross), rabbit anti-human β1C globulin (Behringwerke, Marburg), and mono-specific fluorescein isothiocyanate conjugated rabbit antisera to goat and horse globulin and goat antiserum to rabbit globulin (Nordic, Tilburg).

All sera utilized in case G. G. were obtained from Behringwerke, Marburg. Observations and photographs were made with a Leitz Ortoplan microscope.

Case Reports

Patient K. A. (see Fig. 1), 3 years and 8 months old boy

In June 1966 a ventriculo-atrial shunt (Pudenz-Heyer) was inserted at the age of 8 months because of rapidly increasing communicating hydrocephalus. The patient was readmitted in September 1968 because of spiking fevers and episodes of gross hematuria. Urinalysis disclosed only trace proteins and some red blood cells (RBC) per high power field (hpf). Glomerular function and serum protein (7 g/100 ml) were normal. Cultures of urine and cerebrospinal fluid were negative. The cause of the hematuria was not determined, and the patient was sent home. Eight months later, i.e., three years after insertion of the shunt, he was readmitted because of

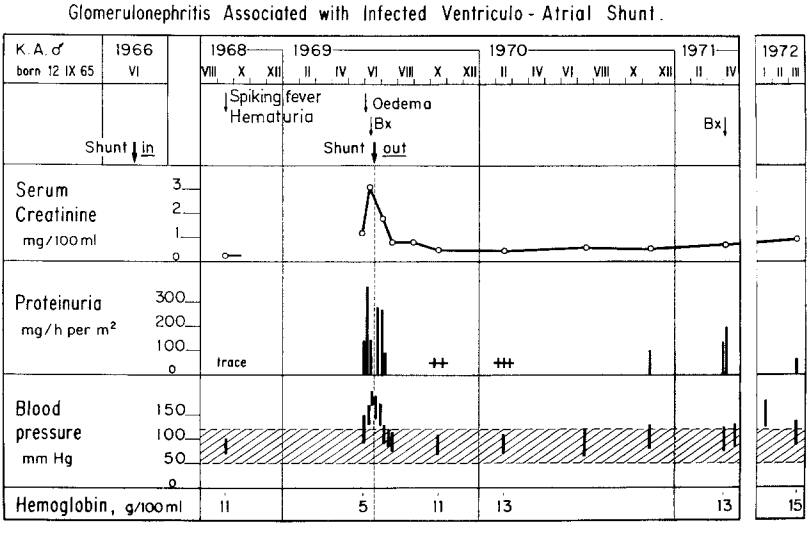

Fig. 1. Clinical course of patient K. A. (Bx: renal biopsy)

fever, vomiting, and edema. On admission this 3 years and 8 months old boy was severely ill, pale, and grossly edematous. Work-up revealed rapidly progressive azotemia, the nephrotic syndrome, hypertension (blood pressure recordings up to 200/160 mm Hg), severe anemia (hemoglobin concentration 5 g/100 ml), and hepatosplenomegaly. Serum values: blood urea nitrogen (BUN) rising from 17 to 81 mg/100 ml, total protein 4.1 g/100 ml, albumin 2.6 g/100 ml, cholesterol 185 mg/100 ml. There was massive proteinuria and gross hematuria. The ASO titer was normal (< 50 Todd units), and β1C globulin in the serum was low. Cultures of Staphylococcus albus were grown from the spinal fluid and valve, but not from either blood or renal tissue. An open kidney biopsy was performed and the infected shunt was removed. Rapid clinical improvement followed, and serum β1C globulin returned to normal values. Repeated spinal taps were only initially required since the hydrocephalus arrested spontaneously. However, the serum concentration of creatinine has remained slightly elevated, and significant proteinuria without the nephrotic syndrome was still present two years later. At this time, a second renal biopsy was performed. The patient has remained clinically well since, but is receiving antihypertensive drugs because of elevated blood pressure (180/125 mm Hg). At follow-up in March 1972 clearance of creatinine was 53 ml/min per 1.73 m^2, maximum osmolality in urine was 570 mosmol/kg, serum proteins were 5.7 g/100 ml, and serum albumin was 3.1 g/100 ml. Only borderline microscopic hematuria was observed.

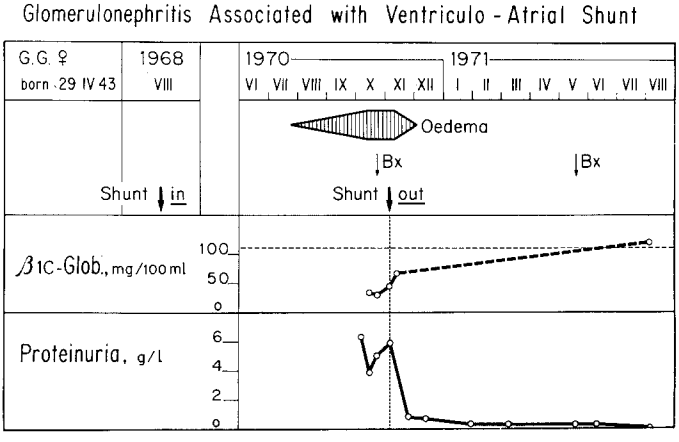

Fig. 2. Clinical course of patient G. G.

Patient G. G. (see Fig. 2), 27 year old female

Obstructive hydrocephalus caused by a tumor of the basal ganglia was diagnosed in July 1968 and was treated by inserting a ventriculo-atrial shunt (Spitz-Holter) and by local irradiation. The patient did quite well for the next two years. In July 1970 she first noticed swelling of her legs and had an occasional spiking temperature. On admission in October 1970 the nephrotic syndrome was diagnosed. There was only slight anemia (hemoglobin concentration 9.0 g/100 ml) and no hepatosplenomegaly. Laboratory values: BUN 20 mg/100 ml, serum creatinine 0.9 mg/100 ml, serum protein 3.5 g/100 ml, albumin 1.9 g/100 ml, cholesterol 190 mg/100 ml, massive proteinuria, microscopic hematuria (10–40 RBC per hpf) and pyuria (30 to 70 WBC per hpf), in spite of repeated negative urine cultures. Tests for lupus erythematosus and antinuclear antibodies were negative; the ASO titer was below 50 Todd units. No microorganism could be cultured from the blood or valve, and the spinal fluid could not be examined. A percutaneous renal biopsy was performed, and the shunt, which no longer functioned, was removed resulting in rapid clinical improvement and sudden decrease in proteinuria. Seven months later, a second renal biopsy was done. Serum creatinine was then 0.8 mg/100 ml, and urinalysis showed only trace protein and microscopic hematuria (8–10 RBC per hpf). At her fast follow-up in August 1971, serum albumin was 4.1 g/100 ml, and only minimal hematuria (3–5 RBC per hpf) persisted.

Histopathological Observations

Patient K. A.

First Biopsy (HZ 6598/69):

Light Microscopy. 30 glomeruli are seen. More than 90 percent exhibit extra capillary proliferation with crescent formation, and all show diffuse intracapillary proliferation (Fig. 3). Some of the crescents are already sclerosed. Deposits of fibrin are occcasionally seen between the proliferating epithelial cells. Isolated tufts are compressed by crescents. The tubules are dilated and their epithelium is flattened. There is interstitial edema with predominantly periglomerular infiltrates of round cells. The blood vessels are normal.

Diagnosis. Diffuse intra- and extracapillary glomerulonephritis, type III[1] (subacute glomerulonephritis).

1 Nomenclature according to Habib (1970).

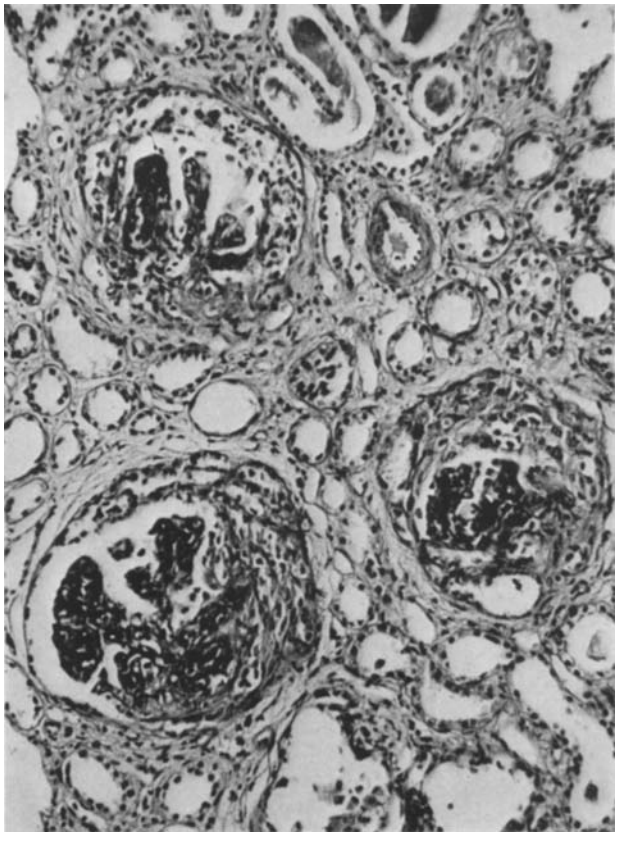

Fig. 3. Patient K. A., first biopsy. Diffuse intra- and extracapillary glomerulonephritis type III. Over 90 percent of the glomeruli exhibit extracapillary proliferation with crescent formation, and all show diffuse in tracapillary proliferation PAS, × 160, HZ 6598/69

Immunofluorescence Study (Dr. H. J. Plüss, Laboratory of Oncology, University Children's Hospital, Zurich). All glomeruli contain IgM, and to a lesser extent, IgG and β1C complement in a coarsely granular pattern. No IgA was detected.

Second Biopsy (HZ 8220/71):

Light Microscopy. The histological picture is entirely different from the first biopsy. Approximately half of the seventeen glomeruli are hyalinized. Only one crescent is still distinguishable. In the remaining glomeruli, there is no epithelial, but slight mesangial proliferation with small areas of sclerosis, some capsular adhesions, and occasional thickening of the wall of capillary loops (Fig. 4). There is focal tubular atrophy and interstitial fibrosis. The epithelium of the remaining tubules is intact. The blood vessels appear normal.

Immunofluorescence Study (Dr. H. J. Plüss). Antisera produced minimal (against IgG and fibrinogen) or no (against IgM, IgA and β1C globulin) staining, but only two glomeruli could be examined.

Ultrastructural Findings. Only a few completely normal capillary loops are present. There is irregular thickening or proliferation of endothelial and

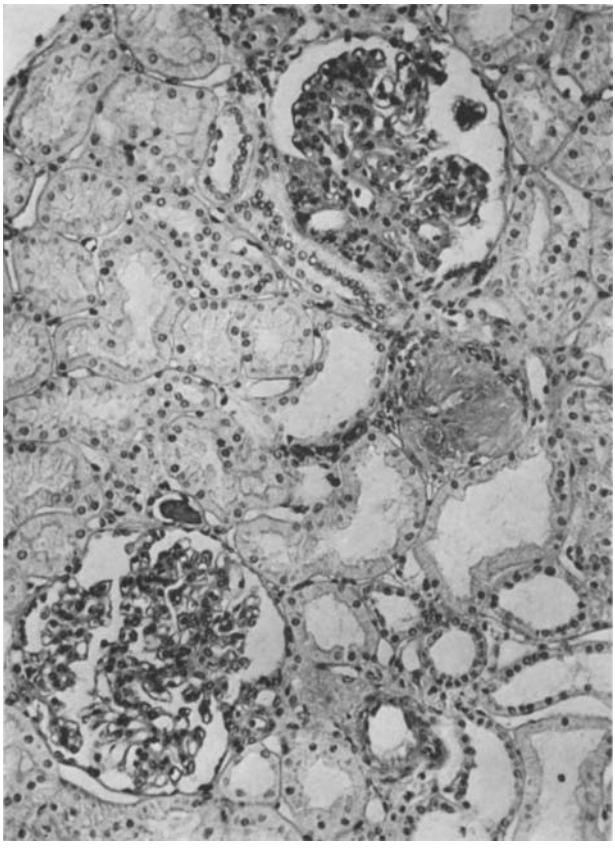

Fig. 4. Patient K. A., second biopsy. Approximately 50 percent of the glomeruli are sclerosed. In the remaining glomeruli, there is focal intracapillary proliferation with some capsular adhesions. HE, × 100, HZ 8220/71

mesangial cells and an increase of mesangial matrix. In some loops there is partial or total circumferential mesangial interposition. The border on the epithelial side of the glomerular basement membrane is smooth, but there is slightly nodular thickening on the endothelial side of the membrane. Less frequently, fine granular subendothelial deposits in both obliterated and relatively normal capillary loops are found (Fig. 5). The epithelial foot processes are often coalesced.

Patient G. G.

First Biopsy (HZ 20,322/70):

Light Microscopy. The biopsy contains 8glomeruli. One is sclerosed, and the remaining seven are uniformly altered. There is distinct intracapillary prolifer ation with partial or total obliteration of the capillary lumen and accumulation of polymorphonuclear leucocytes (Fig. 6). In addition, there are areas of fibrinoid necrosis in some capillary loops. The tubules, interstitium, and blood vessels are normal with the exception of isolated foci of round cell infiltration.

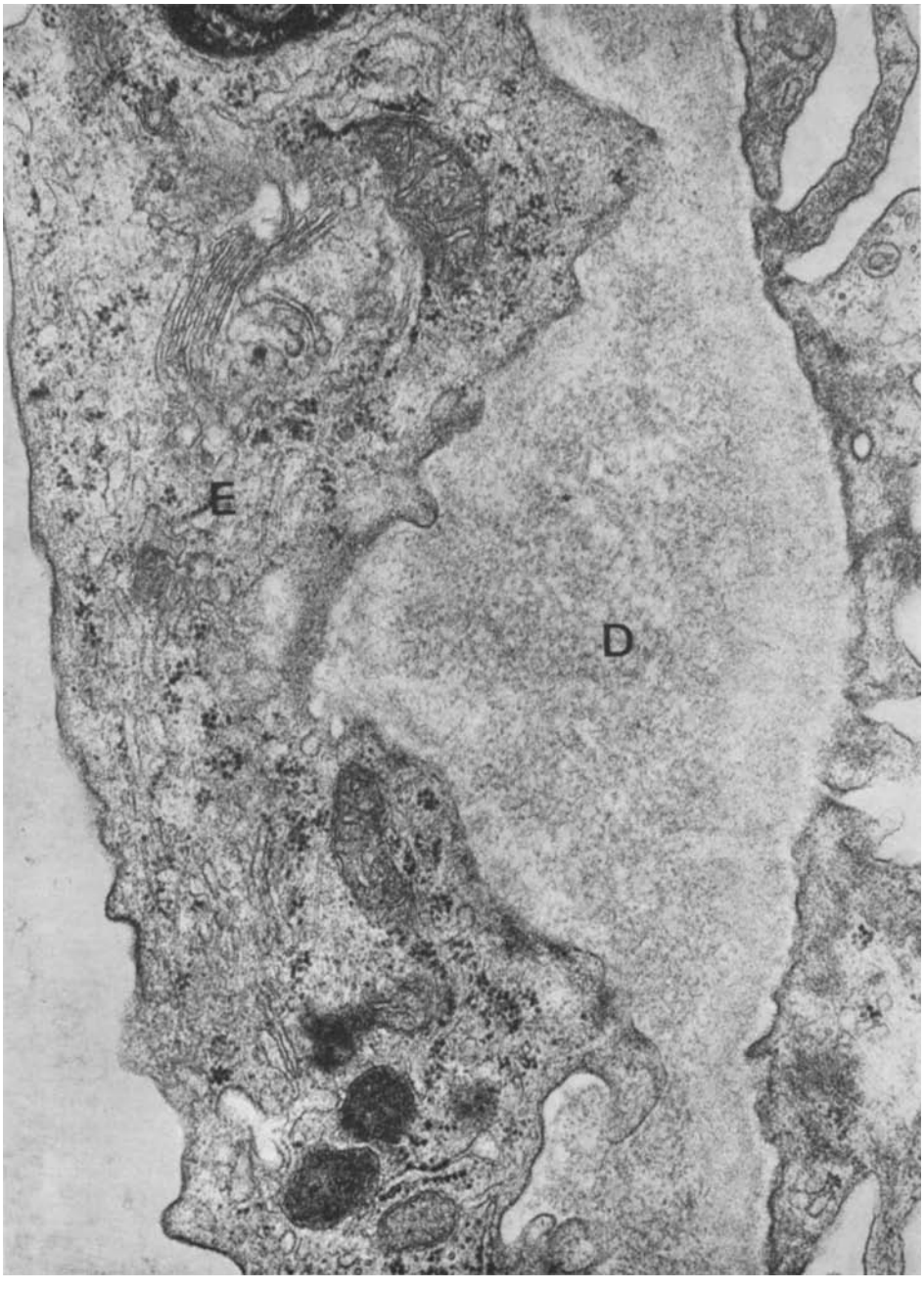

Fig. 5. Patient K. A., second biopsy. Detail of a glomerular capillary loop with a hyperplastic endothelial (*E*) cell and with a fine granular subendothelial deposit (*D*). Epithelial foot processes are partially fused. Electronmicrograph 1386/71. × 42000 (reduced to 7/9)

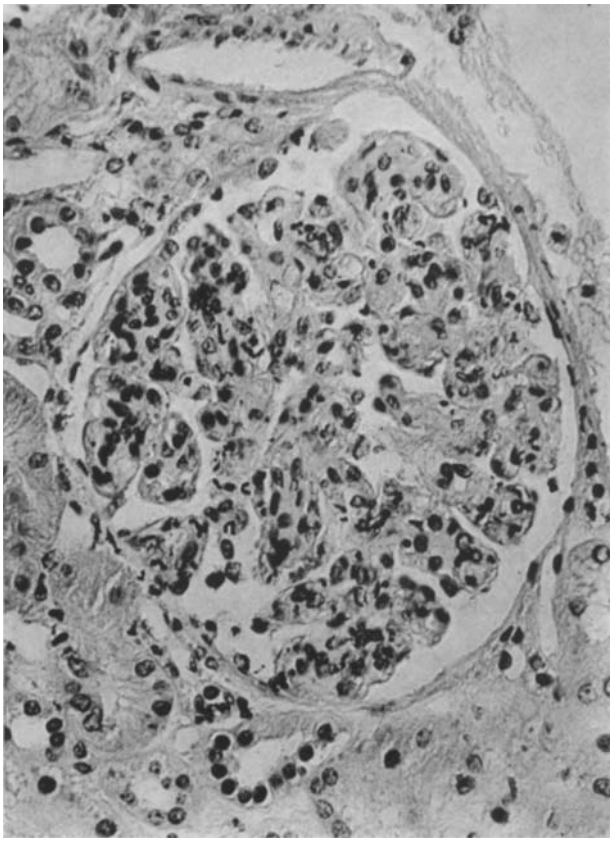

Fig. 6. Patient G. G., first biopsy. There is diffuse intracapillary proliferation with accumulation of polymorphonuclear leucocytes. HE, × 350, HZ 20,322/70

Diagnosis. Diffuse intracapillary proliferative and exudative glomerulonephritis.

Ultrastructural Findings. The lumen of most glomerular capillary loops is narrowed or totally obstructed by endothelial or mesangial cells and by mono- and polymorphonuclear leucocytes (Fig. 7). Numerous small and large, fine granular electron-dense deposits are located between the glomerular basement membrane and the endothelial cells (Fig. 7). The basement membrane itself is not thickened, and its lamina densa is intact. Polymorphonuclear cells are often found between the endothelial cells and the basement membrane next to the endothelial deposits (Fig. 8). Some polymorphonuclear cells are necrotic. There is occasional fusion of the epithelial foot processes. The mesangial matrix is slightly increased.

An immunofluorescence study was not performed.

Second Biopsy (HZ 11,825/71):

Light Microscopy. In contrast to the first biopsy, the glomerular capillary loops are no longer obstructed, but there is still distinct mesangial proliferation with lobulation of the glomerular tuft (Fig. 9). The basement membrane of some

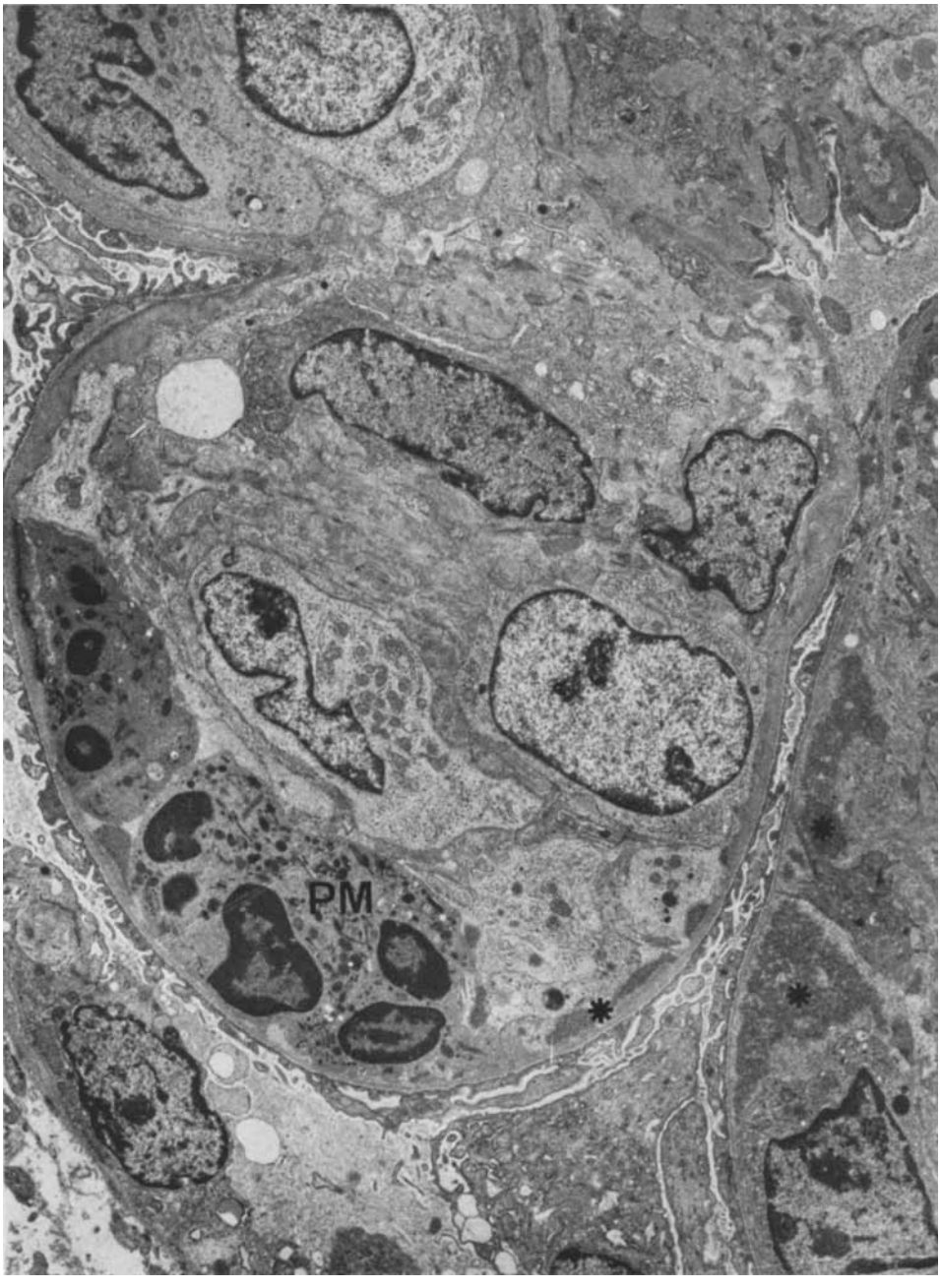

Fig. 7. Patient G. G., first biopsy. Most glomerular loops are totally obstructed by proliferating endothelial and mesangial cells and polymorphonuclear leucocytes (*PM*). Subendothelial electron-dense deposits (*) differing in size are seen. Electronmicrograph 2181/70. × 9000 (reduced to 7/9)

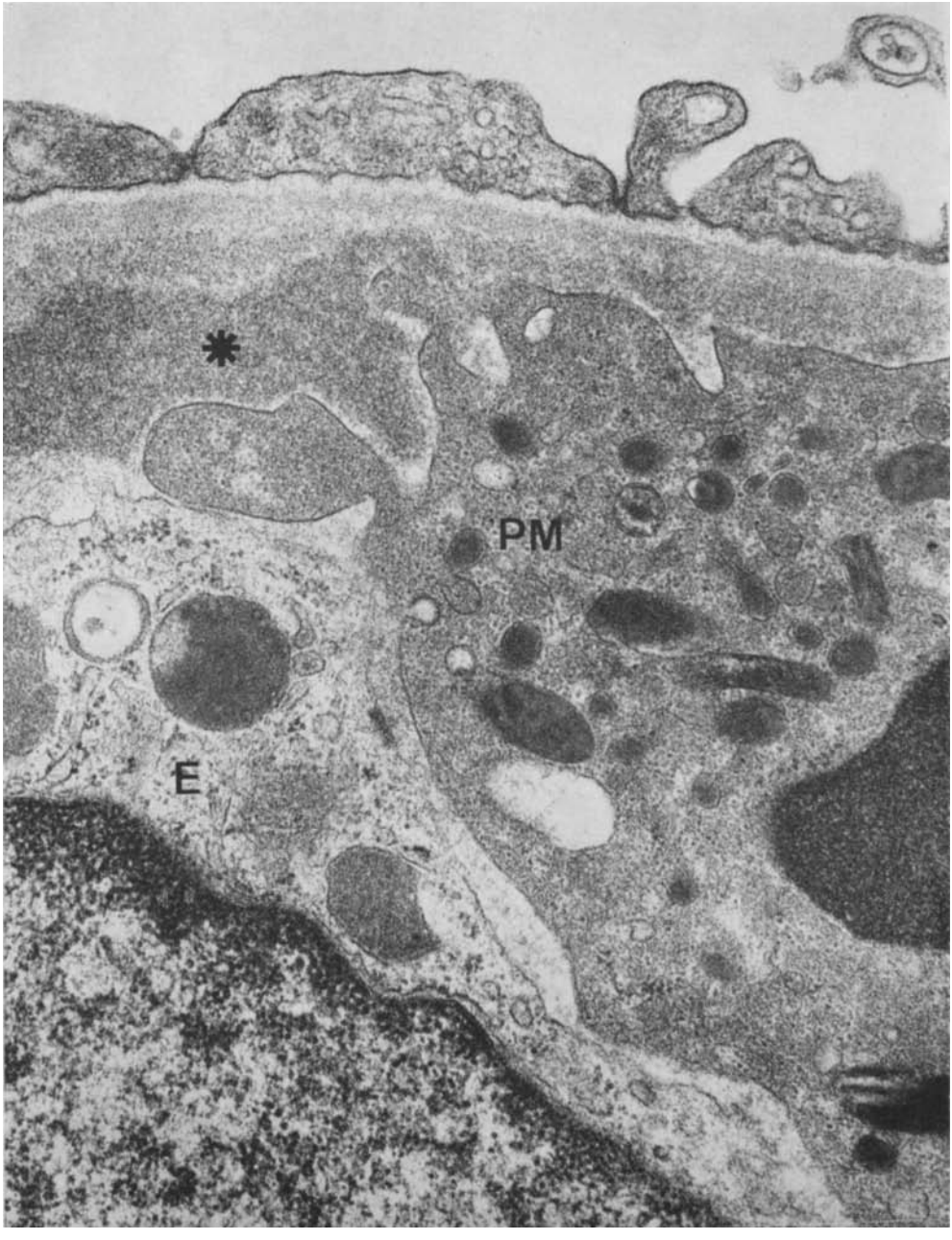

Fig. 8. Patient G. G., first biopsy. Detail of a glomerular capillary loop. An endothelial (*E*) cell is separated from the underlying basement membrane by a polymorphonuclear leucocyte (*PM*) which lies in close proximity to an electron-dense deposit (*). Epithelial foot processes are partially fused. Electronmicrographs 2180/70. × 42000 (reduced to 7/9)

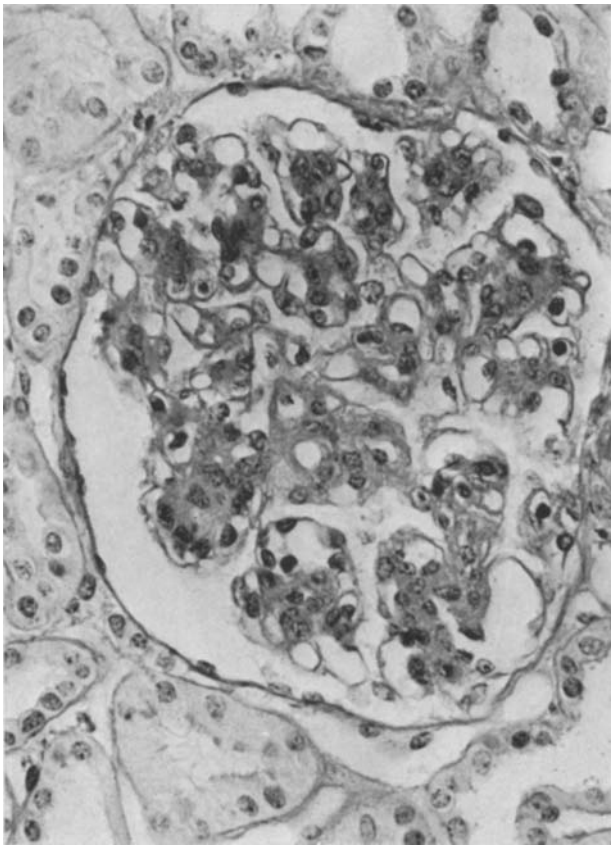

Fig. 9. Patient G. G., second biopsy. There is distinct lobulation of the glomerulus with predominant mesangial cell proliferation and slight centrolobular sclerosis. PAS, ×400, HZ 11,825/71

glomerular capillaries is focally thickened and appears split on silver staining. There are rare areas of tubular atrophy and interstitial fibrosis. While there is distinct intimal thickening of the arteries, the arterioles appear normal.

Immunofluorescence Study (Dr. P. Grob, Laboratory of Immunology, University Hospital, Zurich). It showed positive staining in a coarsely granular pattern of the glomerular basement membrane for IgG, IgM and β1C globulin and rarely for fibrinogen.

Ultrastructural Findings. The walls of many capillary loops are thickened because of interposition of mesangial cells between the basement membrane and the endothelial cells resulting in formation of a second basement membrane-like layer on the endothelial side (Fig. 10). Subendothelial osmophilic deposits, some with central cores of diminished electron density, are still visible in many capillary

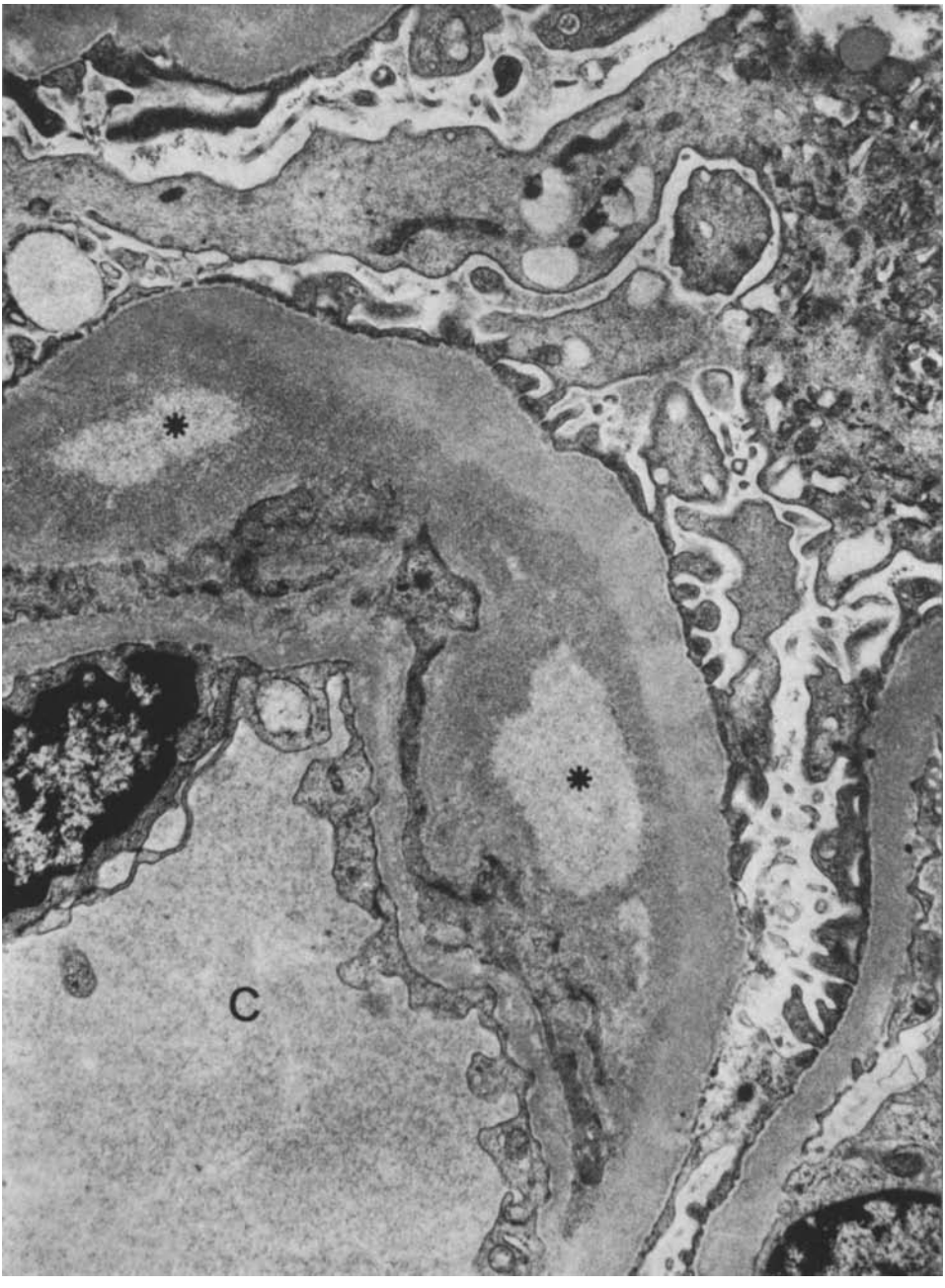

Fig. 10. Patient G. G., second biopsy. Detail of a glomerular capillary loop. Two subendothelial deposits (*) with central cores of diminished electron density are seen. The capillary wall is thickened by mesangial interposition and deposits. The capillary lumen (*C*) is patent. Electronmicrograph 1567/71. × 10000 (reduced to 7/9)

loops (Fig. 10). Mesangial proliferation and formation of mesangial matrix in the center of the lobules are much more pronounced than in the first biopsy. The foot processes of the epithelial cells are only moderately coalesced.

Discussion

In most cases of glomerulonephritis associated with infected ventriculo-atrial shunts, S. albus has been cultured from the valve. This microorganism was not considered to be pathogenic until S. albus septicemia was described in patients having prostheses in the circulatory system (see Smith *et al.*, 1958). Only occasionally have other microorganisms, e.g., S. aureus (Stickler *et al.*, 1968), Micrococcus (Holland, 1967; Kaufman *et al.*, 1969) and B. cereus (Campbell *et al.*, 1971), been observed in patients with shunt nephritis. Although no organism could be cultured from the valve of patient G. G., the clinical course and renal biopsy findings strongly suggest that infection of the valve must also have occurred. Absence of hepatosplenomegaly in this case is rather unusual and is probably related to removal of the shunt at a relatively early stage of the disease. In addition, nearly all cases reported so far were children in whom enlargement of the liver and spleen occurs more rapidly than in adult patients.

There is strong evidence that the pathophysiology of glomerulonephritis associated with infected ventriculo-atrial shunts has an immunological basis. Theoretically, two other mechanisms are possible; namely, direct bacterial embolization, and thrombotic microangiopathy. The first is excluded as a result of consistently negative bacterial cultures from renal tissue and negative Gram stains (Stickler *et al.*, 1968; patient K. A.). Thrombotic microangiopathy presents with a different clinical picture and pathology; there is thrombosis of the afferent arterioles and glomerular capillary loops, as well as splitting of the glomerular basement membrane (Habib *et al.*, 1969). Furthermore, no signs of hemolytic anemia (burr cells, thrombocytopenia), characteristic of thrombotic microangiopathy, have been reported in cases of shunt nephritis except for one observation by Campbell *et al.* (1971). An immune pathogenesis of the antigen-antibody complex type is strongly suggested by the presence of 1) granular deposits of IgG and β1C globulin on the glomerular basement membrane, 2) subendothelial electron-dense deposits, and 3) hypocomplementemia returning to normal levels after removal of the shunt. Labeled antibodies against S. albus would be expected to produce positive staining along the glomerular basement membrane on immunofluorescent study. This has indeed been observed in the patient described by Kaufman and McIntosh (1971). Electron-dense deposits on the endothelial side of the glomerular basement membrane most likely correspond to immune complexes. Deposits similar to those seen in our study have been described in patients of Rames *et al.* (1970), Bauby (1972) and Moncrieff *et. al.* (1973). The deposits resemble those observed in patients with lupus nephritis. No deposits on the epithelial side of the glomerular basement membrane (so-called humps), frequently seen during the acute stage of poststreptococcal glomerulonephritis and also described in patients with endocarditis due to a coagulase positive Staphylococcus (Gutman *et al.*, 1972), have been observed in patients with shunt nephritis. The statement of Kaufman and McIntosh

(1971) that "the morphological and immunohistological characteristics of shunt nephritis and poststreptococcal glomerulonephritis are indistinguishable" may therefore be debatable.

Infection of a ventriculo-atrial shunt does not necessarily lead to glomerulonephritis. In a retrospective study, glomerulonephritis occurred in only one patient (Patient K.A.) in a series of 13 patients with infected ventriculo-atrial shunts (Molz and Doswald, 1970). Development of glomerulonephritis probably depends on a favorable immunological environment as suggested experiments of Dixon *et al.* (1961).

A striking feature of both repeat renal biopsies was the finding of numerous subendothelial electron-dense deposits even 7 and 22 months, respectively, after removal of the shunt, and of granular deposits of IgG, IgM and β1C globulin on immunofluorescence microscopy in the second biopsy of patient G. G. Repeat renal biopsies after removal of the shunt have only been reported in two instances (Stickler *et al.*, 1968; Bauby, 1972). Stickler *et al.* (1968) noted in their first case (biopsy nine months after shunt removal) that on light microscopy 20 out of 24 glomeruli were hyalinized and that the remaining four had hypercellularity in the center of the lobules and thickening of the capillary basement membrane. Unlike in our two patients, in the first case described by Bauby (1972), finely granular electron-dense deposits which were seen on the original biopsy could not be detected at the second biopsy eight months after removal of the shunt. Formation of deposits is unlikely to occur once the antigen is removed. It is rather suggested that the original deposits persist for an extended period of time in certain situations. The continuing presence of subendothelial deposits may cast some doubt on the long-term outcome in certain patients. Lasting proteinuria and secondary elevation of blood pressure were indeed observed in patient K. A.

The difficulty in evaluating the prognosis from the renal biopsy alone is strikingly documented by patient K. A. The first renal biopsy was interpreted by different pathologists as: subacute glomerulonephritis, malignant glomerulonephritis, rapidly progressive glomerulonephritis, and intracapillary and extracapillary glomerulonephritis type III of Habib (1970). The prognosis in any case was expected to be extremely poor. In a series of patients with similar renal biopsy findings observed by R. Habib, all expired in terminal renal failure within 20 months (Proesmans, 1971). Following more recent investigations of Sonsino *et al.* (1972), simple extracapillary glomerulonephritis should be carefully distinguished from combined extra- and intracapillary glomerulonephritis. In their series of 31 observations all presenting with crescent formation in more than 60 percent of the glomeruli, 20 patients, many of them with signs of systemic disease, belonged to the group with simple extracapillary proliferation. Immunofluorescence studies were negative in seven of eight of these patients, and only four were alive at the time of the report. On the other hand, only a minority (two of eleven) of the latter group of combined extra- and intracapillary glomerulonephritis went into terminal renal failure. These patients were generally younger and often had preceding upper respiratory infections in their history. On immunofluorescence study, positive staining in a granular pattern was observed in three of five cases examined. Our first case and others with shunt nephritis (Black *et al.*, 1965; Stickler *et al.*, 1968) clearly belong to the latter group with intra- and extracapillary proliferation. A

relatively good prognosis may thus be anticipated even in the presence of severe renal damage, especially as the antigen can successfully be eliminated by removal of the shunt.

We are indebted to the late Dr. W. Scheitlin, Department of Medicine, for performing the renal biopsies in patient G. G.; to Dr. H. J. Plüss, Department of Pediatrics, University Children's Hospital, for the immunofluorescence studies in case K. A.; to Dr. P. Grob, Department of Medicine, for the immunofluorescence studies in case G. G.; and to Dr. U. Stauffer, Department of Pediatric Surgery, and Dr. A. Ganzoni, Department of Medicine, for providing clinical data.

Appreciation is expressed to Mrs. M. Schneeberger for skillful technical assistance.

Reference

Bauby, C.: Contribution à l'étude de la néphrite de shunt. Thèse, Faculté de Médecine, Paris Lariboisière. St. Louis: 1972.

Black, J. A., Challacombe, D. N., Ockenden, B. G.: Nephrotic syndrome associated with bacteremia after shunt operations for hydrocephalus. Lancet **1965 II**, 921–924.

Campbell, A., Futrakul, P., Musgrave, J. E., Surapathana, La-Or, Eisenberg, C. S.: Bacillus cereus prosthesis nephritis. (Abstract) Proc. Second International Symposium of Pediatric Nephrology, Paris 1971, p. 167. Paris: Editions Sandoz 1971.

Dixon, F. J., Feldman, J. D., Vazquez, J. J.: Experimental glomerulonephritis: Pathogenesis of laboratory model resembling spectrum of human glomerulonephritis. J. exp. Med. **113**, 899–920 (1961).

Gutman, R. A., Striker, G. E., Gilliland, B. C., Cutler, R. E.: The immune complex glomerulonephritis of bacterial endocarditis. Medicine (Baltimore) **51**, 1–25 (1972).

Habib, R.: Classification anatomique des néphropathies glomérulaires. Pädiat. Fortbild. Praxis **28**, 3–47 (1970).

Habib, R., Courtecuisse, V., Leclerc, F., Mathieu, H., Royer, P.: Etude anatomo-pathologique de 35 observations de syndrome hémolytique et urémique de l'enfant. II. Arch. franç. Pediat. **26**, 391–416 (1969).

Holland, N.: Hypocomplementemic glomerulonephritis associated with Micrococcus infection of ventriculo-atrial shunt. (Abstract) 37th Annual Meeting Society for Pediatric Research, Atlantic City, N. J., p. 125 (1967).

Kaufman, D. B., Logan, L., McIntosh, R. M.: The nature of the antibody in a patient with immune complex renal disease. (Abstract) Pediat. Res. **3**, 363 (1969).

Kaufman, D. B., McIntosh, R. M.: The pathogenesis of the renal lesion in a patient with streptococcal disease, infected ventriculo-atrial shunt, cryoglobulinemia and nephritis. Amer. J. Med. **50**, 262–268 (1971).

Molz, G., Doswald, T.: Diffuse Glomerulonephritis bei Staphylokokken-infizierter ventrikuloatrialer Liquordrainage. Schweiz. Arch. Neurol. Neurochir. Psychiat. **107**, 223–230 (1970).

Moncrieff, M. W., Glasgow, E. F., Arthur, L. J. H., Hargreaves, H. M.: Glomerulonephritis associated with Staphylococcus albus in a Spitz Holter valve. Arch. Dis. Child. **48**, 69–72 (1973).

Proesmans, W.: Proliferative glomerulonephritis with crescents. (Abstract) Proc. Second International Symposium of Pediatric Nephrology, Paris 1971, p. 91–92. Paris: Editions Sandoz 1971.

Rames, L., Wise, B., Goodman, J. R., Piel, C. F.: Renal disease with Staphylococcus albus bacteremia. A complication in ventriculoatrial shunts. J. Amer. med. Ass. **212**, 1671–1677 (1970).

Smith, I. M., Beals, P. D., Kingsbury, K. R., Hasenclever, H. F.: Observations on Staphylococcus septicemia in mice and men. Arch. intern. Med. **102**, 375–388 (1958).

Sonsino, E., Nabarra, B., Kazatchkine, M., Hinglais, N., Kreis, H.: Les glomérulonéphrites prolifératives extracapillaires dites „glomérulonéphrites malignes". In: Actualités Néphrologiques de l'Hôpital Necker, p. 119–161. Paris: Editions Flammarion 1972.

Stauffer, U. G., Csomor, A., Plüss, H. J., Hitzig, W. H.: Diffuse Glomerulonephritis infolge infizierten ventrikuloatrialen Shunts. Schweiz. Med. Wschr. **100**, 1288–1291 (1970).

Stickler, G., Shin, M. H., Burke, E. C., Holley, K. E., Miller, R. H.: Segar, W. E.: Diffuse glomerulonephritis associated with infected ventriculo-atrial shunt. New. Engl. J. Med. **279**, 1077–1082 (1968).

PD Dr. W. Wegmann
Institut für Pathologische Anatomie
Schmelzbergstr. 12
CH-8006 Zürich
Switzerland

Dr. E. P. Leumann
Universitäts-Kinderklinik
Steinwiesstr. 75
CH-8032 Zürich
Switzerland