THE AMERICAN JOURNAL OF PATHOLOGY

VOLUME XII NOVEMBER, 1936 NUMBER 6

THE EARLY STAGES OF GLOMERULONEPHRITIS*

E. T. BELL, M.D.

(From the Department of Pathology, University of Minnesota, Minneapolis, Minn.)

INTRODUCTION

The structure of the glomerulus in clinical acute diffuse glomerulonephritis has been studied by various investigators and it is generally agreed that the essential lesion is an increase in the number and size of the endothelial cells with resulting capillary obstruction. Polymorphonuclear leukocytes are found in varying numbers among the endothelial cells, but leukocytes alone do not produce complete capillary obstruction except in occasional capillary loops.

Investigators interested in the pathogenesis of human glomerulonephritis have studied clinical examples of the disease in which death occurred shortly after the onset of symptoms. In general they have found appearances similar to, but less prominent than, those occurring in well developed clinical cases.

Gräff, 1916, using Schultze's oxidase reaction, demonstrated a great increase of polymorphonuclear leukocytes in acute glomerulonephritis. He thought that the number of leukocytes in the glomeruli afforded a distinction between simple inflammatory reactions and acute glomerulonephritis.

Gross, 1919, studied the kidneys of a person who died of pulmonary edema a few hours after the onset of symptoms of nephritis. In the glomerular capillaries he noted leukocytes and many large endothelial nuclei embedded in a cytoplasmic network.

Volhard, 1922, 1931, proposed the theory that the primary change in acute glomerulonephritis is a spasm of the afferent glomerular arterioles, the resulting anemia injuring the capillaries and bringing

* Received for publication March 28, 1936.

about a secondary inflammatory reaction. He based his hypothesis on clinical and physiological considerations and on analogy with eclampsia.

Kuczynski and Dosquet, 1926, supported Volhard's theory with anatomical evidence. In a case which they considered early acute glomerulonephritis they noted edema of the wall of the afferent glomerular arteriole near its entrance into the glomerulus. Leukocytes were also found in the wall of the arteriole. They believed that this structural alteration indicated a primary spastic constriction of the afferent arteriole. The leukocytes in the glomerular capillaries were supposed to have entered through the efferent arteriole. An increase of endothelial nuclei was described.

Volhard's theory has received very little support from anatomical studies. It is, of course, difficult to refute since any spasm of the arteriole present in life would probably relax after death, and one would not expect arteriolar spasm to produce structural changes in the wall of the vessel. In some cases of glomerulonephritis the arterioles show an occasional area of hyaline degeneration in the media, but it is certain that the vast majority show no anatomical changes. They are frequently dilated rather than contracted at the point of entrance into the glomerulus.

Endothelial proliferation does not seem to be related to hypertension. It will be shown later in this paper that severe infections without hypertension show much more endothelial proliferation in the glomeruli than is found in primary hypertension. The high frequency of endothelial proliferation in association with infectious and toxic processes indicates that it is a response to soluble toxic substances rather than to injury from anemia.

Fahr, 1926, restated his belief that glomerulonephritis is caused by soluble toxins that produce a primary endocapillaritis. In a person who died of pneumonia 3 days after the onset of symptoms of nephritis he found a definite endothelial proliferation and many leukocytes in the glomerular capillaries. A careful study of the afferent arterioles showed no lesions of any kind.

Hückel, 1929, studied the kidneys from a case of glomerulonephritis of 30 hours duration. He found the glomerular capillaries filled with polymorphonuclear leukocytes and endothelial cells in a cytoplasmic substance. He agreed with Fahr's conception of primary endocapillaritis.

The prevailing opinion in the literature seems to be in accord with Fahr's conception that the primary change in glomerulonephritis is proliferation of the endothelium of the glomerular capillaries and that the earliest clinical examples of acute glomerulonephritis show this lesion. The simplest interpretation of the endothelial increase is an inflammatory reaction to soluble toxic substances.

We may now raise the question as to whether or not acute glomerulonephritis is a specific disease entity, *i.e.* a disease caused by a specific organism or virus and having characteristic anatomical lesions, such as typhoid fever and tuberculosis. Inasmuch as organisms are not found in the glomeruli the etiological agent can only be inferred from the associated infection in the patient. Nearly all observers are agreed that the associated infectious agent is usually a streptococcus, but both hemolytic and non-hemolytic strains are concerned. There is also strong evidence that pneumococci may occasionally cause glomerulonephritis, and in rare instances other organisms may be concerned. Staphylococci apparently do not produce diffuse endothelial proliferation in the glomeruli to any notable extent although they often produce glomerular abscesses. It may be concluded, therefore, that glomerulonephritis is not caused by a specific etiological agent.

As regards the anatomical lesion, the essential feature is proliferation of the glomerular capillary endothelium. Polymorphonuclear leukocytes are usually present in varying numbers but are not an essential feature. Leukocytes alone rarely, if ever, produce widespread capillary obstruction. Epithelial crescents predominate in certain fulminant cases and may be largely responsible for obstruction of the glomeruli.

In 1926 Clawson, Bell and Hartzell published the observation that a moderate degree of diffuse glomerulitis is frequently found in persons dead of subacute bacterial endocarditis. Since that time I have noted a similar glomerulitis in various acute infectious processes, notably puerperal septicemia. These subclinical forms of diffuse glomerulonephritis were illustrated in my "Text-Book of Pathology" in 1934 (Figs. 217 and 218).

In this paper the study of the finer glomerular structure has been extended to include a large number of infectious and non-infectious diseases. It will appear from this investigation that a diffuse proliferation of the glomerular endothelium occurs in many acute and

chronic infectious processes and in some diseases in which no infectious element was found. There are innumerable transitions between this subclinical glomerulitis and clinical acute glomerulonephritis. The clinical disease shows an increased endothelial proliferation and more pronounced capillary obstruction, but fundamentally it is the same type of reaction that occurs in the subclinical forms.

If this interpretation be correct, *i.e.* that subclinical and clinical acute glomerulonephritis differ only in intensity, it follows that acute glomerulonephritis is not a sharply circumscribed entity and a much broader approach to its etiology and pathogenesis is available.

Material and Methods

In this investigation the kidneys from 865 cases have been examined microscopically (see Table II). A wide range of diseases is included and all age groups are represented. Paraffin sections were stained by the Mallory-Heidenhain technique (azocarmine). This stain was first applied to the glomeruli by McGregor. Since the capillary basement membrane is stained sharply, one may easily distinguish cells within the capillaries (endothelial cells and leukocytes) from the glomerular epithelial cells outside them. The stain works to best advantage on tissues fixed in Helly's or Zenker's fluid, but with slight modifications it is satisfactory after formalin fixation unless the tissues have been in formalin for over a year. Tissues kept in formalin several years may often be stained satisfactorily if the deparaffined sections are treated with Zenker's fluid for 24 hours.

In estimating the degree of endothelial proliferation the number of endothelial and epithelial nuclei in several glomerular loops are counted. When the epithelial nuclei definitely outnumber the endothelial the degree of endothelial proliferation is graded "0," and when the two types of nuclei are of approximately equal number it is graded "+." A definite preponderance of endothelial nuclei is graded "1" and a marked preponderance "2." In Grades 1 and 2 the endothelial nuclei are large and show abundant cytoplasm about them. Grade 3 endothelial proliferation corresponds with the structure seen in typical clinical acute glomerulonephritis. Intracapillary fibers are easily seen in Grade 3, and occasionally in very small amount in Grade 2, but are entirely absent in lower grades of proliferation.

In counting the nuclei within the capillaries polymorphonuclear leukocytes were not included, but mononuclear leukocytes were counted as endothelial cells unless they lay entirely free in the capillary lumen. It is very difficult to distinguish a mononuclear leukocyte from a large endothelial cell when the former is flattened against the capillary wall.

This method of enumerating the endothelial nuclei does not, of course, give the total number of cells in a given volume of glomerular tissue and it assumes that the number of epithelial cells is fairly constant.

It is true as Van Waveren points out that fewer endothelial nuclei are visible in a section when the capillaries are distended than when they are empty. In a normal glomerulus, where the endothelial nuclei are smaller than the epithelial, this may lead to underestimation of the relative number of endothelial cells; but in all forms of glomerulitis the endothelial nuclei are as large as the epithelial, and therefore distention or collapse of the capillaries does not alter the ratio of endothelial to epithelial nuclei.

Grades 1 and 2 of endothelial proliferation are immediately recognizable with the high dry lens. Figures 3, 4, 5 and 6 illustrate what is meant by endothelial proliferation — 0, +, 1, and 2 respectively.

The Structure of the Normal Human Glomerulus

In a normal glomerulus the lobulation is usually indistinct since the interlobular fissures are difficult to see. However, in chronic glomerulonephritis the lobules are often shrunken so that the interlobular fissures become conspicuous (Figs. 1 and 2). In midsagittal sections through the vascular pole of such slightly shrunken glomeruli one sees from three to five fissures that penetrate nearly to the vascular pole. Some of the primary lobules thus formed are subdivided peripherally by fissures which extend from one-third to one-half the distance to the vascular pole and form secondary lobules. Capillary loops bulge from the surfaces of the secondary lobules to form small tertiary lobulations. The tertiary lobules are indistinct in the shrunken glomerulus (Fig. 1) but are easily seen in a normal glomerulus. In tangential sections through a glomerulus one sees small isolated, secondary or tertiary lobules, each composed of one or more capillary loops surrounded by epithelium.

Judged from the appearances seen in sections through different

planes one may conclude that there are from four to six primary lobules of irregular conical shape with their apices near the vascular pole and their wide bases at the surface of the glomerulus. Each primary lobule branches distally into secondary and tertiary lobules.

It is clear that the elaborate separation of the glomerulus into lobules serves the purpose of bringing nearly all the capillaries into contact with the surface. There are few capillaries that are not in contact with the surface epithelium at some part of their circumference, and those in the small peripheral tertiary lobules are usually largely or completely surrounded by epithelium. The glomerular epithelium covers the surface of the glomerulus and lines all the shallow intralobular as well as the deep interlobular clefts. There are obviously no capillary anastomoses across any of the fissures.

The glomeruli in newborn infants are smaller and of less complex structure than those of adults. The primary lobules are smaller and secondary lobulation is much less conspicuous.

The finer structure of the glomerulus is best seen in the small tertiary lobules at the surface. These consist of a few capillary loops closely invested by glomerular epithelium (Fig. 3). The epithelium covers the outer surfaces of the capillaries and fills the interstices between them. The nuclei between capillaries probably all belong to epithelial cells.

The Glomerular Epithelium

The glomerular epithelium is the visceral epithelial layer of the capsular space and is continuous around the vascular pole with the capsular epithelium (the parietal epithelial layer of the capsular space). Both the parietal and the visceral epithelial layers of the capsular space have the same embryonic origin as the cells of the convoluted tubules, since the capsular space is formed by invagination of the glomerular tuft into the expanded end of the primitive tubule. This relation is seen in tubular disease of the kidneys in which one may see hyaline granular degeneration, fatty degeneration and necrosis of the glomerular and capsular epithelial cells when these changes are present in the tubular epithelium.

As pointed out above, the epithelial layer lines all the interlobular and intralobular clefts and penetrates into the lobules between the capillaries. It therefore forms a support for the capillaries as well as an external covering. The epithelial cells are much more conspicu-

ous in some kidneys than in others. In infants the surface layer is columnar or cubical in shape and very conspicuous. In adults the cytoplasm of the epithelial cells is sometimes so abundant that the cells seem to compress the capillaries. More often, however, their nuclei are found in the interstices between the capillaries and sparsely distributed over the surface. Wide areas of the capillary surfaces may appear to be denuded of epithelium, but a careful study will always reveal a layer of epithelial cytoplasm separating the capillary basement membrane from the capsular space (Fig. 3). The surface epithelial layer undergoes postmortem autolysis rapidly, and the number and size of the cells are underestimated in poorly preserved tissue.

The parietal epithelium of the capsular space (the capsular epithelium) plays an important rôle in glomerulonephritis, since it is the source of the epithelial crescents; but the glomerular layer shows chiefly degenerative changes and never proliferates sufficiently to compress the glomerulus.

The Glomerular Endothelium

McGregor, 1929, has described and illustrated the finer histology of the normal glomerulus. In preparations stained by the Mallory-Heidenhain method the endothelial nuclei are easily distinguished from the epithelial by their position on the inner surface of the capillary basement membrane. In a large majority of normal kidneys the structure of the glomerulus corresponds to that shown in Figure 3, which I have called Grade 0. The epithelial nuclei greatly outnumber the endothelial. Practically no cytoplasm is seen about the endothelial nuclei or elsewhere on the inner surface of the basement membrane.

In Table I the degree of endothelial proliferation in 107 normal kidneys is recorded, the cases being arranged by decades. The kidneys classified as normal were from individuals who died of trauma or carbon monoxide poisoning not more than 6 hours after the injury was sustained. The majority lived less than 1 hour after the accident. A further requirement was that there should be no gross or microscopic evidence of any disease other than the fatal trauma or poisoning.

It will be noted from the table that 90 of the 107 cases showed Grade 0 endothelial proliferation, which indicates that the epithelial

nuclei were more numerous than the endothelial. A definite preponderance of epithelial nuclei is illustrated in Figure 3. In 16 of the 107 cases epithelial and endothelial nuclei were present in approximately equal numbers. This type of structure is graded + and is illustrated in Figure 4. Inasmuch as about one-seventh of the normal kidneys showed Grade + structure, this must be accepted as a variation within normal limits.

TABLE I

The Endothelium of the Glomerular Capillaries in Apparently Normal Kidneys *

Decade	No. of cases	Endothelial proliferation		
		o	+	1
1	9	9	0	0
2	8	6	2	0
3	17	13	4	0
4	25	21	4	0
5	17	15	1	1
6	11	9	2	0
7	12	12	0	0
8	6	4	2	0
9	2	1	1	0
Total	107	90	16	1

* In the o column the kidneys are listed in which the epithelial nuclei definitely outnumber the endothelial (Fig. 3). Grade + indicates that the epithelial and endothelial nuclei are approximately equal in number (Fig. 4). Grade 1 indicates a definite preponderance of endothelial nuclei (Fig. 5).

In only one instance did an apparently normal kidney show a definite preponderance of endothelial nuclei. This structure is called Grade 1 endothelial proliferation and is illustrated in Figure 5. Although no disease was found at postmortem to account for this endothelial increase, it is probably beyond the limits of the normal variation in structure.

Nussbaum, 1886, demonstrated cell boundaries in the endothelium of the frog's glomeruli. Bensley and Bensley, 1930, were able to see some cell boundaries in human glomeruli by staining with silver; and Zimmermann, 1933, observed cell boundaries in the glomeruli of cats. However, a majority of investigators have failed to demonstrate cell boundaries in the endothelium of the glomerular capillaries although they found them readily in the afferent arteriole.

There is disagreement in the literature as to the number of endo-

thelial nuclei normally present. Langhans, 1885, found only a few endothelial nuclei. Von Möllendorff, 1927, observed in the human glomerulus only a few endothelial nuclei. A little cytoplasm was found about the nuclei but no cell boundaries were demonstrated. Bargmann, 1929, 1931, and McGregor, 1929, agreed with Von Möllendorff that the endothelial cells are few in number, sparsely distributed and greatly outnumbered by the glomerular epithelial cells.

Borst, 1931, found that endothelial nuclei are more numerous than epithelial except in infants and young children where a reverse relation obtains. Borst used a technique which involves boiling of fresh tissue and results in great damage to the cytoplasm of the epithelial cells.

Van Waveren, 1935, used a technique similar to Borst's except for a short preliminary fixation in formalin before boiling. This method gives good pictures of the basement membrane but destroys the cytoplasm of epithelial cells. Van Waveren estimated the number of endothelial and epithelial nuclei in corresponding volumes of glomerular tissue and came to the conclusion that endothelial nuclei always outnumber epithelial. He presents the interesting hypothesis that even in glomerulonephritis the endothelial cells do not increase in number but only in size. It seems, however, that the boiling method damages the epithelial cells so severely that one may be led to underestimate their number. It is also to be noted that the postmortems from which this author apparently obtained his material were performed 36 to 42 hours after death. Ordinarily the surface layer of glomerular epithelial cells has undergone extensive autolysis by this time, and one would not expect to find all of these cells still present.

Van Waveren maintains that the appearances which I have described as glomerulitis do not represent an actual increase of endothelial cells but merely an apparent increase due to contraction of empty capillaries. Empty collapsed capillaries, however, usually show a wavy basement membrane and are easily distinguished from glomerulitis.

Wilbur, 1931, studied the kidneys of 25 apparently healthy subjects dead from accidental causes. He found that endothelial nuclei were from four to six times as numerous as epithelial.

My own observations have been recorded above. The epithelial cells were found to outnumber the endothelial in 90 of 107 normals

and usually the former were much more numerous than the latter. In 16 instances the endothelial and epithelial cells were approximately equal in number. My conclusion is that a definite preponderance of endothelial cells with an increase of their cytoplasm, as shown in Figure 5, represents a glomerulitis. It will be shown presently that the endothelial cells often show a great increase in number and size in infectious and toxic processes, and if one examines the kidneys from a large series of consecutive postmortems he will find that a fairly high percentage of them show more endothelial than epithelial cells in the glomeruli. It appears from Table II that 41.7 per cent of the 865 cases studied showed a definite excess of epithelial over endothelial cells, while in 30.4 per cent the reverse relation obtained. In 27.8 per cent the endothelial and epithelial cells were approximately equal in number. The material studied, however, is not a uniform sample of postmortem material since there is an undue proportion of infectious processes. In a corresponding number of consecutive postmortems the percentage with Grade o endothelium would doubtless be greater.

TABLE II

*Age Distribution of the Endothelial Patterns in All the Cases Studied, Including the Normals**

Decade	Endothelium										Total
	o		+		1		2		3		
	No. cases	Per cent	No. cases	Per cent	No. cases	Per cent	No. cases	Per cent	No. cases	Per cent	
0–10 yrs.	42	79.3	6	11.3	4	7.5	1	2.0	0	0	53
10–20 "	18	30.0	19	31.6	18	30.0	4	6.7	1	1.7	60
20–30 "	34	26.6	34	26.6	46	36.0	12	9.4	2	1.5	128
30–40 "	50	34.0	53	36.0	36	24.5	7	4.8	1	0.7	147
40–50 "	74	42.8	48	27.7	43	24.8	8	4.6	0	0	173
50–60 "	56	47.5	23	19.5	35	29.6	4	3.4	0	0	118
60–70 "	53	46.9	33	29.2	22	19.5	5	4.4	0	0	113
70–80 "	23	41.1	23	41.1	10	17.8	0	0	0	0	56
80–90 "	10	..	2	..	4	..	0	..	0	..	16
90–100 "	1	..	0	..	0	..	0	..	0	..	1
Total	361	41.7	241	27.8	218	25.2	41	4.7	4	0.5	865

* Reading horizontally one sees the number of cases of each endothelial pattern and the percentage of each pattern in the decade. Reading vertically one may compare the frequency of any endothelial pattern in the various decades. Grade o indicates that epithelial outnumber endothelial cells; + indicates that epithelial and endothelial cells are approximately equal in number; 1 indicates a definite preponderance of endothelial cells (Fig. 3); 2 indicates a rather marked glomerulitis but somewhat below the clinical stage; 3 indicates a clinical glomerulonephritis.

The Influence of Age on the Endothelial Pattern

In Table II the distribution of all the cases studied, including the normals, is shown according to the decades and the endothelial pattern. The accuracy of the percentages may be judged by the numbers on which they are based. In the first decade the percentage with Grade 0 endothelium is very high. In infants and young children this endothelial pattern prevails even in association with infectious diseases. The low percentage with Grade 0 in the 2nd, 3rd and 4th decades is no doubt due to the inclusion of a large number of cases of puerperal sepsis and bacterial endocarditis. It is improbable that age influences the endothelial pattern after the first decade.

TABLE III

Distribution of the Endothelial Patterns in the Normals and the Various Diseases that were Studied *

	Number of cases	Endothelium				
		Per cent 0	Per cent +	Per cent 1	Per cent 2	Per cent 3
1. Normals	107	84.1	15.0	0.9	0	0
2. Miscellaneous non-infections	94	55.0	30.8	14.0	0	0
3. Primary hypertension	100	46.0	41.0	11.0	2.0	0
4. Lobar pneumonia	112	51.8	29.5	13.4	5.4	0
5. Acute rheumatic endocarditis	61	44.0	15.0	38.0	3.0	0
6. Acute bacterial endocarditis	37	30.0	27.0	43.0	0	0
7. Subacute bacterial endocarditis	85	3.5	17.6	60.0	16.5	2.4
8. Puerperal sepsis	84	6.0	41.7	38.0	12.0	2.4
9. Pulmonary tuberculosis	73	15.1	45.2	37.0	2.7	0
10. Miscellaneous infections	112	36.6	25.9	29.5	8.0	0

* Explanation as in Table II.

Effect of Disease on Endothelial Pattern

Miscellaneous Non-infectious Diseases (Table III, No. 2): This group includes a large variety of diseases in which infection plays no rôle except as a terminal complication. The diseases included are as follows: old valve defect, 15; malignant tumors (carcinoma of stomach, pancreas, and so on), 19; pernicious anemia, 7; atrophy of liver, 8; diabetic coma, 7; alcoholism, 5; coronary disease, 4; burns, 3; arsenic poisoning, 2; and 1 each of 24 other diseases. The frequency of the various endothelial patterns is shown in Table III, No. 2. A Grade 1 glomerulitis was present in 13 of the 94 cases (14 per cent).

It was present in the following diseases: pernicious anemia, 4 cases (out of 7 examined); old healed valvular heart disease, 5 cases; 1 case each of subacute atrophy of the liver, subacute combined degeneration of the spinal cord, carcinoma of the ampulla of Vater, and right heart failure. Terminal infections may have played a rôle in causing the glomerulitis but this could not be established conclusively.

Primary Hypertension (Table III, No. 3): In this group there were 11 cases of Grade 1, and 2 of Grade 2 glomerulitis. In the 2 cases with Grade 2 glomerulitis death was due to renal insufficiency. The causes of death in the 11 cases with Grade 1 glomerulitis were as follows: myocardial exhaustion with congestive heart failure, 4; renal insufficiency, 2; coronary disease, 2; and 1 case each of cerebral hemorrhage, pyloric obstruction and rupture of the aorta. It is not uncommon to find a definite endothelial increase in hypertension with renal insufficiency — glomerulitis often seems to be an essential part of the renal lesion. Not infrequently patients with primary hypertension die of some complicating infection such as septicemia or pneumonia, and occasionally in such cases clinical acute glomerulitis is found at postmortem; but hypertensives with an obvious terminal infection were not included in this group. The glomerulitis in the 9 cases without renal insufficiency cannot be satisfactorily explained as a result of infection.

We shall now consider the glomerular structure in definite infectious diseases.

Lobar Pneumonia (Table III, No. 4): One-hundred-twelve cases of this disease were studied. It is surprising to find that the frequency of glomerulitis is not significantly greater than in the non-infectious diseases. It is true that there are 6 cases of Grade 2 glomerulitis, but over 50 per cent of the kidneys show the Grade 0 endothelial pattern. No correlation could be found between the degree of endothelial proliferation and the duration of the illness or the age of the patient. Apparently pneumococci do not stimulate the glomerular endothelium to the degree that streptococci do.

It is recognized in the literature that clinical acute glomerulonephritis may follow lobar pneumonia, but postpneumonic nephritis is generally believed to be quite rare. Abrahams, 1920, found that acute nephritis developed in only 2 of 558 cases of typical lobar pneumonia. Eliassow, 1920, described a convincing case of acute

glomerulonephritis in a male 38 years of age, who developed symptoms (albuminuria, edema and moderate hypertension) on the 11th day after the onset of pneumonia. The disease ended in recovery about 6 months later. Seegal, 1935, in a study of 1004 cases of lobar pneumonia found that 7 developed acute glomerulonephritis.

McIntosh and Reimann, 1926, studied renal function during pneumonia. They noted that some previous investigators had found a slight decrease and others a slight increase of kidney function. They studied the elimination of phenolsulphonephthalein after intravenous injection, and also determined the index of urea concentration. The kidneys frequently showed an increased functional ability which began before the crisis and persisted for several days after it. No examples of decreased functional power were mentioned.

Neale, 1928, examined the urine of 287 adult patients with lobar pneumonia. In 3.4 per cent the albumin was +++, in 48 per cent +, and in 47.5 per cent it was absent. No examples of acute glomerulonephritis were found in the 42 postmortem examinations that were made. In 102 cases of pneumococcal infection other than lobar pneumonia, normal urine was found in 46 cases, albumin alone in 45, and albumin casts and blood in 11. In 21 cases of acute pneumococcal infection in children under 7 years of age the urine was normal in 5, contained some albumin in 12, and contained albumin, casts and blood in 4.

Lyttle and Rosenberg, 1929, state that pneumonia in children is frequently followed by nephritis.

Blackman, Brown and Rake, 1931, injected rabbits intravenously with pneumococcal autolysate and intradermally with pneumococci. Eighteen of the rabbits developed generalized edema with ascites. The lesions in the kidneys were interpreted as comparable to human acute and subacute nephritis. These authors also found mild acute and subacute nephritis in 40 to 50 per cent of persons dead of pneumococcal infections. However, there was no anatomical evidence submitted which indicates that any of these renal lesions were true glomerulonephritis. The lesions described were chiefly tubular injuries, thrombosis of glomerular capillaries and occasional epithelial crescents.

Blackman and Rake, 1932, found acute nephritis of considerable intensity in 9.5 per cent of a group of young infants with pneumococcal infections (empyema, organizing pneumonia, otitis media,

meningitis). The diagnoses were made by postmortem examination; no case was recognized as nephritis clinically. They found no cases of nephritis in older children or adults following pneumococcal infections.

Blackman and his associates use the term "nephritis" in a very broad sense to include lesions that are chiefly tubular, and do not restrict it to glomerulonephritis.

The fact that persons suffering with lipoid nephrosis frequently develop pneumococcal peritonitis has led to the belief that pneumococci are responsible for this type of renal disease.

Acute Rheumatic Endocarditis (*Table III, No. 5*): This group includes two clinical types: (*a*) those dying during the first attack from septicemia or a complicating infection such as pericarditis; and (*b*) those dying from a recurrent acute attack in which valvular insufficiency was a contributory cause of death. Glomerulitis was somewhat more frequent in the first type. It may be seen in Table III that glomerulitis was present in 41 per cent. Although the group is small this percentage seems significantly higher than in the preceding group. In rheumatic endocarditis there are comparatively few bacteria in the circulating blood and one would not expect to find as much glomerular irritation as in bacterial endocarditis.

Acute Bacterial Endocarditis (*Table III, No. 6*): This group includes primary bacterial endocarditis of less than 6 weeks duration and bacterial endocarditis secondary to some major infection. The duration of the illness is much shorter than in the subacute form. The number of cases is too small to have much significance, but there is a suggestion that infections of this type cause proliferation of the glomerular endothelium.

Subacute Bacterial Endocarditis (*Table III, No. 7*): In this disease, which is nearly always caused by streptococci, there is usually a prolonged bacteriemia and the glomeruli are exposed to large quantities of bacterial poisons for many months. As might be anticipated, the effects on the glomerular endothelium are very striking. Only 3.5 per cent of the glomeruli show the Grade 0 endothelial pattern, as compared with 84.1 per cent in the normals, and 79 per cent of the cases show glomerulitis. The higher degrees of glomerulitis are numerous, and in 2 instances the typical structure of clinical acute glomerulonephritis was present although it was not recognized

as such clinically. Seven cases were omitted from the table because the glomeruli were so extensively involved with embolic lesions that the endothelial pattern could not be determined. There is no correlation between the number and size of the embolic lesions and the intensity of the endothelial proliferation. Many cases of severe diffuse glomerulitis showed no embolic lesions. The glomerulitis in the cases of acute endocarditis mentioned above is much less intense than in the subacute group, but no definite relation could be established in the subacute group between the duration of the disease and the intensity of the glomerulitis. The glomerulitis may be more pronounced in a case of 2 months duration than in one that lasted over 1 year.

In bacterial endocarditis every transition may be found between kidneys that show the normal Grade 0 endothelial pattern and those that show the structure of typical clinical acute glomerulonephritis. In a large series of these cases one may trace the pathogenesis of the glomerular lesions, and the various stages are illustrated in Figures 4, 5, 6 and 7. The more or less constant presence of streptococci in the blood in this disease over a period of several months would lead us to expect a much higher incidence of clinical acute glomerulonephritis; yet 60 per cent of the cases show only Grade 1 glomerulitis. Evidently the development of the clinical lesion depends on some factor other than the presence of streptococci in the blood stream. Baehr and Lande, 1920, found that 9 of 77 cases of subacute streptococcic endocarditis showed diffuse glomerular damage.

Puerperal Sepsis (*Table III, No. 8*): In this disease, as in subacute bacterial endocarditis, there is a high incidence of glomerulitis, 52.4 per cent. Most of these are Grade 1 glomerulitis; but 12 per cent show the Grade 2 pattern, and there are 2 cases of clinical acute glomerulonephritis. This disease is usually due to streptococci, although other organisms, *e.g.* staphylococci, are occasionally responsible. Peritonitis and bacteremia are the usual fatal complications. As in the case of subacute bacterial endocarditis, there are numerous transitions between mild and severe glomerulitis, and the distinction between subclinical and clinical glomerulonephritis is somewhat arbitrary.

Pulmonary Tuberculosis (*Table III, No. 9*): In this group only those cases are included in which the patient died of chronic pulmonary tuberculosis. In all instances the lungs were extensively

destroyed by cavities and tuberculous tissue. It is probable that the high frequency of glomerulitis, 39.7 per cent, is due to the pyogenic infection in the cavities rather than to any toxic products of the tubercle bacillus. Some of these kidneys contain deposits of amyloid. In a previous publication, 1933, I have called attention to the increase of endothelial nuclei that precedes the deposition of amyloid. It appears from the present study that this endothelial increase is the result of the underlying infection and is independent of the formation of amyloid. Occasionally a clinical acute glomerulonephritis follows pulmonary tuberculosis.

Miscellaneous Infections (Table III, No. 10 and Table IV): This group includes 112 cases of various infectious processes encountered

TABLE IV

*Miscellaneous Infections Arranged According to the Disease and the Degree of Endothelial Proliferation**

Infection	Endothelium				Total cases
	0	+	1	2	
Typhoid fever	3	2	0	0	5
Septicemia	5	4	4	1	14
Peritonitis, appendicitis	8	6	7	2	23
Pyelonephritis	0	0	2	0	2
Acute and chronic suppuration	3	12	9	1	25
Diphtheria	6	1	0	1	8
Scarlet fever	6	0	0	0	6
Bronchopneumonia	2	1	1	1	5
Endarteritis	0	0	1	0	1
Septic sore throat	1	1	2	0	4
Pericarditis or pleuritis	1	2	2	0	5
Meningitis	6	0	3	0	9
Acute hepatitis	0	0	0	1	1
Lupus erythematosus	0	0	1	1	2
Purpura hemorrhagica	0	0	0	1	1
Enterocolitis	0	0	1	0	1
Total	41	29	33	9	112

* Explanation as in Table II.

in a series of consecutive postmortems. No instance of clinical acute glomerulonephritis following an infection was encountered in this series of postmortems, but clinical glomerulonephritis is commonly related to such infections. In a group of 57 cases of clinical acute glomerulonephritis collected from a series of 23,000 postmortems there were 25 cases that followed miscellaneous infections of the type

listed in Table IV: 37.5 per cent of this group show glomerulitis, Grades 1 and 2.

In Table IV the group is arranged according to the disease and the endothelial pattern. The surprisingly high incidence of the Grade 0 endothelial pattern is due to the inclusion of 27 cases in children under 10 years of age, 22 of which showed the normal Grade 0 structure. If these 27 cases are excluded the percentage of Grade 0 type drops from 36.6 to 22 per cent, and is then more comparable to the other groups shown in Table III which are chiefly adults. It is to be noted that diphtheria and scarlet fever do not have much effect on the endothelium. Fahr, 1916, found only 1 case of acute glomerulonephritis from postmortem examination of 110 cases of diphtheria. It is known that glomerulonephritis is rarely found in persons who die during an attack of scarlet fever.

The Relation of Endothelial Proliferation to Albuminuria

In the 246 cases included in Table V the urine was examined at some time during the fatal illness and usually only a few days before

TABLE V

The Relation of Endothelial Proliferation to Albuminuria

Endothelium	Albuminuria				Total
	0 or trace		+ to ++++		
	No. of cases	Per cent	No. of cases	Per cent	
0	47	74.6	16	25.4	63
+	41	67.2	20	32.8	61
1	74	71.8	29	28.2	103
2	10	52.6	9	47.4	19
Total	172		74		246

death. The cases in which the urine contained no albumin or only a trace are listed together. If this group be subdivided, there are 100 with no albumin and 72 with a trace. The cases in which albuminuria was graded + to ++++ are listed together, since these are only rough estimations of the amount of albumin. It is obvious that there is no relation between the presence or the amount of albumin and the degree of endothelial proliferation. A few cases with Grade 0 endothelium showed heavy albuminuria, and some cases with Grade 2 proliferation showed no albumin. It may be argued that this

is evidence that the endothelial proliferation is not an inflammatory reaction, but it is well established that albuminuria depends on some injury of the capillary endothelium which makes it permeable to protein. There is more albumin in the urine in lipoid nephrosis, which often shows little or no endothelial proliferation, than in glomerulonephritis with a pronounced endothelial increase.

Cloudy swelling of the kidneys likewise shows no direct relation to increase of endothelial cells, since it may be as pronounced in those with the Grade 0 endothelial pattern as in those with Grade 2. However, those with the Grade 2 pattern always showed cloudy swelling.

The Rôle of the Polymorphonuclear Leukocyte

Gräff, 1916, emphasized the importance of polymorphonuclear leukocytes in acute glomerulonephritis and expressed the opinion that the number of these cells in the glomerular capillaries affords a distinction between simple inflammatory irritation and true nephritis. In clinical acute glomerulonephritis the polymorphonuclears are often conspicuous and are partly responsible for capillary obstruction when they are distributed among the endothelial cells; but when present alone they rarely cause permanent capillary obstruction since they do not become attached to the capillary wall.

In the subclinical forms of glomerulonephritis which are discussed in this paper, the polymorphonuclears are sometimes present in considerable numbers but usually they are inconspicuous. In estimating the degree of endothelial proliferation these leukocytes were, of course, not enumerated. The leukocytes probably accumulate in the capillaries because the capillary walls have been injured and they may also be held mechanically in capillaries that are partly obstructed by endothelium.

Focal Glomerulonephritis

The embolic glomerulonephritis associated with bacterial endocarditis is a well recognized type. Clinically it is characterized chiefly by hematuria; anatomically there are focal lesions usually considered embolic in origin. But in all probability these focal lesions are thrombotic and proliferative in character and not embolic. They are apparently due to the lodgement of bacteria in the capillary tufts but they are not infarcts (Bell, 1932). They occur frequently in the absence of endocarditis.

Aside from this so-called embolic type associated with endocarditis, focal glomerulonephritis is ill-defined both clinically and anatomically. Clinicians often diagnose as focal glomerulonephritis the transitory hematuria that sometimes accompanies tonsillitis and other infections when no hypertension, edema or renal insufficiency develops. Thus Werboff, 1928, speaks of hematuria accompanying tonsillitis and appendicitis as due to focal glomerulonephritis. Baehr's benign hemorrhagic nephritis, 1926, evidently belongs in this category. The underlying pathology of these transitory hematurias is not known with certainty, but it is probably glomerular bleeding from ruptured capillaries.

There is no clinical condition other than transitory bleeding from the parenchyma of the kidney that can be interpreted as focal glomerulonephritis. Postmortem studies show that albuminuria developing during the course of an infection is due to diffuse and not to focal glomerular injury.

Fahr uses "focal glomerulonephritis" in a pathological sense to include thrombosis or necrosis of individual capillary loops. Only a few glomeruli may be involved and only a part of the affected glomerulus is obstructed. Apparently no constant clinical picture is associated with such focal lesions. Fahr believes that focal glomerulonephritis is due to the lodgement of bacteria in the glomerulus, while diffuse lesions are caused by soluble toxins.

In this series of 865 cases capillary thromboses were rarely seen except in association with endocarditis. Occasionally a few glomeruli show Grade 1 or 2 glomerulitis of a diffuse type when all the others are normal, and usually there are some normal glomeruli when the great majority show glomerulitis. Even in clinical acute glomerulonephritis one may find a few normal glomeruli. A glomerulitis may be focal in the sense that only a small proportion of the glomeruli are involved.

The Significance of Endothelial Proliferation

It is concluded from the foregoing studies that endothelial patterns o and + are normal and that the o type occurs much oftener in the first than in subsequent decades. A large variety of infectious and toxic processes irritate the glomerular capillaries and cause an increase in the number and size of the endothelial cells. The most pronounced endothelial reactions result from severe streptococcic in-

fections, notably subacute bacterial endocarditis and puerperal sepsis. In these infections the endothelial reaction often approaches and sometimes reaches the intensity that is found in clinical acute glomerulonephritis. It appears that a wide variety of irritants produce glomerulitis of a subclinical type and it is only when a definite capillary obstruction is produced that the clinical symptoms of acute glomerulonephritis develop.

Subclinical glomerulitis differs from clinical acute glomerulonephritis only in the extent of the endothelial proliferation. The fundamental pathological reaction is endothelial proliferation in both conditions; and it seems justified, therefore, to consider subclinical glomerulitis as an early stage of clinical glomerulonephritis. The numerous transitions between the two diseases and the similar etiology also support this interpretation. Cases of acute glomerulonephritis that terminate in complete healing may possibly resemble the severe subclinical forms more than they resemble the fatal acute cases.

The Nature of the Endothelial Reaction: The usual interpretation of the endothelial reaction is that it is a proliferative inflammation, *i.e.* the increase in the number of cells is due to division of preexistent endothelial cells. It is recognized that the endothelial nuclei become larger and that the amount of cytoplasm about them increases greatly. The objection to this interpretation is that no mitoses are to be seen in the endothelial cells. Numerous investigators have confirmed the absence of mitoses. In this study of subclinical glomerulitis no mitoses were seen. One is therefore forced to conclude that if cell division actually occurs it is largely of the amitotic type.

Another theory that merits consideration is that the increase of cells is due to the lodgement of mononuclear leukocytes in the capillaries. It is difficult to distinguish mononuclear leukocytes from endothelial cells unless the former lie free in the lumen of the capillary. In Figures 5 and 6 there are some cells that are obviously mononuclear leukocytes and there are others that may belong to this group. In fact the study of glomerulitis of Grades 1 and 2 brings out considerable evidence that at least some of the increase of intracapillary cells is due to the lodgement of mononuclear leukocytes.

A third theory suggested by Van Waveren is that the endothelial

cells increase only in size and not in number. He explains the appearances of glomerulitis, which I have described, as due to contraction of the capillaries. He is also inclined to believe that true glomerulonephritis may be explained similarly as merely an increase in size of endothelial cells. The drawings (Figs. 3–8) were all made at the same magnification and most of the capillaries are distended, except in Figure 4. It seems incredible that these appearances could all be due merely to increase in the size of the endothelial cells.

We may conclude that glomerulitis is due in part to enlargement of the preexistent endothelial cells and in part to lodgement of mononuclear leukocytes, but endothelial proliferation is probably the most important feature of the reaction.

To what extent is glomerulitis a reversible process? No definite information is available on this problem. On theoretical grounds we may believe it reversible until an intensity is attained that results in the formation of hyaline intracapillary fibers between the cells. The formation of fibers leads to fixation of the cells and permanent obliteration of the capillary. The presence of intracapillary fibers may be used to distinguish the clinical from the subclinical stage of glomerulitis.

If one accepts the theory I have sought to establish in this paper that subclinical glomerulitis differs from clinical glomerulonephritis only in intensity, a broader approach to the etiology of glomerulonephritis is available. A large group of infectious and toxic processes is concerned in the etiology of the disease. The glomerular capillaries are injured probably by various toxic substances. Sensitization to bacterial or other protein may play an important rôle, but it is unnecessary to assume that sensitization is essential in the development of the lesion. Masugi, 1933, has shown that glomerulonephritis develops readily in a sensitized animal when the antigen is injected into the renal artery, but this experiment is about the same as the Arthus phenomenon, and is not duplicated in the clinical development of nephritis. The cases of acute glomerulonephritis that develop within a week after the onset of an acute infection are not easily explained as a result of hypersensitiveness. A widespread sensitization to bacterial protein must be assumed if one is to explain subclinical glomerulitis on this basis.

Summary and Conclusions

A microscopic study of the kidneys was made in 107 cases of death from accidental causes, in 194 cases of death from non-infectious diseases, and in 564 cases of death from various infectious processes.

In the 107 normals the glomerular epithelial cells definitely outnumbered the endothelial in 84.1 per cent, the endothelial outnumbered the epithelial cells in only 1 instance (0.9 per cent), and the two types of cells were approximately equal in number in 15 per cent. It was concluded that a definite preponderance of endothelial over epithelial cells represents a glomerulitis.

A Grade 1 glomerulitis was found in 14 per cent of non-infectious processes.

In lobar pneumonia glomerulitis was found in only 18.8 per cent, but in the other infectious groups it varied from 37.5 to 78.9 per cent.

The highest incidence of glomerulitis was found in puerperal sepsis (52.4 per cent) and subacute bacterial endocarditis (78.9 per cent).

It is evident that a variety of toxic substances, especially those derived from streptococci, may irritate the glomerular capillaries and produce an increase of endothelial cells.

In a Grade 2 glomerulitis the glomerular capillaries are filled with cells and occasionally a few intracapillary fibers are present. The distinction from clinical glomerulonephritis is somewhat arbitrary.

The glomerulitis is probably due chiefly to endothelial proliferation, but the lodgement of mononuclear leukocytes in the capillaries seems to play a rôle of some importance.

There is no relation between the presence or the amount of albumin in the urine and the degree of endothelial proliferation.

There is no anatomical basis for a diagnosis of focal glomerulonephritis except in instances of transitory glomerular bleeding not associated with symptoms of nephritis, and in cases of bacterial endocarditis.

BIBLIOGRAPHY

Abrahams, Adolphe. Lobar pneumonia. A clinical analysis of 558 consecutive cases. *Lancet*, 1920, **2**, 543–546.

Baehr, George, and Lande, Herman. Glomerulonephritis as a complication of subacute streptococcus endocarditis. *J. A. M. A.*, 1920, **75**, 789–790.

Baehr, George. A benign and curable form of hemorrhagic nephritis. *J.A.M.A.*, 1926, **86**, 1001–1004.

Bargmann, W. Zur Morphologie des Nierenglomerulus. *Ztschr. f. Zellforsch. u. mikr. Anat.*, 1929, **8**, 765–771.

Bargmann, W. Über Strucktur und Speicherungsvermögen des Nierenglomerulus. *Ztschr. f. Zellforsch. u. mikr. Anat.*, 1931, **14**, 73–137.

Bell, E. T. A Text-Book of Pathology. Lea & Febiger, Philadelphia, 1934, Ed. 2 (see Figs. 217 and 218).

Bell, E. T. Amyloid disease of the kidneys. *Am. J. Path.*, 1933, **9**, 185–203.

Bell, E. T. Glomerular lesions associated with endocarditis. *Am. J. Path.*, 1932, **8**, 639–664.

Bensley, R. R., and Bensley, Robert D. The structure of the renal corpuscle. *Anat. Record*, 1930, **47**, 147–165.

Blackman, Sam S., Brown, J. Howard, and Rake, Geoffrey. The production of acute nephritis by means of a pneumococcal autolysate. *Bull. Johns Hopkins Hosp.*, 1931, **48**, 74–79.

Blackman, Sam S., and Rake, Geoffrey. Acute pneumococcal nephritis. *Bull. Johns Hopkins Hosp.*, 1932, **51**, 217–233.

Borst, J. G. G. Der Bau des normalen Glomerulus. *Ztschr. f. mikr.-anat. Forsch.* 1931, **23**, 455–483.

Clawson, B. J., Bell, E. T., and Hartzell, T. B. Valvular diseases of the heart, with special reference to the pathogenesis of old valvular defects. *Am. J. Path.*, 1926 **2**, 193–234 (see page 230).

Eliassow, Walter. Über akute Nephritis nach Pneumonie und Grippe. *Ztschr. f. Urol.*, 1920, **14**, 433–440.

Fahr, Th. Beiträge zur Diphtherie-Frage. *Virchows Arch. f. path. Anat.*, 1916, **221**, 38–66.

Fahr, Th. Herdförmige Glomerulonephritis. Handbuch der speziellen pathologishen Anatomie und Histologie, Henke, F., and Lubarsch, O. J. Springer, Berlin, 1925, 348–362.

Fahr, Th. Zur Pathogenese der akuten Glomerulonephritis. *Deutsche med. Wchnschr.*, 1926, **52**, 735–737.

Gräff, Siegfried. Untersuchungen über das Verhalten der Leukozyten im Glomerulusgebiet bei der akuten Glomerulonephritis. *Deutsche med. Wchnschr.*, 1916, **42**, 1092–1093.

Gross, W. Frische Glomerulonephritis (Kriegsniere). *Beitr. z. path. Anat. u. z. allg. Pathol.*, 1919, **65**, 387–422.

Hückel, R. Beitrag zu den Veränderungen im Beginn der diffusen Glomerulonephritis. *Virchow's Arch. f. path. Anat.*, 1929, **271**, 211–225.

Kuczynski, Max H., and Dosquet, H. Zweiter anatomischer Beitrag zur Pathogenese der Glomerulonephritis. *Krankheitsforschung*, 1926, **3**, 201–247.

Langhans, Th. Ueber die entzündlichen Veränderungen der Glomeruli und die acute Nephritis. *Virchows Arch. f. path. Anat.*, 1885, **99**, 193–250.

Lyttle, John D., and Rosenberg, Lester. The prognosis of acute nephritis in childhood. *Am. J. Dis. Child.*, 1929, **38**, 1052–1063.

Masugi, Matazo. Über das Wesen der spezifischen Veränderungen der Niere und der Leber durch das Nephrotoxin bzw. das Hepatotoxin (zugleich ein Beitrag zur Pathogenese der Glomerulonephritis und der eklamptischen Lebererkrankung). *Beitr. z. path. Anat. u. z. allg. Pathol.*, 1933, **91**, 82–112.

McGregor, Leone. The finer histology of the normal glomerulus. *Am. J. Path.*, 1929, **5**, 545–557.

McIntosh, John F., and Reimann, Hobert A. Kidney function in pneumonia. *J. Clin. Investigation*, 1926–27, **3**, 123–130.

Neale, A. Victor. The kidneys in pneumococcal infections. *Brit. M. J.*, 1928, **2**, 891–892.

Nussbaum, M. Ueber den Bau und die Thätigkeit der Drüsen. *Arch. f. mikr. Anat.*, 1886, **27**, 442–480.

Seegal, David. Acute glomerulonephritis following lobar pneumonia. Analysis of seven cases. *Arch. Int. Med.*, 1935, **56**, 912–919.

Van Waveren, E. K. Over de Anatomie en histologische Diagnostiek van Glomerulonephritis. Van Gorcum & Comp., Assen, 1935, 1–213.

Volhard, F. Über Wandlungen in der Nephritislehre. *Wien. med. Wchnschr.*, 1922, **72**, 430–435.

Volhard, F. Handbuch der inneren Medizin, von Bergmann, G., and Staehelen, R. Julius Springer, Berlin, 1931, 1183–1203.

Von Möllendorff, W. Einige Beobachtungen über den Aufbau des Nierenglomerulus. *Ztschr. f. Zellforsch. u. mikr. Anat.*, 1927, **6**, 441–450.

Werboff, S. Nephritiden als Folge von Tonsillitis und Appendicitis; Einfluss der Tonsillektomie und Appendektomie auf ihren Verlauf. *Ztschr. f. Urol.*, 1928, **22**, 592–609.

Wilbur, Dwight L. The normal renal glomerulus of man; histologic consideration. *Arch. Path.*, 1931, **12**, 413–428.

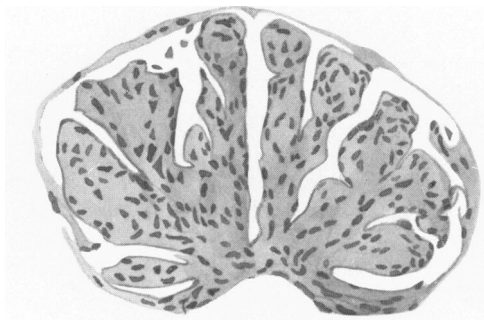
Zimmermann, K. W. Über den Bau des Glomerulus der Säugerniere. Weitere Mitteilungen. *Ztschr. f. mikr.-anat. Forsch.*, 1933, **32**, 176–278.

DESCRIPTION OF PLATES

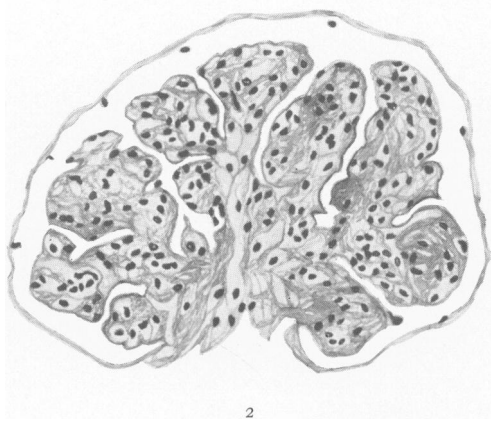
PLATE 129

FIG. 1. Glomerulus from chronic glomerulonephritis. This is a stage just preliminary to hyaline degeneration. The shrinkage of the lobules accentuates the interlobular septa. Drawing. Low magnification.

FIG. 2. Glomerulus from chronic glomerulonephritis. The shrinkage is not so great as in Fig. 1, and secondary lobules are more distinct. Drawing. Low magnification.



1



2

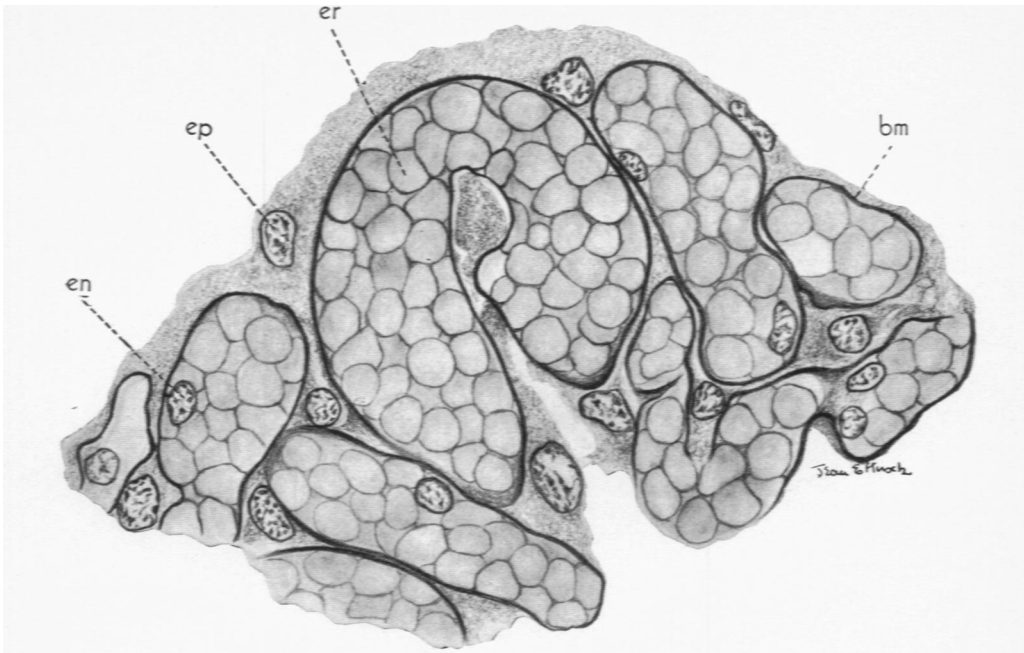
PLATE 130

FIG. 3. Lobule of a glomerulus showing the normal, Grade o, endothelial pattern. The capillaries are distended. Note that epithelial outnumber the endothelial nuclei. From a case of influenzal pneumonia.

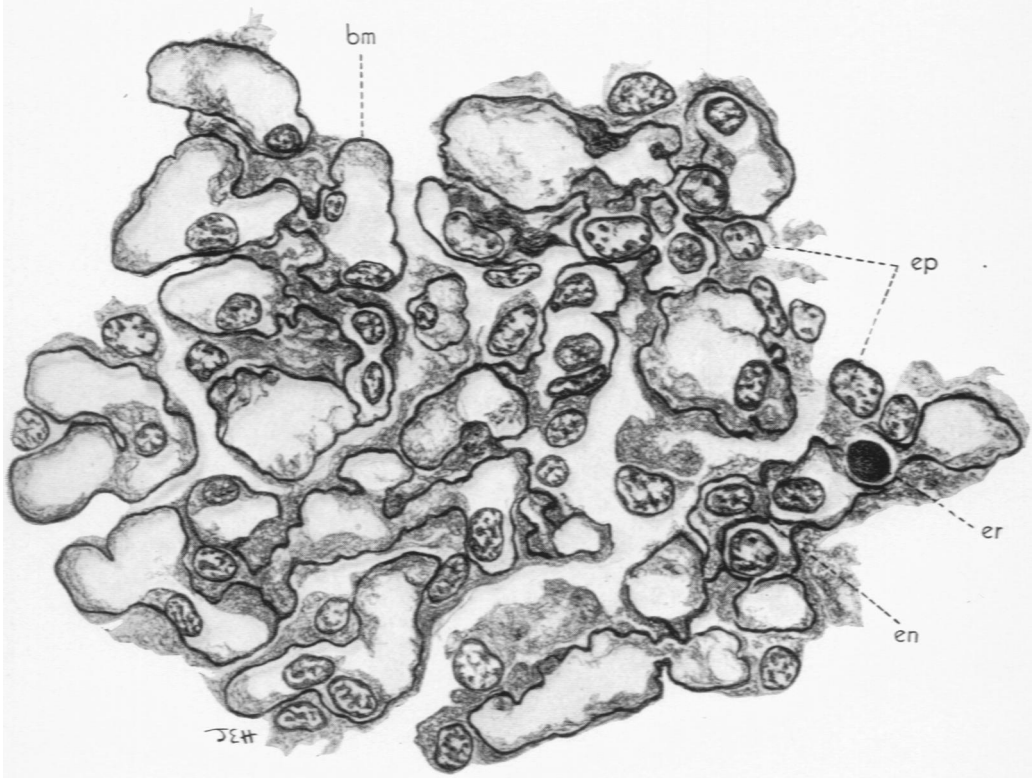
bm = basement membrane of capillary; en = endothelial nucleus; ep = epithelial nucleus; er = erythrocyte. Mallory-Heidenhain stain. Drawing × 1200.

FIG. 4. Lobule of a glomerulus showing the normal, Grade +, endothelial pattern. Note that the endothelial and epithelial nuclei are approximately equal in number. The capillaries are empty of erythrocytes but are not collapsed. The basement membrane is somewhat wavy because of the absence of distention. From a case of puerperal septicemia.

Lettering as in Fig. 3. Mallory-Heidenhain stain. Drawing × 1200.



3



4

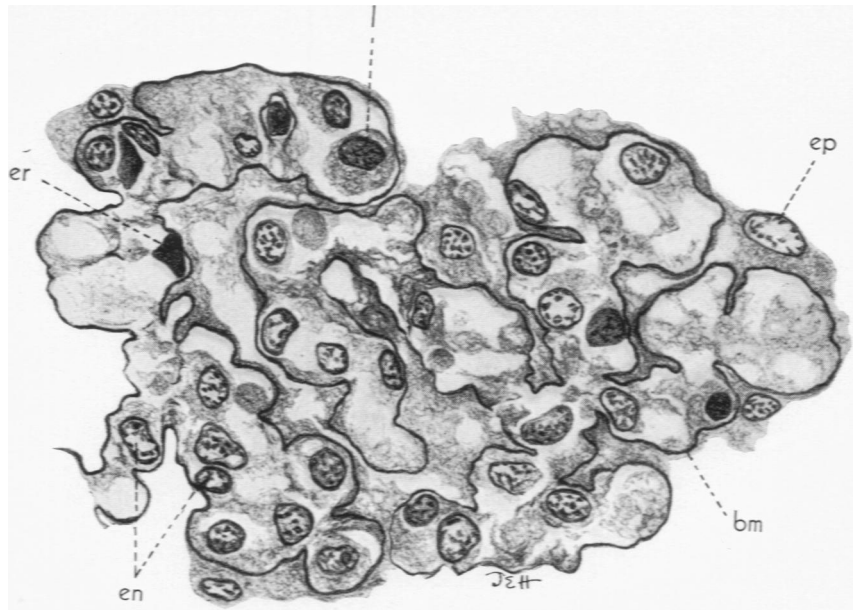
PLATE 131

FIG. 5. Lobule from a glomerulus showing Grade 1 glomerulitis. The endothelial cells definitely outnumber the epithelial and have produced a partial capillary obstruction. Nearly all the cells within the capillaries appear to be of endothelial origin, but one definite mononuclear leukocyte is shown. From a case of septicemia.

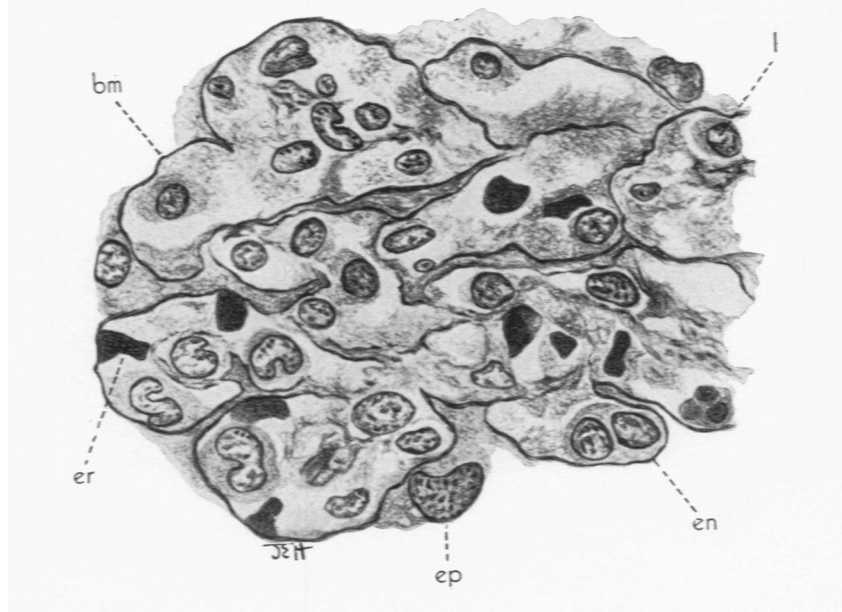
l = mononuclear leukocyte. Other lettering as in Fig. 3. Mallory-Heidenhain stain. Drawing × 1200.

FIG. 6. Lobule from a glomerulus showing Grade 2 glomerulitis. The capillaries are somewhat more closely packed with cells than in Fig. 5. A few erythrocytes are seen which are distorted by pressure. An occasional definite mononuclear leukocyte is seen, and the cells with indented nuclei may be leukocytes. From a case of septicemia.

l = mononuclear leukocyte. Other lettering as in Fig. 3. Mallory-Heidenhain stain. Drawing × 1200.



5



6

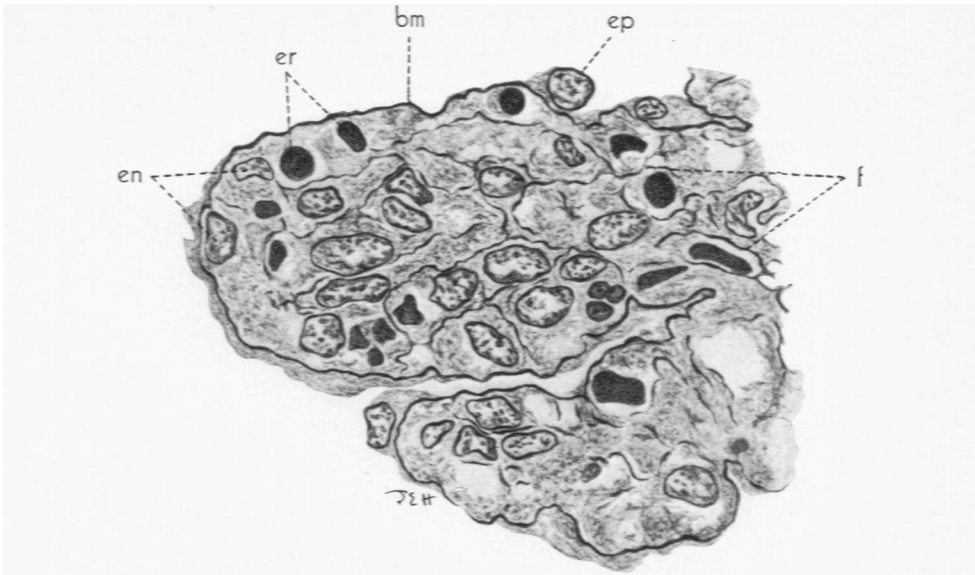
PLATE 132

FIG. 7. Lobule from a glomerulus showing the Grade 3 endothelial pattern. This is clinical acute glomerulonephritis in an early stage. Death from an associated infection. The capillaries are greatly distended.

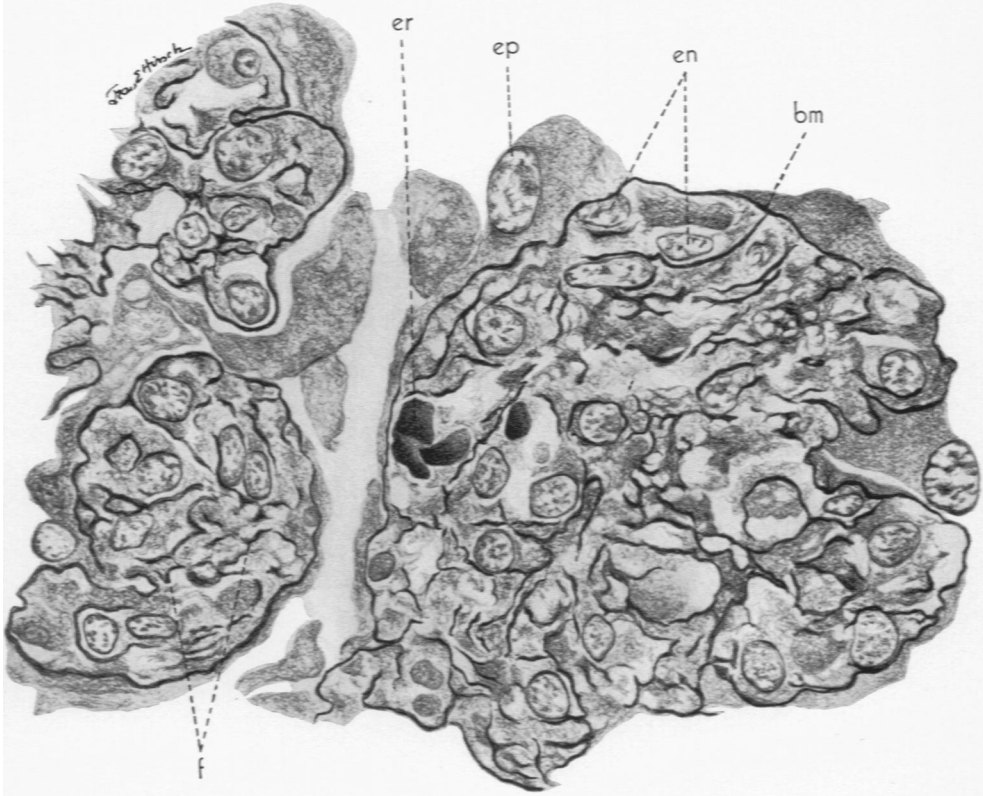
Note the intracapillary fibers, f. Other lettering as in Fig. 3. Mallory-Heidenhain stain. Drawing × 1200.

FIG. 8. Lobules of glomerulus from a typical case of acute glomerulonephritis, more advanced than in Fig. 7. Death from uremia.

Note numerous intracapillary fibers, f. Other lettering as in Fig. 3. Mallory-Heidenhain stain × 1200.



7



8