INTERCAPILLARY LESIONS IN THE GLOMERULI OF THE KIDNEY *

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INTRODUCTION

Since the existence of an intercapillary connective tissue, not only confined to the hilum but also extending to the periphery, has been definitely recognized in the normal glomerulus,[1, 2, 3] more attention has been paid to the pathological changes in this connective tissue framework. MacCallum, in particular,[4] has recently analyzed the changes in the intercapillary connective tissue which are associated with various pathological conditions in the kidney. He describes edema, amyloid degeneration, hyalinization and growth of the connective tissue. Of special interest in relation to the material we present is his statement that intracapillary glomerulonephritis consists in an increase of intercapillary connective tissue. For this reason he suggests the term "intercapillary" in place of "intracapillary" glomerulonephritis. From his description it is not quite clear whether he restricts the term "intracapillary glomerulonephritis" to the cases so-called by Fahr [5] or includes also the common "extracapillary glomerulonephritis."

One of us [6] has recently described the frequently observed broadening of the connective tissue of the glomerulus as an aging process which apparently develops independently of hypertension and arteriosclerosis. Further studies show that in a certain group of cases this change may so dominate the histological picture as to give a characteristic appearance. Since the clinical findings may be equally characteristic, it seems justifiable to describe these cases as a special group. In attempting to do so, however, considerable difficulties are encountered, especially in advanced cases, in differentiating them from so-called intracapillary glomerulonephritis (Fahr). We have, therefore, contrasted the features of this special group with those of

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true intracapillary and extracapillary glomerulonephritis. A detailed study of the basement membrane enables us to make a definite distinction in the majority of cases.

Staining Method

1. Lithium carmine 1½ hours at 55° C.
   (Stain contains 2½ gm. carmine in 100 cc. saturated lithium carbonate.)
2. Without contact with water transfer to 1 per cent hydrochloric acid in 70 per cent alcohol for 3 minutes. Change once.
3. Wash with distilled water.
4. 1 per cent phosphomolybdic acid 30 seconds.
5. Wash with distilled water once.
6. Aniline blue-orange G stain ¾ hour at 55° C.
   (0.5 gm. aniline blue with 2 gm. orange G in 100 cc. 1 per cent phosphomolybdic acid. Stir well and allow to stand a few hours. Filter.)
7. Wash with distilled water several times.
8. 1 per cent phosphomolybdic acid 45 seconds.
9. Wash with distilled water once.
10. Differentiate in 95 per cent alcohol to which is added 1 cc. 15 per cent sodium hydroxide per 100 cc. until first traces of reddish stain appear.
11. Wash quickly in excess of 95 per cent alcohol. The stain washed out turns blue. Continue until no further blue appears.
12. Absolute alcohol, xylol, balsam.

Fresh Zenker-fixed material must be used. Paraffin embedding and thin sections are necessary. If the section is not differentiated enough it may be brought back to alkaline alcohol for a very short time.

Results: Connective tissue and basement membranes deep blue, nuclei red with clear structure. Cytoplasm grayish pink, hyaline droplets blue. Red blood cells golden yellow or occasionally greenish. The colors are more delicate than in the Heidenhain stain and details of the cytoplasm and basement membrane are clearly brought out.

A. Intercapillary Glomerulosclerosis

The term intercapillary glomerulosclerosis has been applied to the group of cases under discussion, of which we present 8 examples showing different stages of the glomerular lesion.

Case 1. B. P., female, aged 62 years, on admission complained of shortness of breath and drowsiness. There was a 3 years history of diabetes with 2 months known hypertension.

Physical Examination: The patient was semicomatose with signs of cardiac failure, and generalized edema including arms, face and neck was present. Blood pressure 180/100 mm. Hg.

Urine: Specific gravity 1004–1010; large trace of albumin; many leukocytes in sediment; sugar negative.

Blood: Non-protein nitrogen 58 mg. per 100 cc.

Autopsy Findings

Anatomical Diagnosis: Myocardial failure.

Gross Appearance of Kidneys: Combined weight 300 gm. Average in size. The capsule strips with difficulty from a granular reddish brown surface with occasional stellate scars. On section the cortex averages 5 mm. in thickness, is reddish brown with normal striations and clearly demarcated from the medulla.

Case 2. H. G., male, aged 60 years, was admitted in extremis complaining of pain in the chest and cough. No previous history was obtainable.

Physical Examination: Generalized edema including the hands and face was present. Blood pressure 160/70 mm. Hg. Signs of bronchopneumonia and cardiac failure were present and the patient died 3 hours after admission.

Autopsy Findings

Anatomical Diagnoses: Chronic nephritis, bronchopneumonia.

Gross Appearance of Kidneys: Combined weight 380 gm. The capsule strips with ease, leaving a finely granular surface. On section the cortex is pale grayish purple, 5 mm. in thickness, with grayish white medulla.

Case 3. A. T., female, aged 63 years, was admitted with a complaint of gradually increasing edema for 10 months with shortness of breath on exertion. There was a previous history of diabetes.

Physical Examination: Edema of legs, thighs, abdomen, arms and face was present. Blood pressure 120/80 mm. Hg.

Urine: Specific gravity 1017–1024; large trace of albumin; sugar ++.

Autopsy Findings

Anatomical Diagnoses: Myocardial failure, arteriosclerosis and diabetic nephrosis.

Gross Appearance of Kidneys: Combined weight 240 gm. The capsule strips with difficulty from a grayish brown, very finely nodular surface containing several smooth depressed scars. Cut surface reveals a cortex 3–5 mm. broad, grayish brown in color, and clearly demarcated from darker red medulla.

CASE 4. M. H., female, aged 51 years, was admitted in a semicomatose condition with twitching of muscles, vomiting and shortness of breath. There was a 10 years history of diabetes.

Physical Examination: Edema of ankles, bilateral cataract and severe arteriosclerosis were present. Blood pressure 190/80 mm. Hg.

Urine: Specific gravity 1012; large trace of albumin; many leukocytes and occasional red cells in sediment.

Blood: Non-protein nitrogen 170 mg. per 100 cc.

Autopsy Findings

Anatomical Diagnoses: Generalized arteriosclerosis, bronchopneumonia.

Gross Appearance of Kidneys: Combined weight 230 gm. The capsule strips easily leaving a yellowish gray, coarsely granular surface. On section a very pale grayish yellow, finely granular cortex 5 mm. thick, with pale grayish red medulla is seen. Marked atheroma and calcification of renal vessels is present.

CASE 5. L. S., female, aged 48 years, was admitted with a complaint of swelling of legs and blurring of vision. There was a 3 years history of diabetes.

Physical Examination: The patient was stuporous with Cheyne-Stokes respiration and generalized edema was present. There were retinal exudates and hemorrhages. Blood pressure 230/110 mm. Hg.

Urine: Large trace of albumin; sugar +.

Blood: Non-protein nitrogen 133 mg. per 100 cc.; blood sugar 275 mg. per cent.

Autopsy Findings

Anatomical Diagnoses: Generalized anasarca, myocardial failure.

Gross Appearance of Kidneys: Combined weight 370 gm. The surface is granular. On section the cortex is 6 mm. thick, and yellowish gray-white in color.

CASE 6. A. H., female, aged 49 years, was admitted with a 2 weeks history of vomiting and oliguria. There was a 15 years history of diabetes. Right nephrectomy for renal calculi was performed 18 years before.

Physical Examination: The patient was comatose with Cheyne-Stokes respiration.

Urine: Albumin present; many leukocytes in sediment; sugar ++.

Blood: Non-protein nitrogen 150 mg. per 100 cc.

Autopsy Findings

Anatomical Diagnoses: Generalized arteriosclerosis, chronic nephritis.

Gross Appearance of Kidney: Weight 280 gm. (left). The capsule strips with difficulty leaving a coarsely granular surface. On section the cortex is grayish red with multiple irregular scars scattered throughout and poorly demarcated from the medulla.

CASE 7. C. H., male, aged 68 years, was admitted complaining of dyspnea on exertion and edema of feet. There was a 6 years history of diabetes.

Physical Examination: Edema of ankles was present. Blood pressure 230/110 mm. Hg.

Urine: Specific gravity 1010–1022; large trace of albumin; sugar +.
Blood: Non-protein nitrogen 25 mg. per 100 cc.

Autopsy Findings

Anatomical Diagnoses: Hypernephroma, pulmonary infarction.
Gross Appearance of Kidneys: The right kidney weighs 375 gm. The capsule strips easily leaving a smooth, pale, swollen surface. On section the cortex is 7 mm. broad and appears pale and swollen. The left kidney contains a hypernephroma.

CASE 8. A. F., male, aged 58 years, was admitted complaining of increasing swelling of the feet, legs and abdomen. There was a 5 years history of diabetes.
Physical Examination: Bilateral cataract present. Pitting edema of legs and abdomen and marked ascites. Blood pressure 190/100 mm. Hg.
Urine: Specific gravity 1007–1015; large trace of albumin; many leukocytes and red cells in sediment.
Blood: Non-protein nitrogen 87 mg. per 100 cc.

Autopsy Findings

Anatomical Diagnoses: Generalized atheroma, myocardial failure.
Gross Appearance of Kidneys: Combined weight 400 gm. The capsule strips with difficulty from a finely granular surface. The cut surface is mottled gray and yellow. The cortex is 6 mm. broad, well demarcated from the medulla.

Microscopic Appearances in the Kidney

(1) *The Glomeruli:* The most striking feature is the great regularity with which the hyalinization of the glomerulus is confined to its center, or even to the center of one lobule (Fig. 1). With the eosin-methylene blue stain an entirely homogeneous mass is seen, suggestive of amyloid, but negative reactions are obtained with all the amyloid stains. Fat stains (Sudan III) usually give a homogeneous pinkish color, while double refraction is only exceptionally present in smaller circumscribed areas. Toward the periphery of the glomerulus the basement membrane of the capillaries seems to emerge from the hyaline mass but its outline is sharply defined and usually surrounds a widely patent lumen (Fig. 2). The basement membrane may be delicate like the normal one, or somewhat thickened, but is never wrinkled or split (Fig. 3). The number of capillaries is apparently reduced — in many cases there remains only a ring of open capillaries surrounding the central hyaline mass (Fig. 1). The remainder appear to have been buried in it and to have disappeared.

The hyaline mass itself obviously represents a broadening of the intercapillary connective tissue. This can be observed particularly

well at the hilum. A very high degree of arteriosclerosis with fatty degeneration of the arterioles is present in most of the cases and the hyaline material is seen to be continuous from the vasa afferentia into the intraglomerular mass as it extends from the center of the lobules to the periphery (Fig. 4). The intercapillary hyalinization is not, however, to be regarded merely as an extension of the degenerative process from the vas afferens since it is found in glomeruli where the vas afferens is normal. Not infrequently pictures are encountered similar to those recently described by one of us as an "aging process of the glomerulus," but the axial thickening is much more massive and striking. It must be emphasized, however, that there is only a difference in degree between the less marked changes frequently observed in senile kidneys and the lesion here described. Although the basement membrane of the capillaries seems to be well preserved for a long time, the change gradually extends to the periphery. This mode of extension is most characteristic. Eventually the capillary walls thicken homogeneously and near the central hyaline mass they collapse and finally merge with the central hyalin (Fig. 5). It is also possible, as MacCallum points out, that the capillaries are partly pushed toward the periphery and preserved there for a long time.

While the capillaries are fusing with the central hyalin, the nuclei, especially those of the endothelial cells, appear well preserved and are crowded together (Fig. 6). This process may be observed step by step: the lumen of the capillaries becomes a narrow slit, the endothelial nuclei increase in density but retain their elongated form and are finally entirely embedded in a homogeneous hyaline mass (Fig.7). This may give rise to an apparent increase in nuclei which simulates an insidious proliferative process, thereby leading to misinterpretations, as we shall see later. The nuclei are often arranged in "onion layers" at the periphery of the hyalin (Fig. 6), presumably originating from the endothelial cells of the collapsed capillary loops. Two reasons prevent one from attributing this appearance to true proliferation: (1) Immature nuclei and mitoses are never seen — on the contrary the nuclei are almost invariably pyknotic and in a state of necrobiosis; (2) The mode of development of the apparent increase in nuclei can be seen to be the result of a regressive process. There is, furthermore, no definite proof of an inflammatory process. Regarding the origin of the nuclei many observations have led to the con-

viction that sometimes at least they originate from the endothelial cells of collapsed capillaries. Whether in addition there is a true "growth" of interstitial tissue as MacCallum assumes, it is difficult to decide. The more centrally situated nuclei lie in a dense homogeneous mass which certainly originates from the intercapillary connective tissue, but in later stages the capillaries with their endothelial and epithelial cells become embedded, and the origin of the nuclei cannot be recognized.

(2) *Capsular Changes:* Severe changes also occur in the glomerular capsule. A substance is deposited which at first appears translucent with a slightly pinkish stain, and later becomes more homogeneous, hyalin-like, and often contains abundant lipoid. The mass lies between the basement membrane and the epithelial layer of Bowman's capsule lifting the epithelial cells (Fig. 8). It may be deposited in such quantity that the capsular space is greatly narrowed (Fig. 9). A connective tissue reaction appears in the outer layers in later stages only — apparently a resorptive or organizing process. Broadening of the connective tissue occurs by the formation of concentric layers of fibrils and nuclei. The mode of development of this capsular change, which frequently accompanies the glomerular lesion, definitely indicates the primary degenerative character of the whole process.

The intercapillary process described above is practically diffuse, in the sense that almost all the glomeruli are affected. Although the severity of the lesion may vary, in a few cases it is the only lesion which can be found. In others, however, a scanty focal glomerulitis is present of the type we have described in decompensated benign nephrosclerosis and malignant nephrosclerosis. There are, in these instances, as in decompensated benign nephrosclerosis, definite signs histologically and clinically of renal insufficiency and we interpret these cases as decompensated benign or malignant nephrosclerosis complicated by intercapillary glomerulosclerosis.

The tubular changes have no special significance. The degenerative processes common to all arteriosclerotic processes are found. There is, however, in most cases a striking deposition of fat and doubly refracting lipoid in the tubules and in the interstitial tissue. No diagnostic significance, however, is attached to lipoid deposition in our cases since the amount was never sufficient to give the gross appearance of a lipoid nephrosis. Moreover, many cases of severe

uncomplicated arteriosclerosis of the kidneys show a fairly high degree of lipoid infiltration of the tubules and interstitial tissue. One case grossly appeared to resemble a nephrosis but lipoid deposition was not extraordinary, the tubules showing chiefly albuminuric and hyaline droplet degeneration.

Comment

The Clinical Picture: The separation of the above group of cases, especially from intracapillary glomerulonephritis, has been made on histological grounds which are discussed later. On reviewing the clinical data it was surprising to find a previous history of diabetes in all these cases, with the exception of one (Case 2) in which death occurred 3 hours after admission and no history was obtainable.* It must be emphasized that only a small proportion of cases of diabetes appears to show this lesion at autopsy. A second striking feature was severe and widespread edema. The clinical picture appears in fact to be almost as characteristic as the histological one: the patients are relatively old; hypertension is present, usually of the benign type, and the kidneys frequently show signs of decompensation; there is a history of diabetes usually of long standing; the presenting symptoms may be those of edema of the nephrotic type, renal decompensation or heart failure; the urine contains large amounts of albumin and there is usually impairment of concentrating power with or without nitrogen retention.

Although some degree of cardiac failure is frequently present, the edema is out of all proportion to this and may be extreme when no signs of heart failure can be demonstrated. Furthermore, its generalized distribution, especially its extension to the arms and face, leads us to regard it as nephrotic rather than cardiac in type, and this conclusion is supported by the constant finding of severe albuminuria.

The Pathological Picture: The gross appearance of the kidneys is not characteristic. They present the picture of arteriosclerotic contraction which may be in part or completely obscured by the signs of

* Since the investigation was completed several other instances of intercapillary glomerulosclerosis have been encountered. All were cases of diabetes except one in which a questionable reducing reaction was present in the urine, but no information was available in regard to the previous history.

nephrosis, *i.e.* they may be enlarged and swollen with grayish or yellowish external and cut surfaces.

The histological picture is, however, very characteristic. Arteriosclerosis is present, usually of very high degree, fatty degeneration of the arterioles being unusually conspicuous. Intercapillary hyaline change is discernible in most of the glomeruli even under low power. The special stain is necessary to demonstrate the earlier stages of the process but when this is used the lesion cannot be overlooked. All degrees of this hyaline change can be observed down to those produced simply by the aging process, and the cases described above represent an extremely severe type.

The tubules very often show fatty degeneration, and lipoid is frequently found in the interstitial tissue.

In addition to these characteristic features the signs of true renal decompensation we have previously described are commonly found, and when this is the case the capsular adhesions though focal in distribution may be surprisingly frequent.

B. Intracapillary Glomerulonephritis (Fahr)

We have referred to the great difficulties which may arise in differentiating late stages of intercapillary glomerulosclerosis and so-called intracapillary glomerulonephritis. The latter differs from the common extracapillary glomerulonephritis in the absence or very scanty occurrence of capsular proliferation. In the subchronic stage, intracapillary glomerulonephritis is frequently complicated by the "nephrotische Einschlag." Histologically a peculiar hyalinization of the glomerulus occurs which accentuates its lobulation in the same way as in intercapillary glomerulosclerosis (Fig. 10). In the early stages abundant leukocytes appear in the capillaries and emigrate into the capsular space and convoluted tubules. In the later stages the only finding may be an increase in nuclei which Fahr interprets as an insidious endothelial proliferation. He believes that hyalinization is due to fusion of the thickened capillary walls. Adhesions are frequently found and thickening of the connective tissue of Bowman's capsule is often present. During the earlier stages there is little difficulty in diagnosing the inflammatory nature of the disease on account of the presence of leukocytic infiltration. In the chronic stages, however, where leukocytic infiltration is almost absent, capsular ad-

hesions may occur only focally and a definite decision may be very difficult. True endothelial proliferation — or at least increase in endothelial nuclei — can sometimes be recognized, but such a finding is inconstant; in general the apparent increase in nuclei cannot be regarded as proof of an inflammatory process. Pyknotic nuclei are embedded in a hyaline mass and it may be impossible to say whether they originate from endothelial or connective tissue cells and whether there is an actual increase in nuclei or merely a crowding effect. The clinical evidence is frequently negative since the acute stage of the glomerulonephritis may pass unnoticed. Intercapillary glomerulosclerosis may, in fact, so resemble intracapillary glomerulonephritis in the late stages that a distinction is impossible. We encountered one such case.

Detailed examination of cases of intracapillary glomerulonephritis shows that in most glomeruli the main mass of hyalin is localized at the center of the lobules; and as in intercapillary glomerulosclerosis a ring of open capillaries is left at the periphery. Although red blood cells are frequently seen in these peripheral capillaries, the lumen is rather narrow and never distended. The hyalinization is easily distinguished from that which occurs in the more common extracapillary glomerulonephritis. In this condition there is irregular thickening of the capillary loops and the lumen is narrowed by the broadening and splitting of the basement membrane. The process often affects the glomerulus focally leaving the unaffected parts free. Moreover, the hyalinization tends to start in the periphery, whereas in intracapillary glomerulonephritis it begins at the center of the lobule.

The central origin of hyalinization in intracapillary glomerulonephritis with preservation of the peripheral capillaries indicates that the degeneration of the connective tissue framework occurs independently of and is superimposed on hyalinization of the capillary wall. If the latter alone were present we should expect the hyalinization of the glomerulus to be diffusely distributed, since in the earliest stages of the disease all the capillaries are involved. The following observation gives more definite proof that hyalinization of the intercapillary tissue occurs as an independent process. In some cases one encounters occasional glomeruli which are not involved in the otherwise diffuse inflammatory lesion and which show hyalinization of the intercapillary connective tissue framework without any change in the peripheral zone. In some of these instances a marked swelling

and hyaline droplet degeneration of epithelial cells is present but in others the glomerulus is normal except for the change in the intercapillary tissue (Fig. 11).

It has already been emphasized that the apparent increase in nuclei in the hyaline mass in intracapillary glomerulonephritis may be attributed to crowding of the endothelial nuclei of collapsed capillaries and does not furnish proof of an inflammatory process. Changes occur, however, in the basement membrane of the preserved peripheral capillaries which in our experience are characteristic of such a process. These are blurring of outline and splitting of the basement membrane, which are also commonly found in extracapillary glomerulonephritis (Fig. 12). The development of intracapillary hyaline fibers, described by McGregor, is rare in the intracapillary form.

Diffuse involvement of the capillaries by these changes definitely indicates a primary diffuse lesion of the glomerular capillaries in contradistinction to intercapillary glomerulosclerosis, even though no actual inflammatory infiltration may be demonstrated. A marked swelling of epithelial cells, which is found even in the later stages, further indicates the inflammatory nature of the process and when diffusely distributed may be regarded as a diagnostic sign. The same change is found in intercapillary glomerulosclerosis but is focal in distribution.

The capsular changes closely resemble those of intercapillary glomerulosclerosis. The same formation of connective tissue layers is present without, however, any epithelial proliferation (crescent formation). Volhard [7] considers this as a reaction to waste products which diffuse outwards from the capsular space. Fahr believes the process to be inflammatory, in keeping with the "insidious endothelial proliferation" in the glomerulus. One can, however, only state that the same capsular change occurs in association with a purely degenerative process in intercapillary glomerulosclerosis, and hence does not necessarily indicate an insidious inflammatory reaction.

Comment

In intracapillary glomerulonephritis capsular proliferation (crescent formation) is inconspicuous, but a most characteristic feature is the massive degeneration of the connective tissue framework of the glomerulus which complicates the capillary lesion. Blurring and

splitting of the basement membrane are regarded as indicative of the inflammatory nature of the process even in the late stages when cellular infiltration and proliferation are absent, and this capillary lesion differentiates the condition from intercapillary glomerulosclerosis. It is noteworthy that in cases of both arteriosclerosis and intracapillary glomerulonephritis the intercapillary degeneration tends to be accompanied by fatty tubular nephrosis and interstitial deposition of doubly refracting lipoid.

C. Extracapillary Glomerulonephritis

The changes in the basement membrane of the peripheral capillaries in intracapillary glomerulonephritis are also found in the extracapillary form. Our observations are based on McGregor's [8] detailed description of structural changes in the glomerulus in glomerulonephritis which are brought out by combined nuclear and basement membrane stains. She claims that a most characteristic sign is the development of intracapillary hyaline fibers, either from fibrin threads or from the basement membrane itself. Hyalinization of the glomerulus is assumed to result from thickening and fusion of these fibers. Our observations essentially confirm these findings with the following additions:

(1) Certain changes in the basement membrane are found in inflammatory lesions of the glomeruli and are no less characteristic than intracapillary hyaline fibers. They may in fact be present in the absence of the latter. Such changes include splitting of the basement membrane which appears blurred and definitely thickened, though not wrinkled. The membrane appears as if teased out into a meshwork of delicate fibers which narrow the lumen. Where the fibers are thick and the section cuts a loop tangentially, they give the impression of being intracapillary. It cannot be stated whether or not all the intracapillary fibers are to be explained in this way; some may well be actually split off the basement membrane. In any case the distribution of both intracapillary fibers and splitting of the basement membrane is irregular throughout the glomerulus. It may be diffuse or confined to small areas, but the peripheral loops are as severely involved as the more central ones. MacCallum states that he has not observed intracapillary occlusions in "intracapillary glomerulonephritis." This holds true for intracapillary glomerulone-

phritis in Fahr's sense, but in the common (extracapillary) form our observations support McGregor's contention that such occlusions are of frequent occurrence.

(2) In extracapillary glomerulonephritis there is frequently, in addition to the above changes, thickening of the intercapillary connective tissue. The points of difference from the similar lesion in intracapillary glomerulonephritis have been outlined above. In particular, the thickening is irregular and focal in its distribution throughout the glomerulus, and does not appear to have any characteristic significance.

Comment

In the common or extracapillary glomerulonephritis thickening of the intercapillary connective tissue is irregular or focal in distribution and is relatively insignificant. Intracapillary fibers, which are found in all inflammatory lesions of the glomerulus, are associated with an equally characteristic change, namely, broadening and splitting of the capillary basement membrane.

Discussion

The glomerular changes in glomerulonephritis include two characteristic elements: (1) alteration of the basement membrane leading to "intracapillary" fibrillation; and (2) a purely degenerative process, the deposition of intercapillary hyaline material. This intercapillary glomerulosclerosis is apparently an independent lesion since it may be superimposed on pure arteriosclerosis as well as on inflammatory changes in the glomeruli. It may therefore be considered as a "complication" of glomerulonephritis.

It has been shown that intercapillary glomerulosclerosis and intracapillary glomerulonephritis have in common a degenerative process in the intercapillary connective tissue. They present also a striking clinical similarity in their frequent association with the nephrotic type of edema — the "nephrotische Einschlag," which has been attributed to a general metabolic disorder. The invariable finding of diabetes in cases of pure intercapillary glomerulosclerosis lends support to such a theory.

Summary and Conclusions

Cases are described which show a striking hyaline thickening of the intercapillary connective tissue of the glomerulus. Evidence is presented which indicates that the change is degenerative in nature and suggests that arteriosclerosis and diabetes may play a part in its causation. The lesion is therefore termed intercapillary glomerulosclerosis. The characteristic clinical features are a previous history of diabetes, severe and widespread edema of the nephrotic type and gross albuminuria. Hypertension is frequently present, in many cases associated with renal decompensation.

The same histological picture frequently complicates intracapillary glomerulonephritis but in the later stages this condition is differentiated histologically by blurring and splitting of the capillary basement membrane.

In extracapillary glomerulonephritis thickening of the intercapillary connective tissue is relatively insignificant and the basement membrane changes are more pronounced.

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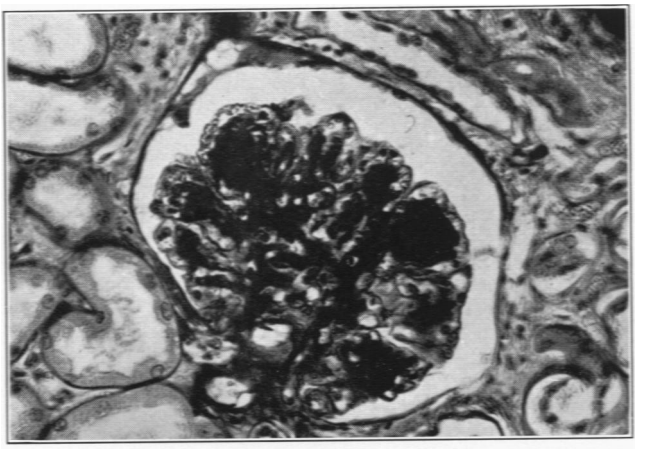
DESCRIPTION OF PLATES

PLATE 9

FIG. 1. Intercapillary glomerulosclerosis. Central hyalinization of all glomerular loops. Peripheral capillaries patent. Special basement membrane stain.

FIG. 2. Central hyalinization of peripheral loop. Capillaries wide open and contain red blood cells. Basement membrane clearly delineated and delicate. Special basement membrane stain. High power.

FIG. 3. Intercapillary hyalinization. Peripheral capillaries patent, nuclei of endothelial and epithelial cells clearly recognizable. Capillary basement membrane somewhat thickened. Special basement membrane stain. High power.



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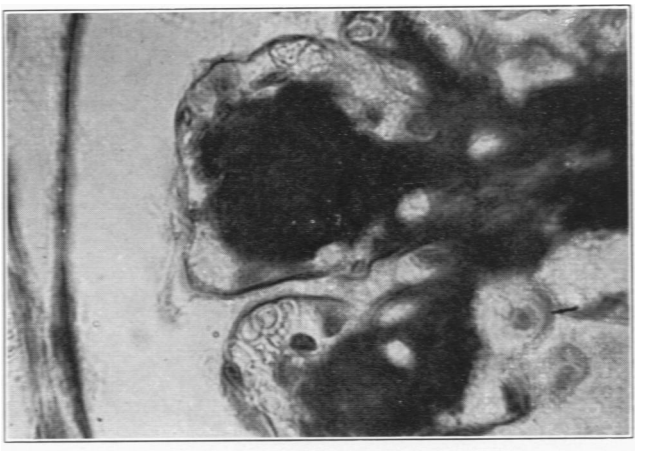

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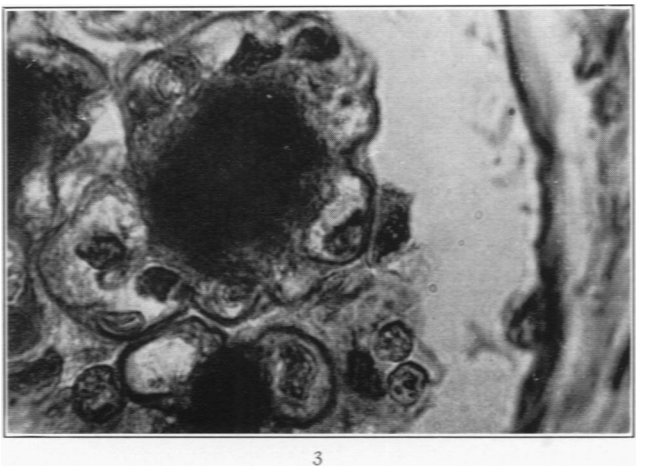

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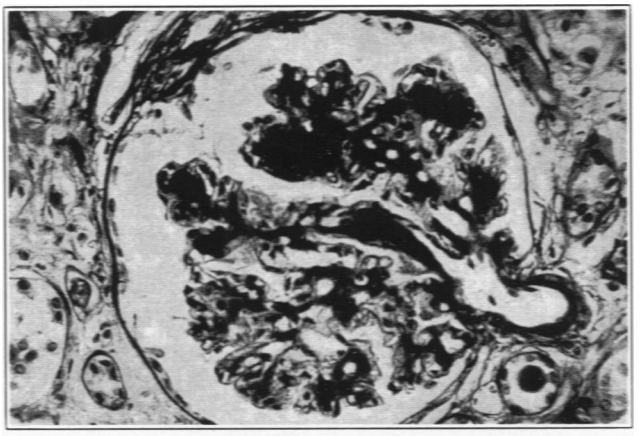
PLATE 10

FIG. 4. Hyalinization of intercapillary connective tissue extending into most of the loops, in direct continuity with the hyaline material of the vas afferens. Special basement membrane stain. Medium power.

FIG. 5. Intercapillary hyalinization in several loops; the hyaline material encroaches upon the capillary wall which is homogeneously thickened. The capillaries are collapsed and their lumen reduced to a narrow slit. Special basement membrane stain. Medium power.

FIG. 6. Central hyalinization clearly seen even with eosin-methylene blue stain. Crowding of endothelial nuclei around collapsed capillaries gives appearance of "onion layers." Eosin-methylene blue stain. High power.



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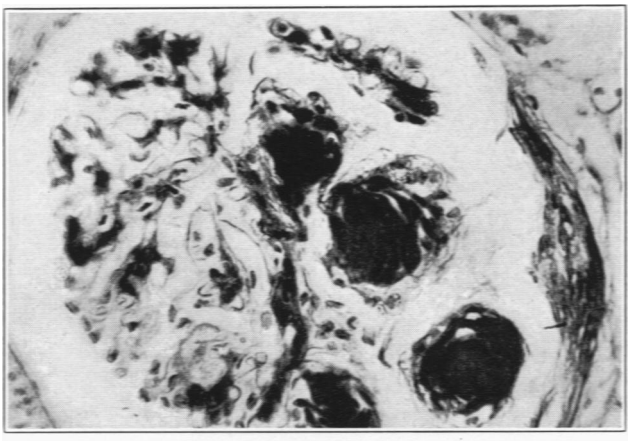

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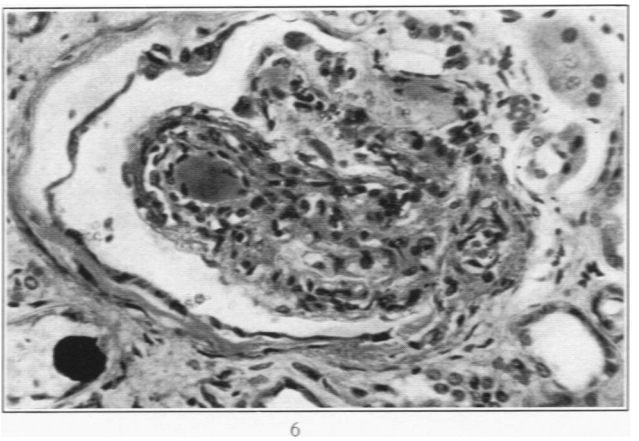

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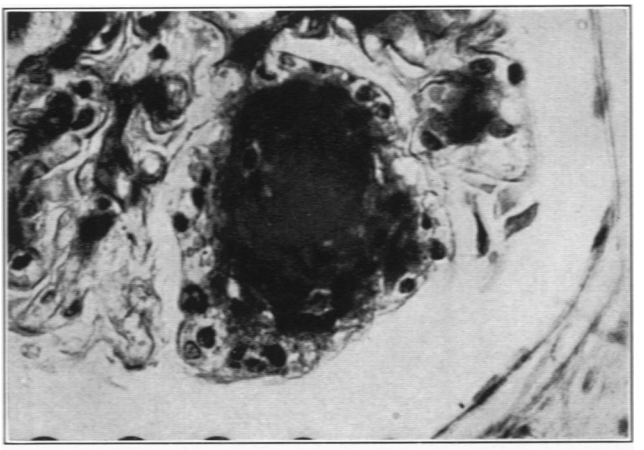
Plate 11

Fig. 7. Well preserved endothelial nuclei are seen embedded in central hyaline mass. Special basement membrane stain.

Fig. 8. Hyaline fatty mass seen between basement membrane and epithelial cells of Bowman's capsule. Special basement membrane stain. High power.

Fig. 9. Sudan III fat stain shows large fatty mass between epithelial cells and basement membrane of Bowman's capsule. The picture also shows fat in the vas afferens, some fatty degeneration of capillary loops and fat in the tubular epithelial cells. Sudan III stain. High power.



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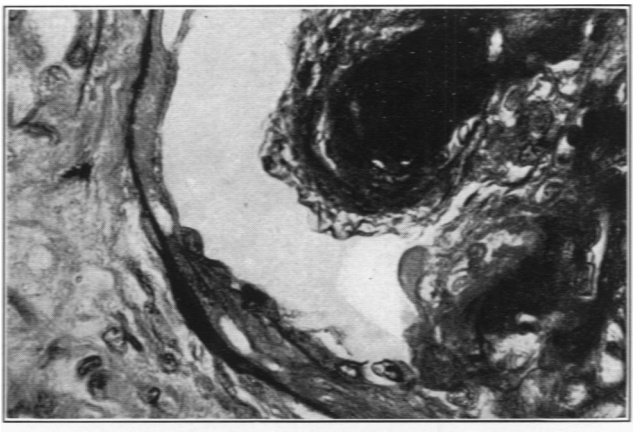

8

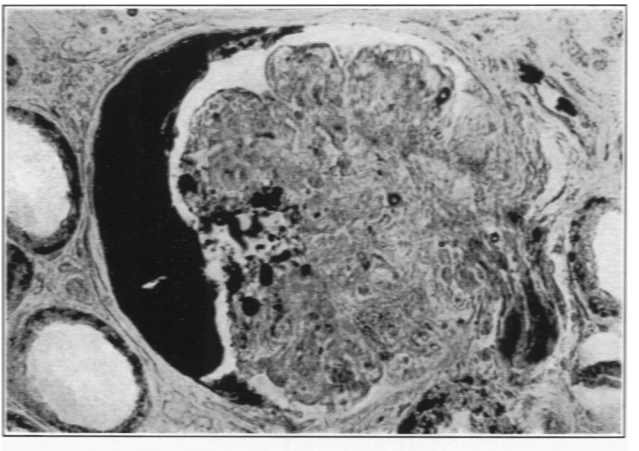

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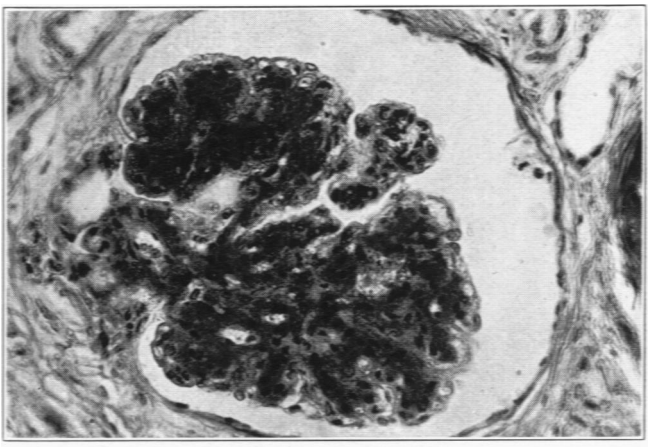
PLATE 12

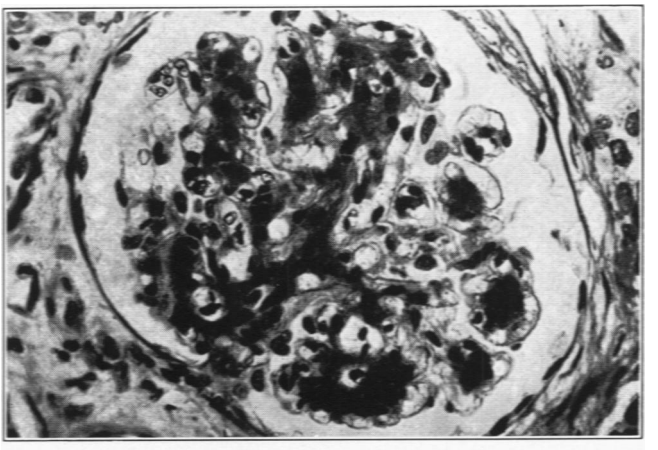
FIG. 10. Intracapillary glomerulonephritis. Central hyalinization identical in situation with that of intercapillary glomerulosclerosis (see Fig. 1). Notice open capillaries in the periphery. Special basement membrane stain. High power.

FIG. 11. Single glomerulus in an otherwise diffuse intracapillary glomerulonephritis. There is no other change but a severe central intercapillary hyalinization. Special basement membrane stain. High power.

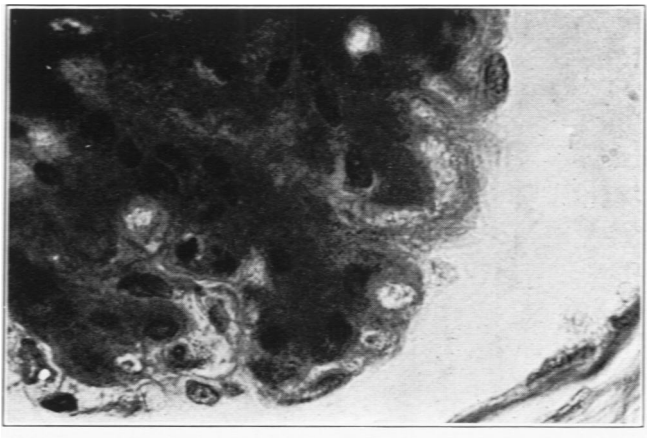
FIG. 12. Intracapillary glomerulonephritis showing blurred outline of peripheral capillaries. Special basement membrane stain. High power.



10



11



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