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<td>Author(s)</td>
<td>Moriyama, Nobuo</td>
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<tr>
<td>Citation</td>
<td>Acta medica Nagasakiensia. 1975, 19(1-4), p.59-81</td>
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<tr>
<td>Issue Date</td>
<td>1975-03-25</td>
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<td>URL</td>
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Pathogenesis of the Lesions of Glomerulus and Renal Arteriole in Experimental Hypertension

II. Morphological Changes in Basement Membrane of Renal Arteriole and of Glomerulus in Experimental Hypertension

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Received for publication, March 10, 1975

Electron microscopic studies were carried out in pursuit of the difference and interrelationship between the changes of the basement membrane of renal glomerulus and the changes of the basement membrane of renal arteriole in experimental hypertension.

The changes of the basement membrane of arteriole and basement membrane like material of mesangium and lacis show their occurrence at about the same time and their progress in the same degree. The changes first observed are the beads-like thickening and reticular change of the basement membrane of vascular wall and also the increase of basement membrane like material in mesangium and lacis. These changes are followed by the deposit of dense material and fibrin on the vascular wall and the increase of basement membrane like material of mesangium and lacis so as to compress their cells and tear them to pieces. About this stage, the thickening of the basement membrane of glomerular capillary loop is intensified and moreover the wrinkle and tortuosity of the basement membrane of glomerular capillary loop and the collapse of glomerular capillary lumen became remarkable.

The above findings suggest that the basement membrane of renal arteriole and the basement membrane like material of mesangium and lacis are interrelated, and may be the portions in the kidney most liable to changes and injury in hypertension.

INTRODUCTION

Many studies on glomerular changes in experimental hypertension by light microscopy and electron microscopy have been reported. Likewise, morphological studies on vascular changes in experimental hypertension, particularly on changes of the medial smooth muscle cells and on hyperpermeability have been performed with the renal
artery and cerebral artery and various results have been obtained. The basement membrane of glomerular capillary loop, the basement membrane like material of mesangium, and the basement membrane of vasa afferens et efferens are anatomically continued to each other through the basement membrane like material of lacis. Despite the same morphological appearance, however, these functional roles are different. While the basement membrane of glomerular capillary loop is primarily related to filtration, the basement membrane like material of mesangium and the basement membrane of vasa afferens et efferens mostly play the role of supporting tissues.

Morphological studies on the basement membrane of glomerular capillary loop and the basement membrane like material of mesangium not necessarily in hypertension have been numerous, but there has hardly been any report in pursuit of their relation with the basement membrane of renal arteriole particularly at the vascular pole. Since experimental hypertension presents changes of the basement membrane and basement membrane like material of glomerulus and the basement membrane of renal vessel, an attempt was made to study these changes as well as the differences and interrelationship between these changes.

The oral administration of a silver nitrate solution is a simple method to label the basement membrane particularly of glomerulus. Three weeks' oral administration of a silver nitrate solution, 0.25%, results in distinct identification of silver granules even electron microscopically and in no such findings as considered renal changes due to silver nitrate. Therefore this method was also used in the present experiment in order to label the basement membrane before onset of hypertensive glomerular changes.

METHODS

Adrenal regeneration hypertension was produced in young Wistar rats.

Group A: Female rats weighing 50 g were subjected to right nephrectomy and adrenalectomy followed by left adrenal enucleation under anesthesia with ether, and were administered with 1% of a saline solution as a drinking water.

Group B: Rats weighing 25 g were administered with 0.25% of a silver nitrate solution for 3 weeks before the above-stated operation. After the operation, they were administered with 1% of a saline solution as a drinking water.

The body weight and blood pressure in all rats were determined weekly. These rats whose systolic pressure exceeded 200 mmHg in 4~6 weeks after operation were sacrificed for observation of the kidney. In group A and B, the kidneys of rats below 200 mmHg of blood pressure including normotensive kidneys were also observed for comparison.

The kidney of each rat was processed by perfusion fixation with 1.5% glutaraldehyde, double fixation with 3% glutaraldehyde and 1% osmic acid, dehydration with alcohol series, embedding with Epon 812, and ultra-thin sectioning with Porter Blum
I type microtome. The ultra-thin sections were stained with uranyl acetate and lead citrate, and were examined and photographed by the use of JEM 7A type and JEM 100B type electron microscopes.

Blood pressure was determined on weekly basis without anesthesia using Model USM-105-RAT automatic recording apparatus (tail-cuff-method).

Of the 120 rats used in the experiment, 23 rats showed the postoperative systolic pressure exceeding 200 mmHg. Electron microscopic examination was done for 6 rats in Group A and 4 rats in Group B, and also for a total of 12 rats with the blood pressure below 200 mmHg including 3 normotensive rats.

RESULTS

The rats orally administered with a silver nitrate solution during the preoperative 3 weeks showed less increase of body weight as compared with the rats administered with tap water. However, the kidneys showed no morphological difference between group A and group B except for the deposition of silver granules in the basement membrane.

Basement membrane of glomerular capillary loop

The basement membrane of glomerular capillary loop in the normotensive rats and also in the seemingly intact portion of the hypertensive rats was of three-laminal structure with lamina rara interna and lamina rara externa of 30~50 μm each in width and with lamina densa of 100~140 μm in width. The lamina densa was of microfibrillar structure, and the mean width of the basement membrane as a whole was approximately 180~200 μm.

In the rats administered with silver nitrate, silver granules of 30~50 μm in diameter were diffusely deposited in the endothelial side of the lamina densa (Fig. 1). The first observed change in hypertension was the thickening of the entire basement membrane, particularly of the lamina densa. Some portions were approximately 300 μm in total width. Partial thickening and tortuosity were also observed. The lamina densa became rough and its microfibrillar structure also became definite. As the tortuosity of the basement membrane of glomerular capillary loop was intensified, the endothelial cytoplasms were detached from the basement membrane and the capillary lumen showed a collapse (Figs. 2 and 3). Whereas the lamina rara externa hardly showed any change, the lamina rara interna was swelled to be 800 μm wide in some portions resulting in the appearance of microfibrils of 5~10 μm in diameter and electron lucent areas. Mesangial interpositions were seen in some portions.

In the group administered with a silver nitrate solution, the deposition of silver granules was observed in the endothelial side of the lamina densa but not in the area of the swelled lamina rara interna (Fig. 4).

The glomerular capillary lumen affected by fibrinoid necrosis was filled with ground
glass like plasma components including fibrin, and the basement membrane of glomerular capillary loop became indistinct. However, in the rats administered with a silver nitrate solution, silver granules were deposited diffusely in the area corresponding to the lamina densa (Fig. 5a).

**Mesangium**

The mesangium in the normotensive rats and also in the seemingly intact portion of the hypertensive rats contained mesengial cells surrounded by some basement membrane like material which was continued to the mesangial basement membrane facing Bowman’s space. The basement membrane like material showed general running of microfibrils and some electron lucent areas. The basement membrane facing Bowman’s space had a lamina rara of 30~50 mμ in width at the both sides and was continued to the lamina rara interna and lamina rara externa of the basement membrane of glomerular capillary loop. The intermediary lamina densa measured 150~200 mμ in width containing microfibrillar structure. The lamina rara interna sometimes appeared indistinct or wider.

In the rats administered with a silver nitrate solution silver granules were deposited in somewhat inner side of lamina densa of the basement membrane facing Bowman’s space (Fig. 1).

The hypertensive change was an increase of the basement membrane like material on the inner side. The basement membrane like material first increased branchedly and irregularly from the basement membrane facing Bowman’s space towards mesangial cells. Microfibrillar structure became rough and electron lucent areas were increased. Cytoplasmic organellae in the mesangial cells were observed to be in normal condition though the cells were slightly compressed. Amongst the microfibrillar structure, many fine granules measuring approximately 50 Å in diameter which seemed to be the cross sections of the microfibrillar structure were observed (Figs. 6 and 8a).

In the rats administered with a silver nitrate solution, the deposition of silver granules in the area of basement membrane facing Bowman’s space was somewhat irregular. Silver granules were observed sometimes in inner side basement membrane like material but not in most of the increased basement membrane like material (Fig. 6).

As the increase of the basement membrane like material was further advanced, the mesangial cytoplasms were compressed or torn to pieces and most of the cytoplasmic organellae disappeared. The above changes of basement membrane like material were accompanied by scattering of cell debris such as vacuoles and dense bodies measuring 250 mμ in maximum diameter (Fig. 7). Occasionally the basement membrane like material increased so diffusely that the basement membrane facing Bowman’s space and the inner basement membrane like material would be indistinguishable. However, even in such cases, the deposition of silver granules was seen only in the portion of basement membrane facing Bowman’s space (Fig. 8b).

At the acute stage of fibrinoid necrosis, the mesangium was filled with fibrin and other plasma components, and the boundary of basement membrane like material was
indistinct. Remaining mesangial cells contained many vacuoles of 1~3 μ in diameter. The basement membrane facing Bowman's space seemed more distinct as compared with the basement membrane like material. In the group administered with a silver nitrate solution, silver granules were deposited in this portion (Fig. 5b). After the acute stage, fibrin masses with various sizes were seen remaining in the increased basement membrane like material and some fibrin masses had electron lucent areas in the surroundings (Fig. 9).

**Basement membrane of vascular pole**

The subendothelial basement membrane and the basement membrane of adventitial area of the vasa afferens et efferens in the normotensive rats and also in the seemingly intact portion of the hypertensive rats were continued by the intercellular basement membrane of media. Before entering the glomerulus, they were connected with the basement membrane of Bowman's capsule and then with the basement membrane of glomerular capillary loop. On the other hand, they were connected irregularly with the basement membrane like material of lacis (Fig. 10). The vascular basement membrane was almost constant in width ranging 200~250 μ. The subendothelial basement membrane of vascular pole and adjacent vessels, which contained nothing identifiable electron microscopically as elastic fibers, manifested in some portions the same three-laminal structure as the basement membrane of glomerular capillary loop. The laminae of both side were electron lucent and approximately 40 μ in width. The middle area was a dense dark stained lamina measuring approximately 160 μ in width. In not a few portions, slightly electron lucent areas were observed in the lamina densa. This lamina also had the microfibrillar structure of brushed-trace like appearance as in the basement membrane of glomerular capillary loop (Fig. 12). The basement membrane of adventitial area had about the same structure but not a few portions of the lamina rara at outer side were indistinct due to the relation with surroundings.

In the rats administered with a silver nitrate solution, the density of silver granules was lower in the portion reversing into the Bowman's capsule than in the basement membrane of glomerular capillary loop and in the mesangial basement membrane facing Bowman's space. Silver granules were deposited around the basement membrane of Bowman's capsule. On the other hand, the silver granules in the vascular basement membrane decreased further from that in the Bowman's capsule, and occasionally the deposition was absolutely absent (Fig. 11). These granules were deposited in the lamina densa as in other portions but loosely (Fig. 12).

The hypertensive change of the vascular basement membrane first observed was the localized thickening of the basement membrane of vascular wall up to several times the normal thickness. In this area beads-like appearance and irregular running were seen. In addition, the general appearance turned to be like a ground glass and there appeared vesicles of 30 μ in diameter. In some areas, reticular change of the lamina densa was seen with many microfibrils and fine granules measuring approximately 50 Å
in diameter, which seemed to be the cross section of microfibrils. An increase of electron lucent areas in the basement membrane was sometimes observed. A greater swelling of the subendothelial basement membrane occasionally resulted in a more remarkable appearance of reticular change (Figs. 13 and 14). Then, the thickening of the basement membrane became remarkable so as to compress the adjacent smooth muscle cells. Dense material was deposited mostly in the intercellular basement membrane of media, and moreover fibrin was educed and deposited. Because of this, smooth muscle cells were either scraped off or torn to pieces, containing some degenerative substance in the cytoplasms (Figs. 15 and 16). Occasionally, cell debris such as small granules and dense bodies were observed as in the mesangial area (Fig. 17).

Corresponding to these changes, the basement membrane of adventitial area was also thickened up to several times the normal thickness and increased irregularly in a pattern of annual rings. The inside became electron lucent and there appeared irregular cell debris and microfibrils. In the surrounding, there appeared fibroblasts and collagen fiber bundles. Silver granules were deposited almost regularly in the innermost basement membrane (Fig. 18).

In the lacis continued to the mesangium, the basement membrane like material was thickened to be several times and increased irregularly but reticular change was hardly observed unlike in the basement membrane of vascular wall. However, dense material was observed scatteringly. The basement membrane like material became electron lucent in vacuolar or worm-eaten shape and these electron lucent areas were fused with one another. They became generally rough showing definite microfibrillar structure (Fig. 19).

In the rats administered with a silver nitrate solution, the deposition of silver granules in the lacis was, like in mesangial area, limited to the external basement membrane facing Bowman’s space, and was hardly observed in the increased inner basement membrane like material (Fig. 20).

In the vascular wall at the acute stage of fibrinoid necrosis, there were observed platelets, fibrin and other plasma components in such manner that the medial cells, subendothelial basement membrane and intercellular basement membrane of media could not be distinguished. Only the basement membrane of adventitial area remained discernible (Fig. 21). After the acute stage, fibrin masses were seen left in the vascular wall. In the rats administered with a silver nitrate solution, the deposition of silver granules was observed in the area corresponding to the lamina densa of the basement membrane of adventitial area (Fig. 22).

_Difference or interrelationship of lesions in the basement membrane and basement membrane like material of vascular pole, mesangium and glomerular capillary loop_

The basement membrane of glomerular capillary loop in the normotensive group and also in the seemingly intact portion of the hypertensive group was similar in
structure to the mesangial basement membrane facing Bowman’s space and to the
basement membrane of vascular wall. In addition, the mesangial basement membrane
like material was no way different in structure from that of lacis (Figs. 1, 11 and 12).

The hypertensive changes in the vascular basement membrane first observed were
localized thickening, beads-shaped thickening and reticular change (Fig. 14). But
these changes were not observed in the basement membrane of glomerular capillary loop.
At a further advanced stage of hypertension, the intercellular basement membrane of
media showed thickening, deposition of dense material and in addition eduction and
deposition of fibrin (Fig. 15, 21 and 22). These changes were similar to the those
in the mesangium and lacis.

The main change in the lacis was an increase of the basement membrane like
material as in the mesangial area (Fig. 19). However eduction of ground glass-like
plasma components including fibrin which was seen in the mesangium was not observed
in the lacis. The changes of the basement membrane of glomerular capillary loop mostly
consisted of wrinkle and tortuosity and general thickening. They were different from the
changes of the basement membrane like material of lacis and mesangium (Figs. 2,
3, 4 and 19).

As to the interrelationship, the localized thickening, beads-shaped thickening and
reticular change of the vascular basement membrane were considered to be the changes
of relatively early stage in this area. During this period, the lacis and the adjacent
mesangium showed a moderate increase of basement membrane like material (Figs. 14
and 23).

Furthermore, the vascular wall showed thickening of the intercellular basement
membrane of media where dense material and fibrin would be deposited. During
this period, the basement membrane like material of lacis and mesangium were further
increased and mesangial cells were at times compressed to be smaller. Moreover, cell
debris such as vacuoles and small granules were seen in the basement membrane like
material (Fig. 17). The basement membrane of glomerular capillary loop showed only
localized thickening which was at times accompanied by wrinkle and tortuosity and
detachment of endothelial cytoplasms. From this period, the medial smooth muscle
cells and JG cells occasionally showed some changes, such as vacuolation of lysosomes and
JG granules. In addition, cytoplasms appeared to be scraped by the increased dense
material (Fig. 15).

As the basement membrane like material of lacis and mesangium was severely
increased, lacis cells and mesangial cells were compressed, scraped off cytoplasms, and
torn to pieces. More vacuoles and granules seemingly cell debris were observed in
the basement membrane like material. In this period, the thickening off the basement
membrane of glomerular capillary loop was intensified and moreover wrinkle and tortuosity,
detachment of endothelial cells and collapse of capillary lumen became remarkable (Fig.
19).

The above findings indicate that the increase of basement membrane like material
in lacis and mesangium and the thickening of basement membrane of vascular wall are the changes of relatively early stage. Then the changes of media smooth muscle cells and of the basement membrane of glomerular capillary loop appear when the mesangial cells and lacis cells are compressed and torn to pieces by the increased basement membrane like material.

DISCUSSION

It has been reported that the main change of the basement membrane of glomerular capillary loop in hypertension is thickening and the thickening is proportional to the duration of hypertension rather than its onset. Generally the thickening of basement membrane is a lamina densa. KURTZ et al. and WALKER have reported that the thickened portion of the basement membrane is produced by epithelial cells. This may be related to the finding that, in formation of the basement membrane of glomerular capillary loop by fusion of the epithelial and endothelial basement membranes, the epithelial basement membrane is more distinct and more electron dense. The thickening of basement membrane is also seen in nephritis and normal aging as well as in hypertension.

The main change of basement membrane of capillary loop in the present experimental study was the thickening mostly of the lamina densa. This thickening was occasionally accompanied by wrinkle and tortuosity of basement membrane and consequent collapse of capillary lumen. These changes were much delayed in occurrence and milder in degree as compared with the changes of the mesangium. Accordingly it is considered that the occurrence of changes of basement membrane of capillary loop requires a durative or intensive effect of hypertension, and that the changes of basement membrane of capillary loop are not the main hypertensive glomerular lesions. The swelling of lamina rara interna (Fig. 4) and the detachment of endothelial cytoplasm due to tortuosity of basement membrane were observed after the lesions of mesangium were greatly advanced. These changes might have been caused by the result that the transportation route from the subendothelial space to the mesangium verified by LATTA et al. and FARQUHAR et al. was broken by the increase of basement membrane like material of mesangium.

The increase of basement membrane like material of mesangium is the main change in hypertensive glomerular lesions. The basement membrane like material first begins to increase branchedly from the mesangial basement membrane facing Bowman's space towards mesangial cells (Fig. 6). As the change is further intensified, the border line between the mesangial basement membrane and basement membrane like material becomes indistinct (Fig. 8b). Accordingly the mesangial basement membrane is mostly responsible for the production of increased portion. However, since silver granules deposited in the lamina densa are hardly irregular, the lamina densa itself is considered to have little responsibility in the production of basement membrane like
material. The basement membrane facing Bowman's space may possibly derives from the adjacent epithelial cells. Participation of mesangial cells and their cell debris in the production of basement membrane like material is also possible. Participation of blood components is another possibility in view of the presence of fibrin.

The main changes of vascular basement membrane are beads-like thickening and reticular change of basement membrane. Similar changes have been noted by SUZUKI et al.\textsuperscript{15} in GOLDBLATT's type hypertensive rats but they do not seem to have placed any emphasis on these changes. Such changes are also reported by PIERCE et al.\textsuperscript{12} to be present in the testicular basement membrane injured by x-ray, chemical and bacteria, and thus these changes are not necessarily characteristic to hypertension. The finding that the beads-like thickening was seen only in the basement membrane of vascular wall may be due to the finding that the basement membrane of vascular wall, unlike the basement membrane of capillary loop, could not be thickened diffusely because of the surrounding medial smooth muscle cells and endothelial cells. The endothelial basement membrane of vessel occasionally shows marked reticular change and marked general swelling (Fig. 13). These changes resemble the postnatal reticular basement membrane like material of aortic endothelium reported by SCHWARTZ et al.\textsuperscript{14}. They stated that the changes were unrelated to endothelial injury. For these changes in the present study, various factors may be considered. For example, the durative increase of blood pressure is one possibility although its definite mechanism is unknown. Permeation of plasma components into vessel may also be a factor.

As to the change of the lacis, it has been reported that in the kidney paired with an ischemic kidney and in animals receiving overdoses of salt and DOCA, the lacis can undergo alterations identical with those occurring in the tunica media of the afferent arteriole and the mesangium: thickening of the intercellular basement membranes\textsuperscript{6}.

In the present experiment, the basement membrane like material of lacis showed several fold thickening and irregular increase, resembling considerably the lesions of the mesangium. One different point was that fibrin was not educed in this area, although it remains questionable if the eduction of fibrin was absolutely negative. However, this may be related to the finding that the lacis is not immediately facing the blood flow. The basement membrane like material increased in this area is continued to the basement membrane facing Bowman's space. Therefore it may be produced by the latter basement membrane and adjacent epithelial cells, and a part may be produced by lacis cells. However, since silver granules deposit regularly in the lamina densa, the lamina densa itself has little responsiblity in this production.

It is revealed by the present experiment that hypertensive renal lesions are first observed in the basement membrane of arterioles and basement membrane like material of mesangium and lacis. It was anticipated that the vascular pole might be the weakest area against pressure and other mechanical factors and might be injured first, but the results of the present experiment failed to support this anticipation. The results rather suggest that the changes of the basement membrane of arterioles and basement
membrane like materials of mesangium and lacis occur about the same time and progress in the same degree but the changes of the basement membrane of glomerular capillary loop occur with a time lag. This suggest that the basement membrane and basement membrane like material of these areas mutually continued and resemble in formation and pathologic changes. In hypertension, the basement membrane of vascular wall and basement membrane like material of mesangium and lacis may be the areas most liable to injury and change.

The roughness and electron lucency observed commonly in all basement membranes and basement membrane like materials may be the morphological appearance of chemical changes such as sclerosis and degeneration of these materials. And the electron lucency may be resemble the electron microscopic appearance of elastic fibers. The thickening of basement membrane and the increase of basement membrane like material may be the morphological expression of abnormal accumulation of these materials.

In fibrinoid necrosis, the basement membrane of adventitial area, the basement membrane of glomerular capillary loop and the basement membrane facing Bowman’s space are hardly destroyed, while the basement membrane like material of mesangium and the intercellular basement membrane of media suffer intensive changes. This may suggest that there is a considerable difference in behavior between these two groups of basement membrane or basement membrane like material.

This paper was partly presented at the 16th Congress of the Japanese Society of Nephrology in 1973 and the 15th Congress of the Japanese College of Angiology in 1974.

The author wishes to thank Professor Issei NISHIMORI and Assistant Professor Nobuo TSUDA in the Department of Pathology, Atomic Disease Institute, Nagasaki University School of Medicine for their teaching and guidance in this study.

REFERENCES


Legends for Figures

Fig. 1 Glomeurlus of normotensive rat
Three-laminal structure is present in the basement membrane of glomerular capillary loop and the mesangial basement membrane facing Bowman’s space (arrows). Silver granules are deposited diffusely in the inner side of the lamina densa. (x 4,500)

Fig. 2 Glomerular capillary loop of hypertensive rat
The basement membrane of glomerular capillary loop is thickened and tortuous. The endothelial cytoplasm (E) is detached from the basement membrane (arrows). (x 16,600)

Fig. 3 Glomerular capillary loop of hypertensive rat
The capillary lumen is collapsed. Some parts of the basement membrane of glomerular capillary loop are thickened and fused. (x 6,000)

Fig. 4 Glomerular capillary loop of hypertensive rat
The lamina rara interna (LI) of the basement membrane of capillary loop is swelled and thickened to approximately 800 m. Irregular running of microfibrils measuring 5~10 m in diameter are seen inside (arrows). Silver granules are deposited in the inner side of the lamina densa. (x 16,600)

Fig. 5 Fibrinoid necrosis, glomerulus (acute stage)
(a) Capillary lumen: Filled with ground glass-like plasma components (PC) including fibrin (F). Silver granules are deposited in seemingly the lamina densa of the basement membrane of glomerular capillary loop. (x 7,500)

(b) Mesangial area: Ground glass-like plasma components (PC) including fibrin (F) are present in the basement membrane like material. Silver granules are deposited in the lamina densa of the basement membrane facing Bowman’s space (BS). (x 7,500)

Fig. 6 Mesangium of hypertensive rat
The basement membrane like material has increased diffusely and silver granules are deposited in the basement membrane facing Bowman’s space (short arrows). Some electron lucent areas are observed in the basement membrane like material. Microfibrillar structure and fine granules are present in some areas (long arrows). (x 7,500)

Fig. 7 Mesangium of hypertensive rat
Mesangial cytoplasms are compressed by the basement membrane like material or torn to pieces. Cell debris such as vacuoles and dense bodies are seen in the basement membrane like material (arrows). (x 4,500)

Fig. 8 Mesangial basement membrane like material of hypertensive rat
(a) Mesangial cytoplasms are torn to pieces in the basement membrane like material, which is fine granular and scattering electron lucent. (x 32,500)

(b) The border of the mesangial basement membrane and basement membrane like material is indistinct. However, silver granules are diffusely deposited in the area corresponding to the lamina densa. (x 17, 500)

Fig. 9 Fibrinoid necrosis, glomerulus (late stage)
(a) Fibrin masses (F) were seen remaining in the increased basement membrane like material. (x 7,500)

(b) High magnification of (a): The surrounding areas of fibrin masses are electron lucent. (x 17,500)

Fig. 10 Lacis of intact glomerulus
The basement membrane like material is narrow and indistinct (arrows). L: lacis cells
(x 3,750)

**Fig. 11** Structure of intact vascular pole
Silver granules are deposited in the basement membrane of Bowman’s capsule (arrows), but not in the vascular basement membrane. (x 6,000)

**Fig. 12** Subendothelial basement membrane of intact vessel
Three-laminal structure is present (short arrows). Some central areas of the lamina densa are slightly electron lucent. Scanty silver granules are deposited in the lamina densa (long arrows). (x 20,800)

**Fig. 13** Subendothelial basement membrane of hypertensive rat
The subendothelial basement membrane (Sb) is swelled. Electron lucent areas show large reticular change and some fine granules measuring 50 Å in diameter (arrows). (x 17,500)

**Fig. 14** Vascular pole of hypertensive rat
The subendothelial basement membrane is thickened in beads-like shape and the interior shows reticular change (arrows). In the lacis, the increase of the basement membrane like material (BM) is considerable, resulting in compression of lacis cells and irregular tearing of cytoplasms. (x 6,000)

**Fig. 15** Vascular pole of hypertensive rat
Dense material (D) is deposited in the vascular basement membrane. Lysosomes and JG granules in JG cells are vacuolated (arrows). The mesangial basement membrane like material adjacent to the vascular pole shows a moderate increase. (x 3,000)

**Fig. 16** Vascular pole of hypertensive rat
Smooth muscle cells are compressed or torn to pieces by an increase of the basement membrane like material (BM). (x 7,500)

**Fig. 17** Vascular pole of hypertensive rat
Cell debris such as small granules and dense bodies are seen scatteringly in the increased basement membrane like material (arrows). (x 3,750)

**Fig. 18** Adventitia of hypertensive rat
Silver granules are deposited in the innermost lamina of the basement membrane of adventitial area (arrows). An increase of collagen fibers (CF) is also seen in part. (x 7,500)

**Fig. 19** Mesangium and lacis of hypertensive rat
(a) The increase of the basement membrane like material of lacis is intensive resulting in a similar change of the mesangium. The basement membrane of glomerular capillary loop is thickened and considerable in wrinkle and tortuosity (arrows). (x 3,000)

(b) The increased basement membrane like material is rough with definite microfibrillar structure (arrows) and some electron lucent areas. Some cytoplasms of lacis cells are torn to pieces and seen in the basement membrane like material. (x 7,500)

**Fig. 20** Vascular pole of hypertensive rat
Silver granules are deposited regularly in the basement membrane facing Bowman’s space but is not seen in the increased basement membrane like material (BM) of lacis. (x 7,500)

**Fig. 21** Fibrinoid necrosis, vascular wall (acute stage)
Eduction of platelets, fibrin (F) and other plasma components is present in the area from the intima to the media. (x 7,500)
Fig. 22  Fibrinoid necrosis, vascular wall (late stage)

Fibrin (F) alone are seen in the media. Silver granules are deposited in the basement membrane of adventitial area (arrows). (x 7,500)

Fig. 23  Vascular pole of hypertensive rat

The subendothelial basement membrane shows beads-like thickening (arrows) and the adjacent lacis indicates a strong increase of basement membrane like material (BM). (x 4,500)