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Pathogenesis of the Lesions of Glomerulus and Renal Arteriole in Experimental Hypertension

I. An Electron Microscopic Study of Glomerulus in Experimental Hypertension

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Rats with adrenal regeneration hypertension were divided by the degree of blood pressure, and the changes in renal glomerulus were studied mainly with electron microscope.

The increase in mesangial basement membrane like material and in the mesangial cells occurred as the early changes in the glomerulus. The mesangial basement membrane like material was extremely increased with an increase in blood pressure or with time. In some cases, fibrinoid necrosis appeared. It was considered that the increased mesangial basement membrane like material was produced anew, since the silver granules which were previously labeled were not deposited into them. Fibrinoid necrosis was considered to arise mainly from the interruption of the blood circulation, such as collapse of the capillary loop and platelet thrombi, and hyperpermeability.

The findings of argyrosis could be ruled out in this study, since there were no findings which were suspected to show the renal lesions caused by the oral administration of a silver nitrate solution used as a label.

INTRODUCTION

Adrenal regeneration hypertension[10)11)] worked out by SKELTON is applicable for observation of renal lesions in animals with hypertension, because it does not make a direct attack on the kidneys, and enables to cause hypertension in a extremely high incidence. There has been almost no report on the study of fine structure of renal lesions

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in cases of adrenal regeneration hypertension except a report by GEER *et al.*[4].

Reports which have been published up to now only described the findings of the glomerulus in hypertension, in which there was no attention to the relationship between the degree of hypertension and of lesions. Therefore, in this study, hypertension was divided into three groups by the degree of the blood pressure, and the lesions and the degree of the damage were studied in each stage.

The oral administration method of a silver nitrate solution is a simple method to label the basement membrane, especially the glomerular basement membrane, and silver granules can be well identified with electron microscope. Therefore, many reports on the usage of this method have been published by KURTZ *et al.* and others[5)14)19)20)]. It was concluded from our previous experiment that silver granules can be fully used as a marker, although there were sequential changes with time[7)17)]. Therefore, this oral administration method of a silver nitrate solution was used in this study, in order to label the basement membrane preceding the hypertensive glomerular lesions.

METHODS

Young Wistar rats were used in this experiment. They were divided into the following two groups.

A group:

Female 70 rats weighing 50 g were used. The enucleation of the left adrenal gland was done after the right nephrectomy and adrenalectomy. In addition, 1% of a saline solution was orally administered.

B group:

Silver nitrate solution, 0.25%, was orally administered before the same operation as that of A group. In this group, rats weighing 25g were used. They received 0.25% of a silver nitrate solution as a drinking water for 3 weeks, and then, 17 rats received the operation mentioned above. In addition, 1% of a saline solution was orally administered. The weight and blood pressure in all rats were determined every week.

All rats in these two groups were sacrificed 4 to 6 weeks after operation, and furthermore, divided into the following group by the blood pressure at the time of the sacrifice.

i) Mildly hypertensive group

…… in which the blood pressure was about 180 mmHg even when six weeks have passed since operation.

ii) Moderately hypertensive group

…… in which the blood pressure was about 180 mmHg 4 weeks after operation, and more than 200 mmHg of the blood pressure was maintained only below one week.

iii) Severely hypertensive group

..... in which the blood pressure was over 200 mmHg 4 weeks after operation, and was maintained at least over one week.

Rats in which the blood pressure was not increased after operation were regarded as the normotensive group. Other groups in which 1% of a saline solution was administered for 6 weeks as a drinking water with no operation and in which 1% of a saline solution was administered for 6 weeks after right nephrectomy, were regarded as controls.

Table 1. Frequency of Hypertensive Rats

Groups	Number of cases	Frequency (%)
Normotension	24	27.6
Mild hypertension	18	20.7
Moderate and severe hypertension	15	17.2
Dead	30	34.5
Total	87	100.0

Table 1 and 2 show the number of rats which received an operation and the number of rats which were electron microscopically studied in detail, respectively.

Each rat for electron microscopic study was fixed by perfusion with 1.5% of glutar-aldehyde. The blocks for the light microscopic study were fixed again with 10% of formalin. (Each rat for light microscopic study only was fixed with 10% of formalin.) In addition, they were embedded in paraffin, and were stained with Hematoxylin and Eosin, PAS, Mallory-Azan and Oil red O. The blocks for electron microscopic study were fixed with 3% of glutar-aldehyde followed by 1% of osmic acid. In addition, they were embedded in Epon 812 after dehydrating with alcohol series. Ultra-thin sections were stained with uranyl acetate and lead citrate, and the glomerulus was observed with the JEM 7A type of electron microscope, and was photographed.

The USM-105-RAT type of the automatic recording apparatus of the blood pressure (tail-cuff-method) was used in the determination of the blood pressure, and the blood pressure was determined with no anesthesia.

In the determination of the width of the basement membrane of capillary loop, three to six rats were used from each group. At least six gromeruli per rat were observed. Twenty pictures with magnification of 17,500 times were taken, and the average values were obtained (Table 2).

RESULTS

The mortality of rats was about 35%, in which about the half died 1 or 2 weeks after operation. The adrenal regeneration of these rats was insufficient (the state of adrenal insufficiency). Thirty of 55 rats in B group died before operation, and most of them were poorly increased in weight.

Table 2. Thickness of Basement Membrane

Groups	Number of the rats	Thickness (mμ)
Not operated+1% NaCl	3	193±4
Unilateral nephrectomy+1% NaCl	3	211±5
Operation for hypertension		
Normotension	3	192±3
Mild hypertension	4	206±5
Moderate hypertension	6	231±5
Severe hypertension	4	230±7

1) *Weight*

There was no significant difference 2 weeks after operation among three groups, the normotensive group, the mildly hypertensive group and the moderately and severely hypertensive group. In the moderately and severely hypertensive group, the increase in weight was blurred from about 3 weeks after operation, especially in one week between the 3rd week and the 4th week. The average weights were 191.1g in the normotensive group, 201.3g in the mildly hypertensive group and 176.0g in the moderately and severely hypertensive group 6 weeks after operation, which suggested the poor increase in weight from 2 to 4 weeks after operation in cases of adrenal regeneration hypertension (Fig. 1).

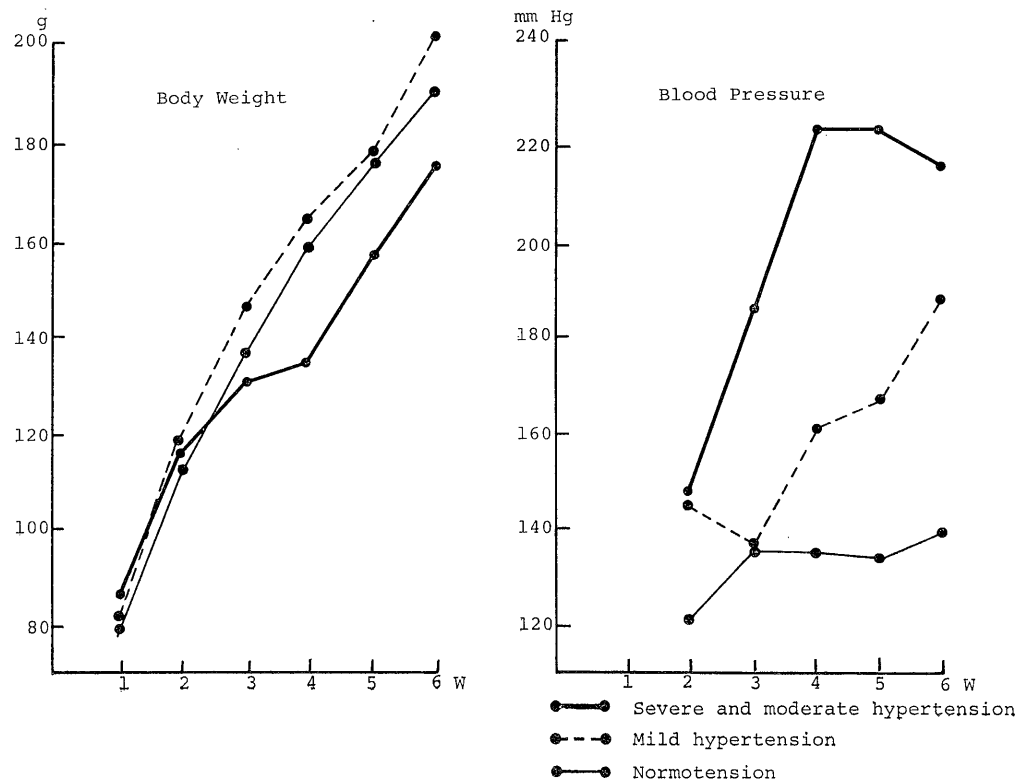

Fig. 1 Body Weight and Blood Pressure of the Rats

The weights of rats in B group were poorly increased before operation, compared with those of a control group with 25g of weight which received a tap water. The average weights were 54g in B group and 102g in a control 3 weeks later (Fig. 2).

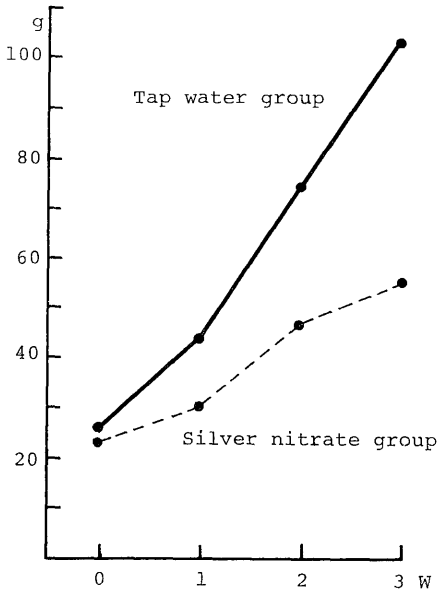

Fig. 2 Body Weight of the Rats given Tap Water and Silver Nitrate Solution

2) *Blood pressure*

The moderately and severely hypertensive group occupied 17.2% (15 rats) and the mildly hypertensive group 20.7% (18 rats) of all number of the rats with operation (Table 1). In the moderately and severely hypertensive group, the blood pressure averaged 147.5 mmHg 2 weeks later, 185.6 mmHg 3 weeks later, and 224.4 mmHg 4 weeks later. From these results, it was found that the blood pressure was increased with an average of 40 mmHg every week from 2 to 4 weeks after operation. This finding corresponded to the finding that the increase in weight was poor during this period. In addition, in the moderately and severely hypertensive group the blood pressure was slightly decreased 6 weeks after operation, but there was statistically no significant difference. In the mildly hypertensive group, the blood pressure was about 140 mmHg 3 weeks after operation. Since then, it was increased at the rate of 10 to 15 mmHg every week. At the 6th week, it reached 188.9 mmHg on the average. In normotensive group, there was no case in which the blood pressure was over 150 mmHg through all weeks. All the cases maintained about 135 mmHg of the blood pressure (Fig. 1).

3) *Macroscopic findings of the kidneys*

The kidneys in rats with operation were more enlarged than those of controls with no unilateral nephrectomy, regardless of the blood pressure. The surface of the kidneys was smooth in normotensive group and mildly hypertensive group. In moderately

hypertensive group and severely hypertensive group, the surface was slightly granulated.

4) *Thickness of the basement membrane of the glomerular capillary loop*

In the moderately hypertensive group and severely hypertensive group, the width of the basement membrane averaged 231 mμ and 230 mμ, respectively, which showed the evident thickness, compared with 206 mμ in mildly hypertensive group and 192 mμ in normotensive group ($p<0.01$). As shown above, in mildly hypertensive group the basement membrane of the glomerular capillary loop was thicker than that in normotensive group ($p<0.05$). But there was no difference in the width of the basement membrane between a mildly hypertensive group and controls with administration of 1% of a saline solution after the unilateral nephrectomy. There was no difference in the width of the basement membrane between a normotensive group and a control group which was given only 1% of a saline solution. The thickness of the basement membrane was evidently seen by the unilateral nephrectomy in controls ($p<0.01$) (Table 2).

5) *Microscopic findings*

a) *Mildly hypertensive group*

The mesangium was increased in a cord-like form under the observation by a light microscope. In addition, the cells were slightly increased in this area, but there was almost no change in the other area. In rats which were given a silver nitrate solution before operation, the other finding such as the deposition of thinly brown silver granules in the basement membrane of the capillary loop was observed.

Electron microscopic findings showed the slight increase of mesangial cells and mesangial basement membrane like material. There was almost no change in the endothelial cells and the fenestration was well maintained. The width of the basement membrane of the capillary loop was slightly thickened, compared with that of a normotensive group. The epithelial cytoplasms were partly swelled. In these cells, 500 to 1000 mμ in diameter of dense ovoid bodies and small vacuoles were scatteringly seen. About 5μ of dense deposit was also sometimes seen (Fig. 3). There was almost no change in the parietal epithelial cells.

In a rat which was orally given a silver nitrate solution before operation, silver granules were diffusely deposited in the endothelial side of the lamina densa in the basement membrane of the capillary loop. In addition, they were deposited in the inner part of lamina densa in the basement membrane faced on the Bowman's space in the mesangium. However, there was no deposition of silver granules in slightly increased basement membrane like material around the mesangial cells (Figs. 4 and 5). Silver granules were deposited in the Bowman's capsule, but the deposition was slighter than that in the basement membrane of the capillary loop.

b) *Moderately hypertensive group*

The glomeruli were remarkably simplified and lobulated in the light microscopic observation. The mesangium was thickened, and the capillary lumen was partly

obstructed. The basement membrane of the capillary loop was slightly thickened. The cells which were suspected to be mesangial cells were increased in a nest-like form. The Bowman's capsule was slightly swelled and thickened (Fig 6). Hyalinization appeared in some glomeruli and the blood vessels. In the group which was orally given a silver nitrate solution before operation, in addition to the findings mentioned above, thinly brown silver granules were deposited in the basement membrane of the capillary loop.

The mesangial basement membrane like material was remarkably increased in the electron microscopic observation. Mesangial cells were more increased than those in the previous group. Mesangial basement membrane like material was irregularly and branchedly increased toward the mesangial cells. There was almost no finding in which mesangial cells were compressed, and the Golgi's apparatus and rough endoplasmic reticula were still observed (Fig. 7). In addition, a large number of colliculi were often present in the region faced on the capillary lumen (Fig. 8). The endothelial cells were not increased, but compressed to the capillary lumen and sometimes shifted to the peripheral area of the capillary loop (Fig. 9). The endothelial cytoplasms were slightly thickened, and the fenestration was slightly decreased (Fig. 10). The capillary lumen was extremely narrowed by the endothelial cells and partly narrowed by the colliculi. It was sometimes completely obstructed (Fig. 9). Many platelets were gathered in the lumen (Fig. 10). There were some regions which seemed to form the platelet thrombi (Fig. 11). The width of the basement membrane of the capillary loop was extremely thickened, and localized or tortuous thickness was seen. The mesangial interpositions were seen in some places, and were factors to produce a thickness of the basement membrane of the capillary loop. The epithelial cells were swelled as the same as those in the previous group. Many Golgi's apparatus and mitochondria were seen and about 500 $m\mu$ of vacuoles and ovoid bodies were scattered in the epithelial cytoplasms. Notches of the epithelial nucleus were increased. Fusion of the foot processes became remarkable (Fig. 11). Several places in the basement membrane of the Bowman's capsule were swelled by several times. In these places, many dense granules and fibrils were seen. The parietal epithelial cells were also swelled.

In rats which were orally given a silver nitrate solution before operation, in addition to these findings mentioned above, silver granules were deposited in the same region as that in the mildly hypertensive group. However, silver granules were not deposited in the mesangial basement membrane like material which was irregularly increased toward the mesangial cells. In addition, silver granules were diffusely deposited in the most external dense layer of the basement membrane of the swelled and thickened Bowman's capsule (Figs. 15, 18 and 20).

c) *Severely hypertensive group*

Hyalinization of the glomeruli and blood vessels was often light microscopically observed. The gromeruli were simplified and the capillary lumen was almost obstructed. Here and there, the hypercellularity was seen in the nest-like form. There were granules

which showed positive fatty staining in some of these cells. The mesangium was thickened (Fig. 12). In a rat of which blood pressure was over 200 mmHg for 2 weeks, many glomeruli showed fibrinoid necrosis. The cells were also decreased and the cytoplasmic vacuoles (positive fatty staining) were scattered. The Bowman's capsule was thickened and adhered to the capillary loop of the glomerulus (Fig. 13).

Electron microscopically, the lesions in the mesangium were progressive. The mesangial basement membrane like material was irregularly and branchedly increased. This material was mainly composed of the usual fine fibrillar basement membrane like material, and sometimes slightly swelled. Vacuoles and granules which seemed to be cell debris, and fibrils which seemed to be collagen fibers were scattered in this area (Fig. 14). In addition, there were electron lucent areas with vacuolar or linear appearance (Fig. 15). Mesangial cells were increased as well as those in the moderately hypertensive group. The mesangial cytoplasms were compressed, torn to pieces and scattered into the basement membrane like material. Golgi's apparatus and mitochondria almost disappeared. There were almost no colliculi, but there were many mesangial interpositions (Fig. 15). The endothelial cells were increased and compressed by an increased mesangial basement membrane like material, and therefore, those cells projected into the capillary lumen, obstructed it, and shifted to the peripheral area of the capillary lumen (Fig. 16). The endothelial cytoplasms were considerably thickened, and often detached from the basement membrane of the capillary loop (Fig. 17). The width of the basement membrane of the capillary loop was extremely thickened with hump-like projections (Fig. 18), remarkable wrinkle and tortuosity. The capillary lumen was obstracted by attaching each other (Fig. 19). Fusion of foot processes became more remarkable (Figs. 15 and 17). The organellae in the epithelial cytoplasms were well developed (Figs. 14 and 15). The basement membrane of the Bowman's capsule showed the similar findings as those in moderately hypertensive group, but those findings were seen more often.

In rats which were orally given a silver nitrate solution, silver granules were deposited in the inner part of the lamina densa in the basement membrane of the capillary loop and of the mesangium faced on the Bowman's space, and in the outer dense layer of the basement membrane of the Bowman's capsule, as well as those in the previous groups (Figs. 15, 17, 18 and 20). However, there was almost no deposition of the silver granules in the basement membrane like material which was increased toward the mesangial cells (Fig. 15).

In the glomeruli with fibrinoid necrosis, the capillary lumen and mesangium were filled with matrix which looked like ground glass and was supposed to be plasma components in the acute state, in which a plenty of fibrin masses and cell debris were observed. The cells which were considered to be mesangial cells contained many vacuoles 1~3μ in diameter. The epithelial cells were degenerated, and the foot processes were fused. They were detached from the basement membrane of the capillary loop (Fig. 21). The ground glass like matrix disappeared after the acute stage. There

remained a plenty of fibrin masses with various sizes in the mesangial basement membrane like material, of which surroundings were electron lucent. The mesangial cells were compressed and slightly gouged out (Fig. 22).

As summarizing these main changes in Table 3, the mesangial basement membrane like material was increased with the degree of hypertension. In addition, the mesangial hypercellularity, the thickness and tortuosity in the basement membrane of the capillary loop and the fusion of the foot processes became remarkable in proportion to the degree of hypertension. More accelerated hypertension caused fibrinoid necrosis in the glomerulus.

Table 3. Main Changes in Hypertensive Glomerulus

	Changes	Mild hypertension	Moderate hypertension	Severe hypertension
Mesangial	Increased basement membrane like material	+	++	+++
	Hypercellularity	±	+	+
	Increased colliculi	−	+	±
	Fibrinoid change	−	+	++
Peripheral	Thickened basement membrane	+	++	++
	Tortuous basement membrane	−	+	++
	Increased endothelial cell	−	+	+
	Platelet thrombi	−	+	+
	Mesangial interposition	−	+	+
	Fibrinoid change	−	+	++
	Fused foot processes	−	+	++

DISCUSSION

It is essential to have the regenerated adrenal cortex in the development of the experimental adrenal regeneration hypertension[12)13)], but the mechanism of this hypertension have not been revealed yet. As this hypertension differs from GOLDBLATT's type of hypertension influenced by renin, it is useful for the follow-up study of hypertensive vascular changes.

In this study, the blood pressure was rapidly increased and the body weight was decreased from 2 to 4 weeks after operation in moderately and severely hypertensive group (Fig. 1). In rats which died 1 to 2 weeks after operation, the adrenal regeneration was little developed. These findings are almost similar to those reported by other previous investigators[4)8)15)].

There are many electron microscopic studies on the changes in glomerulus in cases of hypertension[1)4)9)15)]. GEER *et al.*[4)] mentioned the increase in ovoid bodies in the visceral epithelial and mesangial cells and fusion of foot processes as the early stage of changes in adrenal regeneration hypertension. TAKEBAYASHI[15)] described the

increase in lysosomes and lipid granules in the mesangial cells, and in colliculi in four different experimental hypertension including adrenal regeneration hypertension. On the other hand, OKITA[9] suggested fusion of the foot processes and the changes in the epithelial cells as the first stage of changes in GOLDBLATT's type of hypertension.

Mesangial basement membrane like material was remarkably increased with the exacerbation of hypertension in this study (Figs. 7, 14 and 15). The cells in the tunica media were mainly disturbed as vascular lesions in hypertension[16]. On the reference to the report by DUNIHUE *et al.*[3] that JG cells are similar to mesangial cells, it is easy to explain the results that the mesangium in glomerulus was mainly disturbed in hypertensive lesions. TAKEBAYASHI[15] reported that colliculi were increased in hypertension, and he considered that they were factors to show the activity of the mesangial cells. From the result in this study, it was considered that the colliculi partly influenced the narrowing of the capillary lumen, but are not the significant factors. The basement membrane of the capillary loop was slightly damaged, compared with the mesangial basement membrane like material. If the capillary loop has functionally more extensibility against the mechanical pressure than the mesangium, this may explain the finding above that the changes in the basement membrane of the capillary loop were smaller than those in the mesangial basement membrane like material. OKITA[9] mentioned that the nuclei were shifted to the peripheral area and the fenestration of the endothelial cells was decreased as the second stage of changes in the endothelial cells. The same findings were also obtained in this study. These changes are far smaller those in the mesangium.

The aggregation of the platelets in the capillary lumen and the formation of the thrombi were considered to be important factors to cause the fibrinoid necrosis in the glomerulus (Figs. 10 and 11). The similar findings were seen in cases of hemorrhagic hypotension[2] and cases which received intravenous administration of thrombin and thromboplastin[18]. Toxic factor was suspected as one of other factors. The interruption of the blood circulation, such as collapse of the capillary loop and platelet thrombi, and hyperpermeability would cause the fibrinoid necrosis in the glomerulus. It is uncertain whether the mesangial cells containing vacuoles seen in this case are the same as the foam cells[6] seen in cases of nephrosis and others. This vacuolation was corresponded to the positive fatty staining granules with light microscope. The factor to produce this vacuolation is unknown, but it may be a nonspecific factor in hypertension. These changes at the acute stage would be transferred to the following changes. That is, the mesangium contained fibrin masses connected to the fibrin in the capillary lumen. Its surroundings were partly electron lusent (Fig. 22). These findings seemed not to be opposite to the fibrinoid necrosis at the late stage.

The changes in the basement membrane were more clearly caused by oral administration of a silver nitrate solution. KURTZ *et al.*[5] described that the visceral epithelial cells synthesized the basement membrane, judging from the finding that silver granules were mainly seen in the endothelial side of the basement membrane in the

glomerulus in normal aged rats and rats of aminonucleoside nephritis. WALKER[19] reported the same conclusion as that by Kurtz *et al.*[5]. On the other hand, STRIKER *et al.*[14] held the question of the cellular site of synthesis of the glomerular basement membrane.

In this study, the increased basement membrane like material did not contain the deposition of silver granules, and was considered to be produced anew. Silver granules were deposited in the inner layer of the lamina densa in the basement membrane of the capillary loop and in the mesangial basement membrane faced on Bowman's space (Figs. 10, 15, 17 and 18). This material was considered to be increased by the new production of the outer layer of the basement nembrane. The outer dense layer in the basement membrane of the Bowman's capsules contained silver granules, and was considered not only to be generally thickened but also to be swelled in the inner side. The increased mesangial basement membrane like material was considered to be caused by the mesangial basement membrane faced on the Bowman's space itself, but not to be caused by the lamina densa, because silver granules were almost regularly arranged in the lamina densa. In addition, some of the mesangial basement membrane like material was considered to be produced by the mesangial cells and from their cell debris in this region (Fig. 14). The new production of the basement membrane of capillary loop and the mesangial basement membrane faced on Bowman's space was considered to be influenced by the epithelial cells, judging from the deposition of silver granules. In addition, some of the material which reached this region would influence the new production of the mesangial basement membrane like material by passing into these basement membrane.

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Legends for Figures

Fig. 3 Mildly hypertensive case
The mesangial basement membrane like material was slightly increased. About 5 μ of dense deposit (D) and 500~1000 mμ of dense ovoid bodies and small vacuoles were seen in the epithelial cells. (x 3,750)

Figs. 4 and 5
Cases with administration of a silver nitrate solution before operation

Fig. 4 Normotensive case
There was no increase in mesangial basement membrane like material, but diffuse deposition of silver granules in the inner part of lamina densa in the mesangial basement membrane. (x 7,500)

Fig. 5 Mildly hypertensive case
There was a slight increase of mesangial basement membrane like material, but no deposition of silver granules. (x 7,500)

Figs. 6 – 11 Moderately hypertensive cases

Fig. 10 A case with administration of silver nitrate solution before operation

Fig. 6 The upper glomerulus was simplified and lobulated. The cells were slightly increased in a nest-like form. (H–E staining)

Fig. 7 The mesangial basement membrane like material was considerably increased. The organellae in the mesangial cells were still proven (arrows). (x 7,500)

Fig. 8 A large number of colliculi were present (arrows). (x 5,100)

Fig. 9 The endothelial cells were shifted to the peripheral area of the capillary loop, and almost obstructed the capillary lumen. (x 3,750)

Fig. 10 Many platelets were gathered in the capillary lumen. Silver granules were deposited in the inner part of the lamina densa in the basement membrane (arrows). Endothelial cytoplasms were slightly thickened, and fenestration was slightly decreased. Fusion of the foot processes was also seen. (x 7,500)

Fig. 11 The platelet thrombi (P) were formed in the capillary lumen. Fusion of the foot processes became remarkable. (x 4,500)

Figs. 12 – 22 Severely hypertensive cases

Figs. 15, 17, 18, 20, 21 and 22. Cases with administration of a silver nitrate solution before operation.

Fig. 12 There were many cells in which some granules showed the positive fatty staining. The capillary lumen was almost obstructed. (Oil red O staining)

Fig. 13 The glomerulus showed fibrinoid necrosis. (PAS staining)

Fig. 14 The mesangial basement membrane like material which contained fibrils (arrows), granules and vacuoles were remarkably increased. The mesangial cells were compressed as if the cytoplasms were gouged out. The organellae in the epithelial cytoplasms were well developed. (x 4,500)

Fig. 15 The mesangial basement membrane like material was extremely increased in the electron lucent areas with vacuolar or linear appearance, but no deposition of silver granules. Silver granules were deposited in the inner

part of the lamina densa in the basemenl membrane of the capillary loop and in the mesangial basement membrane faced on the Bowman's space (arrows). In addition, there were mesangial interposition, shift of endothelial cells, fusion of the foot processes and well developed organellae in the epithelial cells. (x 4,500)

Fig. 16 Endothelial cells were increased and occupied almost the area of the capillary lumen. Endothelial cytoplasm was thickened, and fenestration disappeared. The basement membrane of the capillary loop was thickened with wrinkle and tortuosity. (x 4,500)

Fig. 17 Silver granules were deposited in the inner part of the lamina densa in the basement membrane of the capillary loop. The endothelial cytoplasm was thickened and sometimes detached (an arrow). Fusion of foot processes became more remarkable. (x 4,500)

Fig. 18 Silver granules were deposited in the inner part of the lamina densa in the thickend basement membrane of the capillary loop where hump-like projection was seen. The endothelial fenestration disappeared. (x 17,500)

Fig. 19 The basement membrane of the capillary loop was remarkably thickened, wrinkly and tortuous. The capillary lumen disappeared. The organellae in the epithelial cell were well developed. (x 6,000)

Fig. 20 The Bowman's capsule was remarkably swelled and thickened, and the silver granules were deposited in the outer part of a slightly dense (short arrows). The inner part contained many fibrils (long arrows) and granules. (x 7,500)

Fig. 21 Acute stage of fibrinoid necrosis (mesangium) (x 3,000)

Fig. 22 Late stage of fibrinoid necrosis (mesangium) (x 6,000)

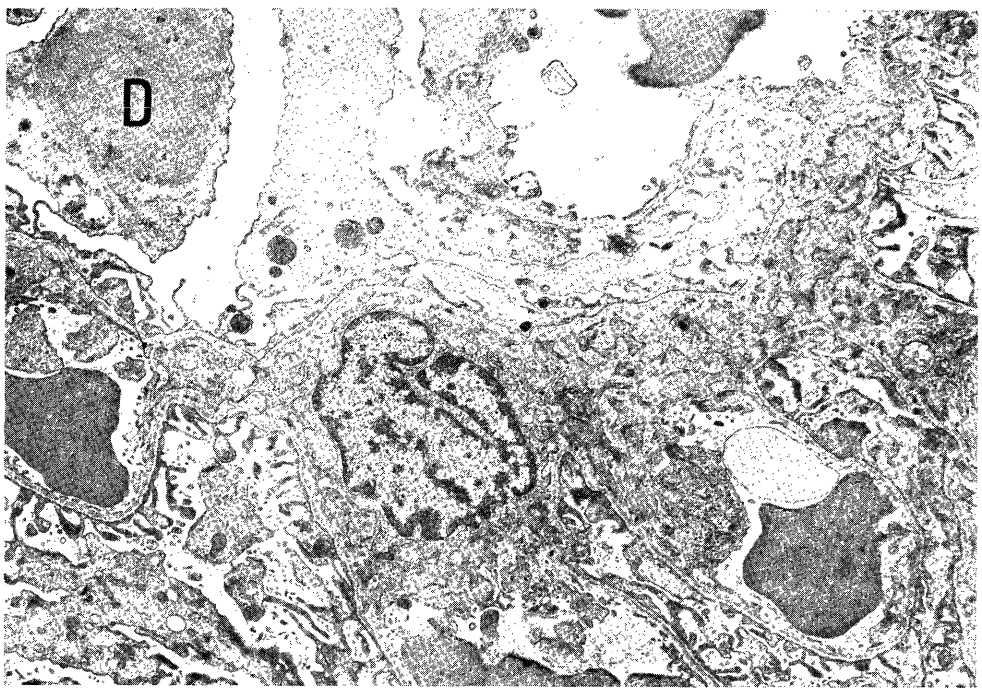


Fig. 3

Fig. 4

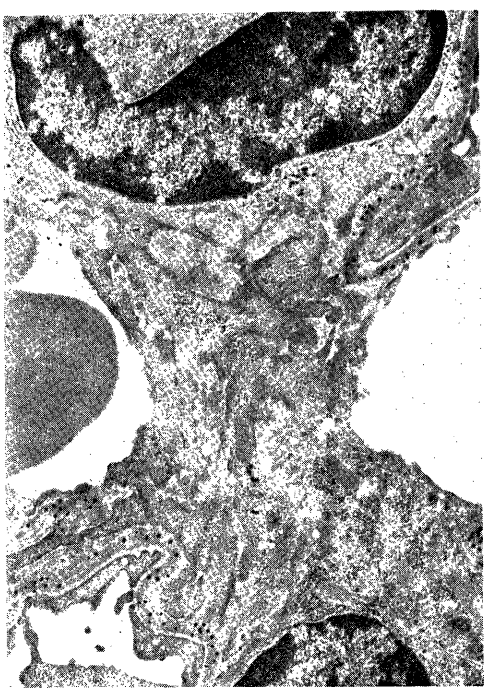


Fig. 5

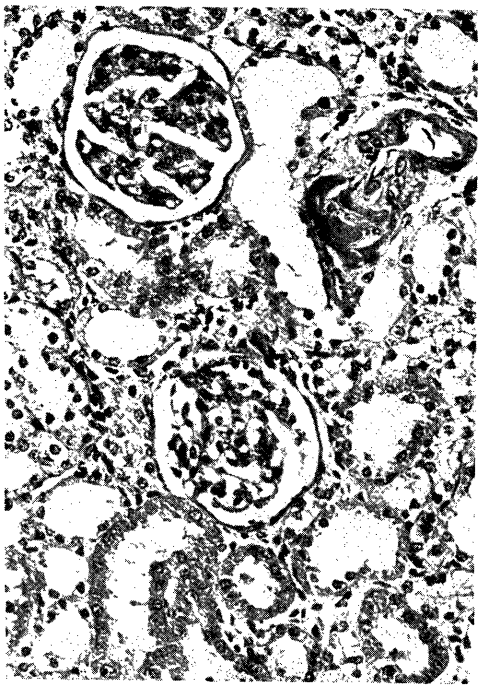


Fig. 6

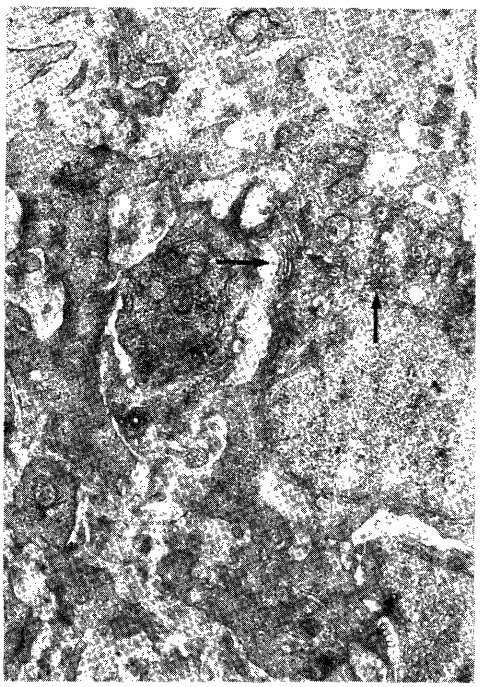


Fig. 7

Fig. 8

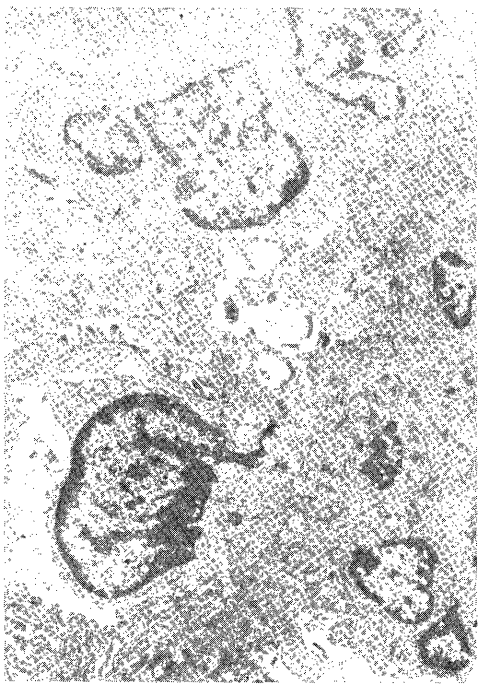


Fig. 9

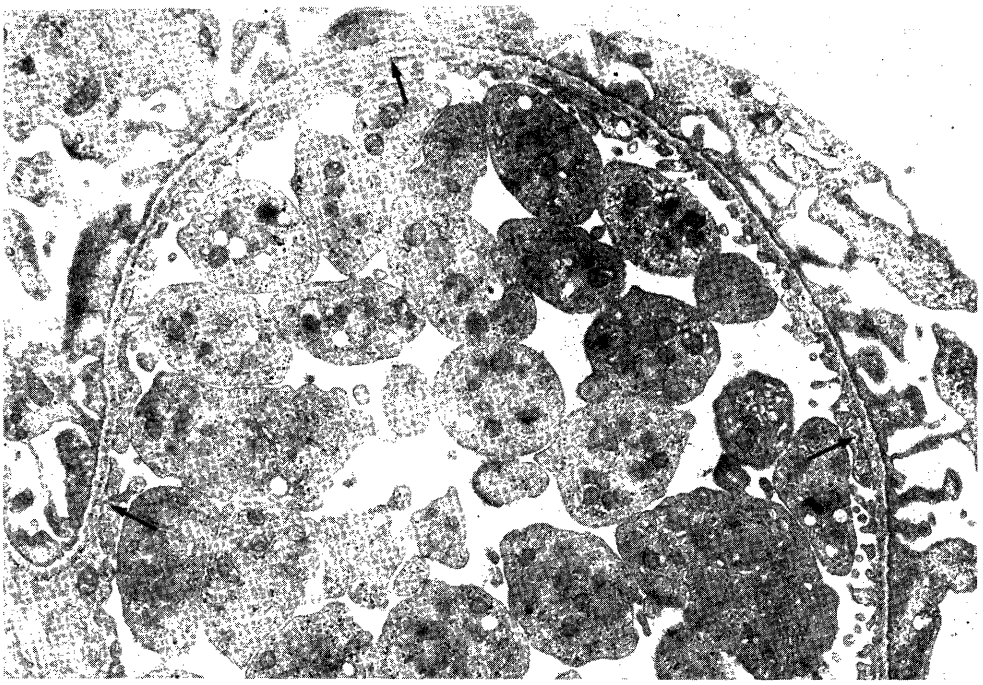


Fig. 10

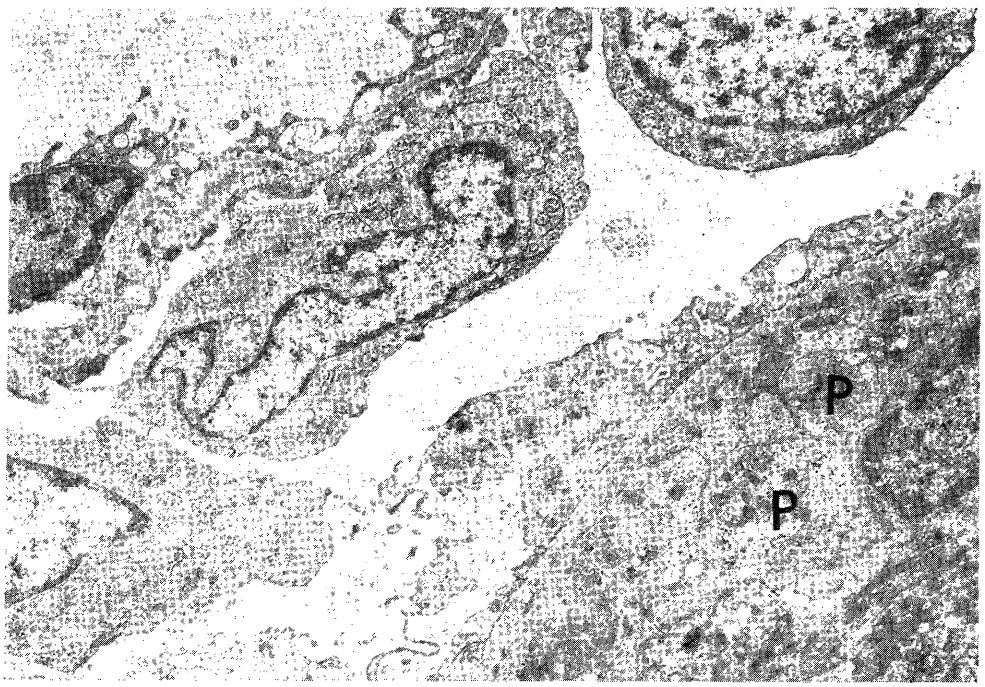
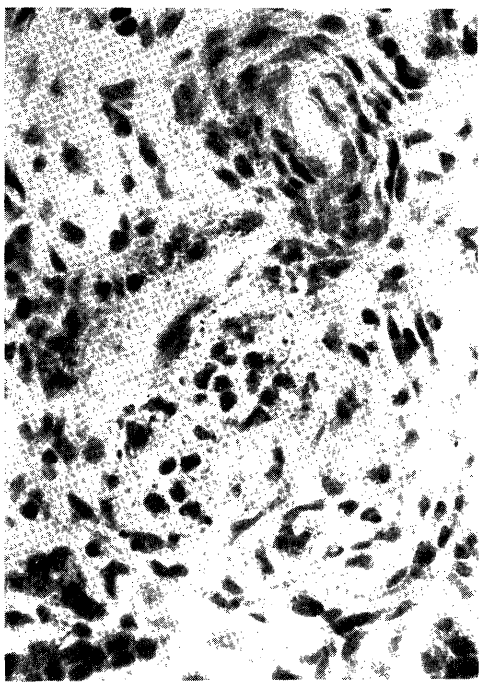


Fig. 11



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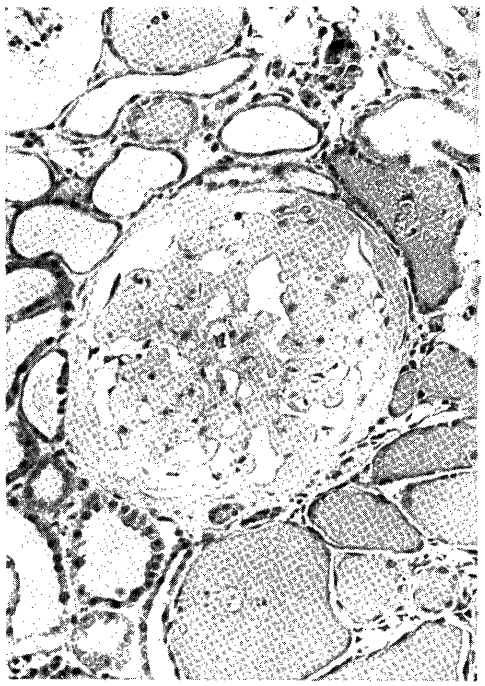

Fig. 13

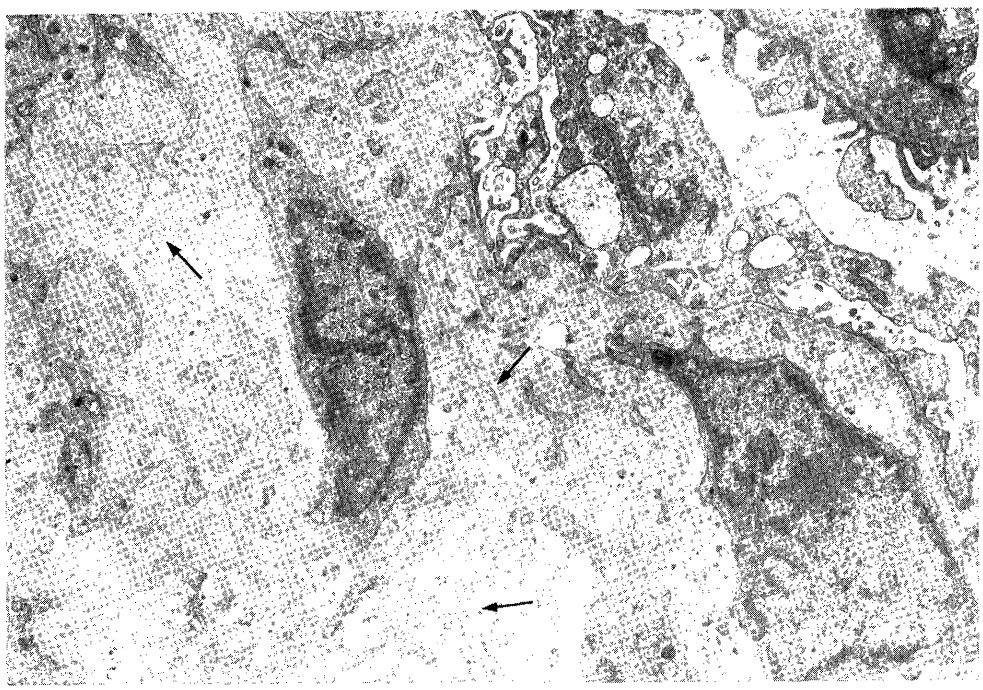

Fig. 14

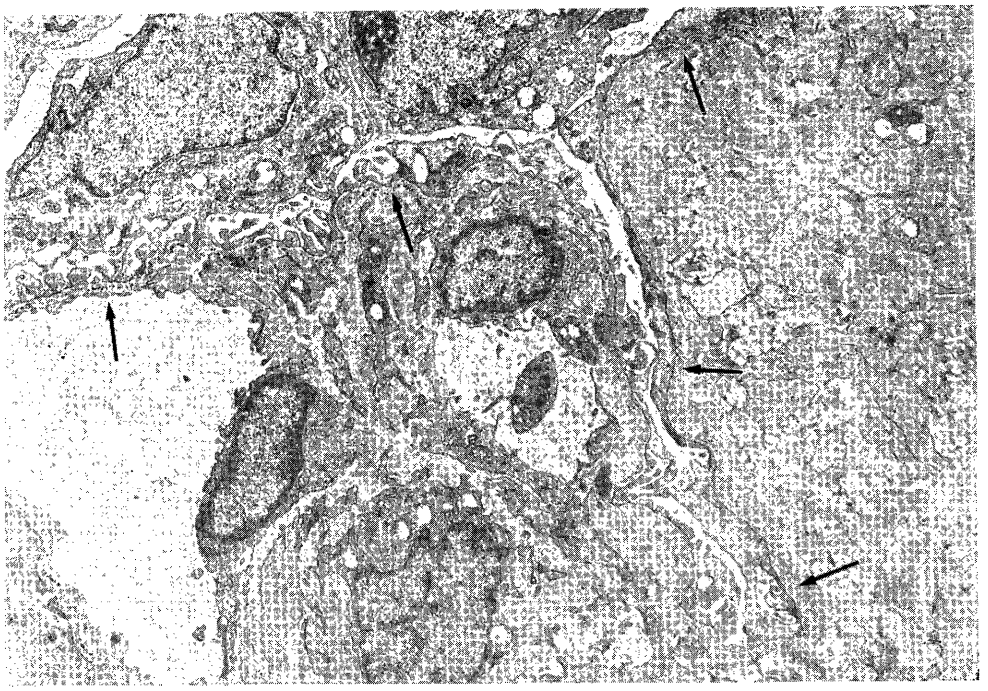

Fig. 15

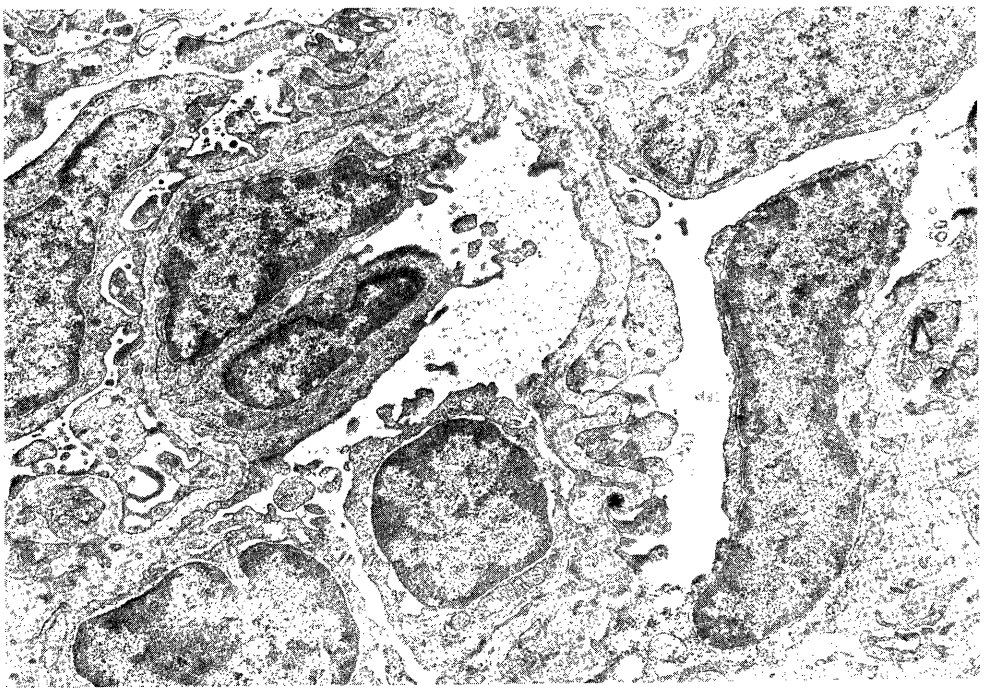

Fig. 16

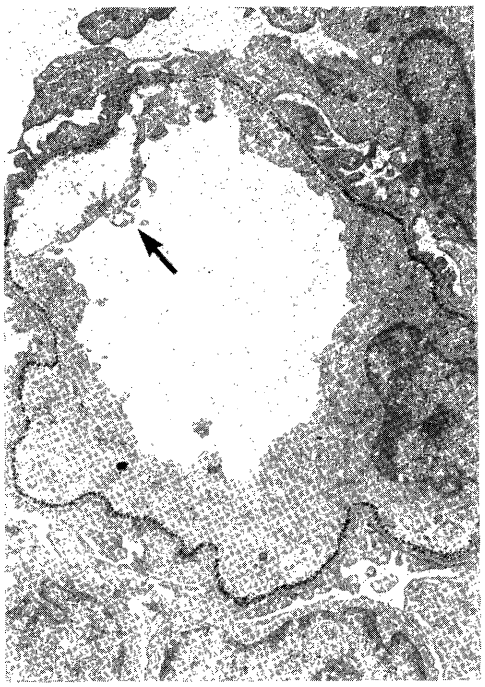

Fig. 17

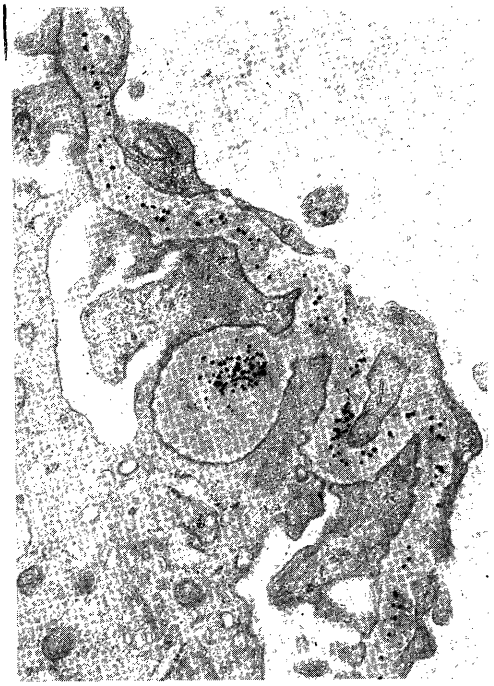

Fig. 18

Fig. 19

Fig. 20

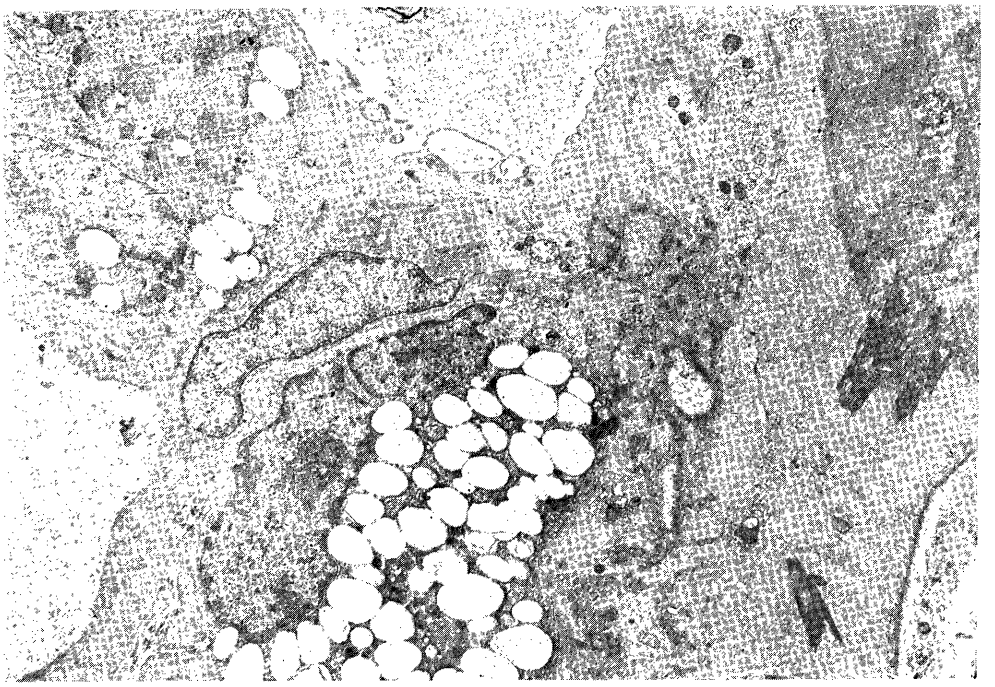

Fig. 21

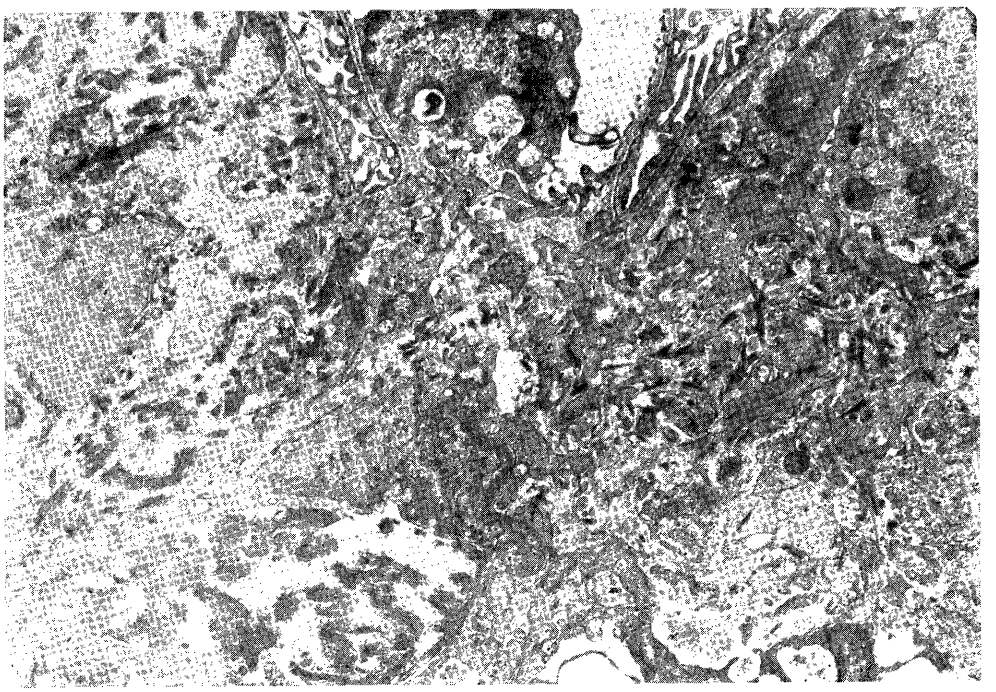

Fig. 22