Nagoya J. med. Sci. 34: 27-39, 1971

FINE STRUCTURE OF ADRENOCORTICAL CELL IN CUSHINGS'S SYNDROME

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ABSTRACT

Adrenocortical tumors or adrenal glands, obtained from cases of Cushing's syndrome consisting of two cases of adrenocortical cancer, three of adrenocortical adenoma, five of adrenocortical hyperplasia and two of adrenocortical nodular hyperplasia were studied by electron microscopy and compared with normal glands. Nodular hyperplasia was differentiated from simple hyperplasia by the unique clinical and fine structural features. The fine structure of adrenocortical cancer cells, which has not been reported up to the present, revealed well developed microvilli and Golgi complex, circular cristae and intramitochondrial body and two kinds of unidentified microbodies in the cytoplasma. Mitochondria of adenoma cells exhibited various sizes and round or oval shape displaying tubulo-vesicular cristae. Smooth surfaced endoplasmic reticulum (s.E.R.) was relatively well developed in many cases of Cushing's syndrome. Rough surfaced endoplasmic reticulum (r.E.R.) was well developed in the case of adenoma, especially in an infant case. Normal lipid droplets were sparse in cases of adenoma and nodular hyperplasia, but small round and homogenous dense bodies were observed in these two groups, especially abundantly in the latter. The fine structure of simple adrenocortical hyperplasia was almost similar to normal adrenal cortex except for the existence of many intramitochondrial bodies.

The fine structural characteristics of adrenocortical tumor or adrenal cortex in Cushing's syndrome were a well developed s.E.R., variety in the size of mitochondria, various cristae of mitochondria and prominent Golgi complex.

INTRODUCTION

In 1955 Lever[1] and Braunsteiner *et al.* independently described the fine structure of the adrenocortical cells in rodents. Subsequently, fine structural descriptions of the adrenocortical cells in many of experimental animals were reported by many investigators[2)-17)], and the morphological features of adrenocortical cells have been said to be characterized by a well developed smooth endoplasmic reticulum (s.E.R.), prominent Golgi complex, mitochondria of various sizes, unique cristae of mitochondria, numerous lysosomes and lipid droplets in greater or lesser numbers depending upon the species. A number of workers have also studied the fine structure of adrenocortical cells under

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Received for publiication January 14, 1971.

various experimental situations[18)-22)] which included stimulation by adrenocorticotropic hormone[23)-26)] and hypophysectomy[27)]. In functionally activated adrenocortical cells, an increase of s.E.R., enlargement of Golgi complex and alteration of mitochondrial cristae have been observed and their functions have been gradually made clear. Many enzymobiochemical studies correlated with electron microscopy have also provided valuable information on their function.

Carr[24)] and Luse[28)] first reported briefly on the fine structure of normal human adrenocortical cells. Recently Jones and Long[29)] have described it in detail. Luse[28)] and Liddle[30)] reported on the fine structure of adrenocortical cells in pathological conditions, and Reidbord[31)] also described it in a case of Cushing's syndrome due to adrenocortical hyperplasia. However, there have been no descriptions of the fine structure of adrenocortical carcinoma cells with Cushing's syndrome. In this paper are reported the fine structural findings of adrenocortical tumors or adrenals which were surgically removed from twelve patients with typical clinicopathological features of Cushing's syndrome, and the adrenals of the patients with breast cancer were comparatively studied as a control.

MATERIALS AND METHODS

Twelve surgically removed adrenals or adrenocortical tumor of patients with Cushing's syndrome and three adrenals of patients with advanced breast cancer were studied.

Immediately after removal of the adrenals or adrenocortical tumors, the materials were immersed in a cold fixative and cut into small pieces. They were then fixed in 1% osmium tetroxide buffered with phosphate at pH 7.4 containing 0.04 g saccharose/ml at 0°C for 1.5 hr. Some of the specimens were fixed, if necessary, in 2% glutaraldehyde solution with 1 mol phosphate buffer of pH 7.4 for two hours and then fixed with osmium tetroxide. The fixed materials were then dehydrated in ascending series of acetone starting with 50%. The embedding was performed according to the method of Luft[32)]. Thick sections were cut with a Porter-Blum ultramicrotome equipped with a glass knife and stained with toluidine blue for precise orientation. Subsequently ultrathin sections were made and stained doubly with uranyl acetate and lead citrate[33)]. These sections were examined and photographed by HITACHI Hu-11 A type electron microscope.

The clinico-pathological data of the patients are shown in Table 1.

The diagnosis of Cushing's syndrome was made by the clinical signs, laboratory findings and histology of removed adrenals and adrenal tumors.

Urinary 17-OHCS was examined by a modification of Kanbegawa's method or Reddy's method and plasma 11-OHCS by the modification of De-Moor's

TABLE 1. Clinical Data

Diagnosis	Sex	Age	Urinary 17-OHCS (mg/day)	Urinary 17-OHCS response to Dexamethasone test 2 mg/day (per os)	Dexamethasone test 8 mg/day (per os)	Metopirone test 4.5 g•day (per os)	Plasma 11-OHCS diurnal rhythm (μg/day) 0.00	6.00	Plasma 11-OHCS response to synth. ACTH rapid test (0.25 mg)**	Weight (gm)
carci-	m	34	36.4 -132.0	moderate	non	non	50.3	54.6	non	r -500
noma	m	22	49.1 -61.5	non	non	non	63.5	54.7	poor	r -700
adenoma	f	45	*16.5 -18.5	non	non	non	30.7	48.1	moderate	r - 14.2
	f	1	* 0.63- 1.54	—	non	—	23.2	25.2	poor	l -170
	m	19	34.3 -38.6	non	non	non	29.9	27.7	good	r - 13.3
hyper-	f	22	* 8.4 - 9.3	—	—	—	—	—	—	—
plasia	f	45	*13.0 -31.0	poor	moderate	moderate	39.9	36.1	good	r - 2.8 l - 3.2
	f	16	*11.9 -28.7	poor	moderate	good	7.1	14.8	good	—
	m	26	46.3 -67.9	non	poor	good	41.3	36.5	poor	r - 11 l - 10
	f	43	5.9 - 9.8	poor	moderate	good	22.4	26.0	good	l - 3.4
Nodular	f	24	39.9 -45.1	non	non	poor	29.8	28.9	non	r - 9.1 l - 12.0
hyper-plasia	f	13	12.7 -42.4	non	non	poor	26.5	27.1	poor	l - 3.7

* modification of Kanbegawa's method.

** intra venous injection.

method. Diurnal rhythm of plasma 11-OHCS wsa studied at four points. Suppression test by dexamethasons, metopirone test and rapid ACTH test using synthetic ACTH were performed in the routine way.

OBSERVATIONS

The fine structure of normal adrenocortical cells was almost similar to the features which were recently reported by Long and Jones[28]. Their structure was compared with the pathological adrenals or adrenocortical tumors with Cushing's syndrome. Up to this time, the adrenals of Cushing's syndrome have been classified into the following three types; adrenocortical hyperplasia, adenoma and carcinoma. However, the bilateral adrenals of two cases which were clinically diagnosed as Cushing's syndrome due to adrenocortical adenoma could not be classified by the above-mentioned criteria. The surface of the enlarged adrenal glands was uneven due to development of large and small nodules. Moreover, their fine structure was completely different from that of others. This type of Cushing's syndrome, therefore, was differentiated as nodular hyperplasia from simple hyperplasia.

1) Adrenocortical Carcinoma

Two cases of adrenocortical cancer were examined. One was a 34 years

old male and the other a 22 years old male. Although radical operation was attempted on them, it was impossible because of advanced metastasis of the carcinoma. The former case showed a more undifferentiated histological type than the latter by the light microscope. However, their findings by electron microscopy were almost similar. By electron microscopy, the carcinoma cells assumed a polygonal or almost round shape with a somewhat irregular contour.

The cell surface had numerous microvilli. The nucleus was round in shape, and, sometimes, intranuclear inclusions (Fig. 3) and desmosome-like structures (Fig. 1) were observed.

The cytoplasm appeared dark due to the well developed cell organelles, which were characteristic in the steroid producing cells. The most specific feature of these cells was the presence of numerous mitochondria with clear matrix and peculiar cristae. They were almost round and varied in size ranging from 0.8 to 3.0 micron in diameter. Their cristae were sparsely distributed. Mainly their cristae were in the form of small vesicles, though they were circular in form in some parts. These circular cristae were not observed in the mitochondria of the adrenal cells in the other types of Cushing's syndrome. Intramitochondrial bodies which were round or rodlike in shape were more frequently encountered in carcinoma cells than in others (Fig. 5).

The s.E.R. was well developed, similar to that in other steroid secreting cells, and distributed among other cell oranelles. It took the form of vesicles or tubules, but anastomosing array of tubular profiles was noticeable in well preserved specimens. The r.E.R. was rarely found and poorly developed as compared with that of adrenocortical cells in other types of Cushing's syndrome.

Lipid droplets were round or irregular in shape and less in number as compared with normal adrenocortical cell.

The most characteristic feature in carcinoma cells was the existence of two kinds of unidenitfied microbodies throughout the cytoplasm. They were almost oval in shape and always partially irregular. One of them showed a clear interior as the mitochondrial matrix, and the others were high in electron density (Fig. 1, 4).

Lysosme appeared in variable shapes (Fig. 4) and was more osmiophylic than the above mentioned microbodies. Lipofuscin granules commonly seen in normal adrenocortical cells were not observed. The Juxtanuclear Golgi complex was composed of stacks of lamellae and many small vesicles. This complex was well developed as in other steroid secreting cells, and was not different morphologically from that in normal adrenocortical cells.

There were many filaments and polysomes dispersed throughout the cytoplasm by glutaraldehyde fixation (Fig. 6).

2) Adrenocortical Adenoma

The fine structure of adenoma cells was studied in three cases consisting

of a one year old female, 45 years old female and 19 years old male. The tumors were 14.2 g, 13.3 g and 170 g in weight.

In the fine structural observation of adult adenoma, the cell was polygonal and larger than normal cells. The cell surface was generally smooth and rarely bore the projection of short microvilli. The nucleus was almost round, and intranuclear inclusion was not observed. Mitochondria were abundant throughout the cytoplasm and varied in shape and size; the shape was generally round or oval and rarely elongated, while the size ranged from 0.8 to 2.0 micron. The cristae were vesicular, tubular or tubulo-vesicular. Intramitochondrial body was rarely observed.

The s.E.R. was more developed throughout the cytoplasm than that of normal adrenocortical cells, and the reticulum was observed as a form of discontinuous vesicles due to the poor fixation. The r.E.R. was more abundant than that of any other type of Cushing's syndrome except the adenoma cell of the infant.

Lipid droplets were less as compared with normal adrenocortical cell, and appeared homogeneously osmiophylic with almost a round shape.

Dense bodies were often observed around the Golgi complex. They were not so abundant as in nodular hyperplasia.

The lysosome was often found throughout the cytoplasm and the Golgi complex was also well developed.

The fine structure of infant adenoma cells was characterized by the existence of large amounts of r.E.R. dispersed throughout the cytoplasm. The reticulum took a lamellar form and was located in some parts of the cytoplasm in the form of parallel array or whorls (Fig. 9). Polysomes not associated with the endoplasmic reticulum also dispersed in the cytoplasm. The s.E.R. also had a tendency to become whorls in a part of the cytoplasm. These whorls sometimes contained lipid droplets in the center (Fig. 10). These two types of reticuli were connected with each other around the whorls. Annulated lamella was also observed (Fig. 11). This organelle was not seen in other materials.

3) *Adrenocortical Hyperplasia*

Five cases of simple adrenocortical hyperplasia were studied.

They were four females from 16 to 45 years old and a 26 years old male. They were diagnosed as Cushing's syndrome by the adrenocortical hyperplasia obtained from laboratory data. Bilateral adrenalectomy in two cases and unilateral adrenalectomy in three cases were performed. Their adrenals were similar to the normal adrenal macroscopically and by light microscopy. Three zones of adrenocortex were thoroughly preserved as observed in the normal adrenal.

The fine structure of these cells was consonant with that of normal

adrenocortical cells except for the existence of large and dense intramitochondrial bodies in the fascicular cells.

4) *Adrenocortical Nodular Hyperplasia*

The fine structure of adrenocortical cells in nodular hyperplasia was studied in two cases. One was a 24 years old female and the other a 13 years old female. In these two cases, the diurnal rhythm of plasma 11-OHCS disappeared and the results of suppression test by dexamethasone, metopirone test and ACTH test revealed that these might be Cushing's syndrome due to adrenocortical adenoma. Surgically removed adrenals were enlarged and rugged with black nodules. Bilateral adrenalectomy was performed in the former case. The weight of the adrenal was 12.0 g in the left and 9.1 g in the right. In the latter case left adrenalectomy was performed and the weight of the adrenal was 3.7 g.

Their fine structure was completely different from other types of Cushing's syndrome. The cell surface was generally smooth, although it bore short or long microvillous projections in some parts. The nucleus was almost round and had no noteworthy features. The most characteristic finding was existence of abundant strongly osmiophylic dense bodies with homogeneous density. The body was almost round in shape and the diameter ranged from 0.2 to 1.0 micron. They were distributed around the Golgi complex. Their content seemed to be lipid in nature.

The s.E.R. was remarkably developed and showed the structure of a network of interconnecting tubules (Fig. 17). The reticulum showed a tendency to localize in one part of the cytoplasm. In the other case in which the fixation was not so satisfactory, the reticulum showed the vesicular form. The r.E.R. was more developed compared with that of normal adrenocortical cells. This reticulum appeared as paralell arrays of flattened lamellae here and there, throughout the cytoplasm. The stack of this reticulum was continuous with the membranes of s.E.R. at the periphery.

Mitochondria were numerous and tended to be concentrated at certain areas where there was noted less s.E.R. They were almost round in shape and varied in size from 0.3 to 3.0 micron and some showed swelling (Fig. 20, 21). Their cristae were of various shapes; vesicular, tubular, vesiculo-tubular and rarely circular. The cristae were sometimes not uniformly distributed but aggregated in some parts of the mitochondria. Conequently, a relatively wide area without cristae was noted in the mitochondria. The matrix appeared clear and somewhat flocculant and sometimes lipid-like substances were observed in the matrix (Fig. 18, 21).

Typical lipid droplets as seen in the normal adrenocortical cell were rarely observed. Continuity of the droplet with the membrane of the s.E.R. was observed. The functional significance of this finding is not clear though

some investigators previously reported a similar phenomenon in animals.

The Golgi complex developed more than that of normal adrenocortical cell and was usually found close to the nucleus (Fig. 21). Often the constituents of the complex were vacuolated and showed a honeycombed appearance as shown in Fig. 21. The Golgi complex was continuous with the tubules of the surrounding s.E.R., in some parts transforming to the latter without a marked boundary. The lysosome was few in number.

DISCUSSION

It is generally accepted that the fine structural features of steroid producing cells are well developed s.E.R., a prominent Golgi complex, variety in size of mitochondria, elaborated cristae of mitochondria and lipid droplets in greater or lesser numbers[28)29)]. The fine structure of normal adrenocortical cell has recently been reported in detail by Long and Jones[29)]. The author studied the fine structure of adrenocortical cells in three normal cases and obtained similar results. In this study, the fine structure of adrenocortical cells or tumors from twelve patients with Cushing's syndrome were examined, and the adrenals in this syndrome were classified into the following four types on the basis of the clinicopathological data shown in Table 1 and the fine structural feature; namely, adrenocortical hyperplasia, nodular hyperplasia, adenoma and cancer.

Two cases of nodular hyperplasia showed the same reaction as cortical adenoma by various hormonal tests; however, the bilateral adrenals were enlarged with many nodules, and their fine structure showed unique features. From the above mentioned reason, nodular hyperplasia was differentiated from simple hyperplasia.

Three zones of the cortex in simple adrenocortical hyperplasia were well maintained, though these were not clear in nodular hyperplasia.

The fine structure of adrenocortical carcinoma cells was characterized by a well developed s.E.R., numerous mitochondria of variable size and with peculiar cristae, unusual intramitochondrial body, abundant microvilli and two kinds of unidentified microbodies. Especially, these unidentified microbodies were prominent features. These microbodies consisted of two types, one showed the same clear interior as the mitochondrial matrix and the other exhibited the density of lysosome. It is not clear whether these unidentified microbodies are lysosome itself or degenerated mitochondria.

The fine structure of adenoma cells was characteristic by the abundant r.E.R. and dense body. Especially in the infant case, there were numerous lamellar concentrations of s.E.R. and r.E.R.

In adrenocortical hyperplasia, three zones of adrenal cortex were well maintained, and the fine structure was similar to that of normal adrenal

cortex. Though Reidboard reported that the intramitochondrial body was abscent in adrenocortical hyperplasia[31], these bodies were often found in this study.

The fine structure of adrenocortical cells in nodular hyperplasia was characterized by the existence of numerous dense bodies around the Golgi complex, a tubular anastomotic network of well developed s.E.R. and a very prominent Golgi complex, relatively abundant r.E.R. and mitochondria of various sizes.

In general, the adrenocortical cell of patients with Cushing's syndrome had a well developed s.E.R., numerous mitochondria and Golgi complex. Christensen and Fawcett[34], and Enders[12] suggested that the steroid-secreting cells have always s.E.R., and Sabantini[10], Scheridan[13] and Zelander[23] reported that the s.E.R. in these cells was generally observed in the form of isolated vesicles. Meanwhile Ross *et al.*[8] and Brenner[14] reported on a tubular anastomotic network of s.E.R. in the foetal zone of the human adrenal and in the adrenal cortex of the rhesus monkey. The author observed a similar structure of s.E.R. in cases of nodular hyperplasia and adrenocortical carcinoma. Recently Long and Jones[29] reported that the s.E.R. was found as a structure of anastomotic network in well fixed samples, while in insufficiently fixed samples, the s.E.R. was observed in the form of discontinuous vesicles. The latter appearance is now thought to be artificial. Christensen and Fawcett[34][35] reported a positive relation between the amount of s.E.R. and the ability of the cell to syntheisze cholesterol from acetate. It may be very difficult to prove the relation between the rate of hormone production and the degree of developement of s.E.R. However it is sure that abundant s.E.R. signify high secretory activity of the adrenocortical cell. Stacks of s.E.R., which were reported by Brenner[14] and Christensen[35], were observed freely or surrounding lipid droplets in the case of infant adenoma. Sato[16] suggested that these small stacks of s.E.R. might include a few mitochondria or lipid droplets and subsequently large lamellated chondriospheres might be founded.

It is said that mitochodrial changes caused by stress are irregularity in its shape, increase in numbers and existence of lamellar cristae[29]. The lamellar cristae were often observed in the mitochondria of adrenocortical cells in hyperplasia, so it might indicate a morphological state of mitochondria in excessively steroid producing cells. However the cristae were few in the mitochondria of adenoma and carcinoma cells which also produce excessive corticosteroids. The functional significance of the lamellar cristae is still unknown. Among the many types of excessive steroid producing cells, there was abundant s.E.R. in the cell of nodular hyperplasia and adenoma, and rather less s.E.R. in carcinoma cells. The significance of this discrepancy is not clear.

Openings of mitochondrial membranes, reported by a number of au-

thors[19)21)36)], were rarely observed in this study (Fig. 20). Napolitano and Fawcett[37)] attributed this appearance to tangential secretioning of the mitochondrial membranes. Long and Jones[29)] suggested that this was an effect of poor fixation rather than a physiologic phenomenon. Intramitochondrial bodies were most frequently observed in carcinoma cells. These bodies are thought to be sites of accumulation of calcium[29)].

Lipid droplets were more or less observed in adrenocortical cells of all cases of Cushing's syndrome. These droplets were rich in quantity in the cell of hyperplasia, though sparse in the cell of nodular hyperplasia, adenoma and carcinoma which secrete more glucocorticoids. Brenner[14)] reported that lipid droplet diminished in size and often disappeared completely during the period of maximum secreting activity of adrenocortical cells. Brenner[14)] described the intimate relation between lipid droplets and s.E.R. and the continuity of the lipid droplets and the membrane of s.E.R. was sometimes observed in the present study. The dense body observed as round osmiophylic granules was characteristic of cells in adult adenoma and nodular hyperplasia. It's content might be lipid.

The Golgi complex was well developed in the cells of carcinoma and nodular hyperplasia and sometimes the constituents of the complex were vaculolated and showed a honeycombed appearance, though it was not a feature peculiar to Cushing's syndrome.

CONCLUSION

The fine structure of adrenocortical tummors or adrenal glands were examined in twelve cases of Cushing's syndrome consisting of two cases of adrenocortical cancers, three of adrenocortical adenoma, five of adrenocortical hyperplasia and two of adrenocortical nodular hyperplasia.

1) Bilateral adrenals of two cases, which were clinically diagnosed as Cushing's syndrome due to adrenocortical adenoma, showed uneven surface due to the developement of large and small nodules. Their fine structure was completely different from that of others. Subsequently, this type of Cushing's syndrome was differentiated as nodular hyperplasia from simple hyperplasia.

2) Well developed microvilli and Golgi complex, abundant mitochondria with circular cristae, intramitochondrial bodies and two kinds of unidentified microbodies were characteristic of carcinoma cells, the last organelles being not observed in other cases.

3) Mitochondria of adenoma cells which had tubular or tubulo-vesicular cristae varied in size and some possessed swelling. Rough endoplasmic reticulum developed most in adenoma, especially infant adenoma cells.

4) Normal lipid droplets were poor in carcinoma and nodular hyperplasia

cells, though small round dense bodies were scattered throughout the cytoplasma in these two groups, especially being abundant in the latter cases.

5) The fine structure of simple hyperplasia was almost similar to normal adrenocortical cells except for the existence of intramitochondrial bodies in the fascicular cells.

6) s.E.R. and Golgi complex were relatively well developed in all cases of Cushing's syndrome, especially in nodular hyperplasia and carcinoma cells.

ACKNOWLEDGEMENTS

The author is grateful to Prof. S. Hoshikawa, Dr. H. Yogo, Dr. T. Sasaki and Dr. T. Yamaoka for their kind advices. The author is indebted to Dr. K. Yamashita of 3rd Department of Anatomy and Dr. M. Hoshino of Aichi Cancer Research Institute for their helpful guidances and suggestions.

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EXPLANATION OF FIGURES

FIG. 1. Adrenocortical carcinoma (34 years old, male)
Numerous mitochondria of various sizes, unidentified microbody and desmosome-like structure seen in lower right corner. Note the abundant microvilli lining intercellular lumen. ×6000

FIG. 2. Adrenocortical carcinoma (34 years old, male)
Mitochondria with circular cristae. ×8000

FIG. 3. Adrenocortical carcinoma (34 years old, male)
Two kinds of unidentified microbodies and intranuclear inclusion seen. ×8000

FIG. 4. Adrenocortical carcinoma (34 years old, male)
Well developed Golgi complex and lysosomes. ×12000

FIG. 5. Adrenocortical carcinoma (34 years old, male)
Peculiar intramitochondrial bodies are observed. ×16000

FIG. 6. Adrenocortical carcinoma (22 years old, male)
Numerous filaments and polysomes throughout the cytoplasm.
(double fixation by glutar aldehyde and OsO_4) ×15000

FIG. 7. Adrenocortical adenoma (19 years old, male)
Well developed Golgi complex and s.E.R. ×6400

FIG. 8. Adrenocortical adenoma (19 years old, male)
Dense body and r.E.R. abundantly observed. ×6400

FIG. 9. Adrenocoatical adenoma (1 year old, female)
Lamellated and paralleled r.E.R. seen throughout the cytoplasm. They are continuous with each other.
(double fixation by glutaraldehyde and OsO_4) ×8000

FIG. 10. Adrenocortical adenoma (1 year old, female)
Mitochondria surrounded by circular e.E.R.
(double fixation by glutaraldehyde and OsO_4) ×10000

FIG. 11. Adrenocortical adenoma (1 year old, female)
Annulated lamellae
(double fixation by glutaraldehyde and OsO_4) ×20000

FIG. 12. Adrenocortical adenoma (1 year old, female)
Concentrated lamellar s.E.R. with lipid droplets in it.
(Double fixation by glutaraldehyde and OsO_4) ×6000

FIG. 13. Glomelular cell of hyperplasia (16 years old, female)
Mitochondria of various shapes and a well developed Golgi complex observed. Elongated mitochondria have tubular cristae. ×6000

FIG. 14. Fascicular cell of hyperplasia (45 years old, female)
Large lipid droplets and relatively round mitochondria seen. The s.E.R. are well developed. Abundant lysosome observed. ×8000

FIG. 15. Reticular cell of hyperplasia (16 years old, female)
Mitochondria of various types and lipofuscin granules seen. ×6000

FIG. 16. Fascicular cell in hyperplasia (45 years old, female)
Abundant intramitochondrial bodies. ×10000

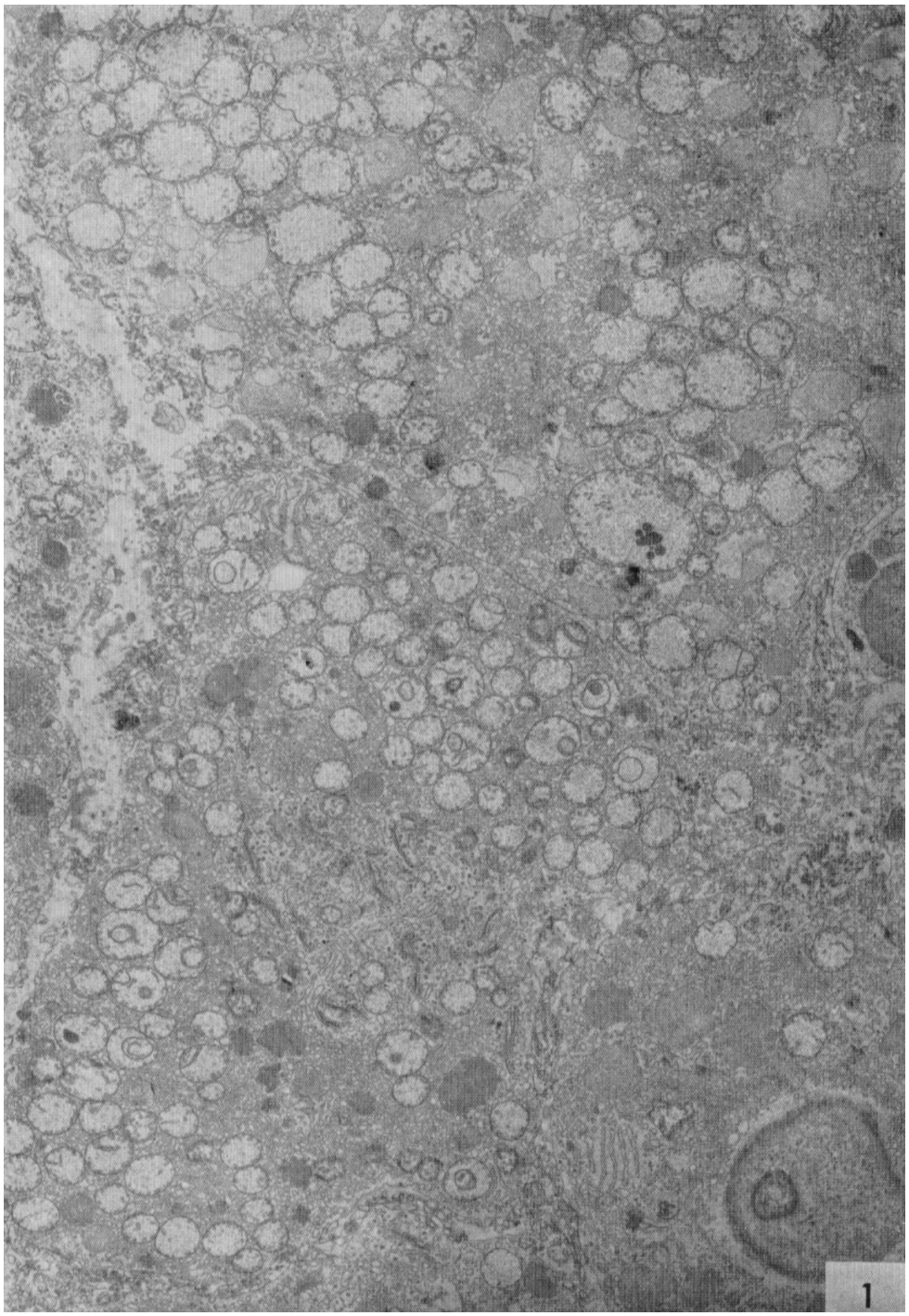
FIG. 17. Adrenocortical nodular hyperplasia (24 years old, female)
Numerous osmiophylic dense bodies. A well developed s.E.R. and abundant mitochondria observed. ×6000

FIG. 18. Adrenocortical nodular hyperplasia (24 years old, female)
Relatively well developed r.E.R. ×4000

FIG. 19. Adrenocortical nodular hyperplasia (13 years old, female)
Segmented mitochonrdia and villiformed microvilli. ×8000

FIG. 20. Adrenocortical nodular hyperplasia (24 years old, female)
The r.E.R. arranged in parallel array are seen. Their peripheries are continuous with membranes of s.E.R. ×16000

FIG. 21. Adrenocortical nodular hyperplasia (24 years old, female)
A well developed Golgi complex and mitochondria of various sizes observed. Some mitochondriamay be swollen and lipidlike substances found in the matrix. ×11000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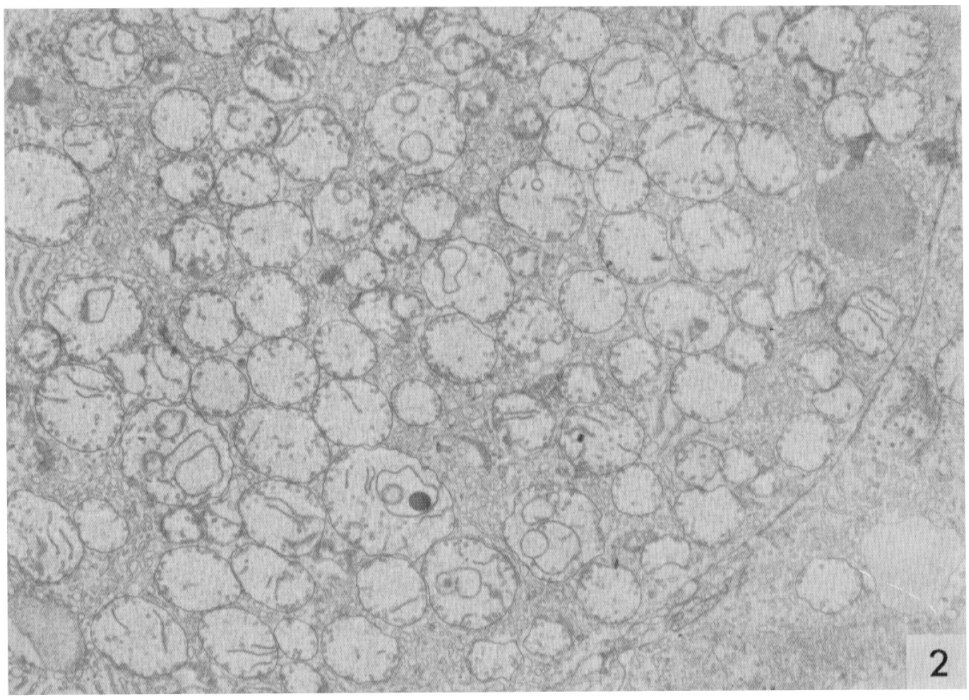
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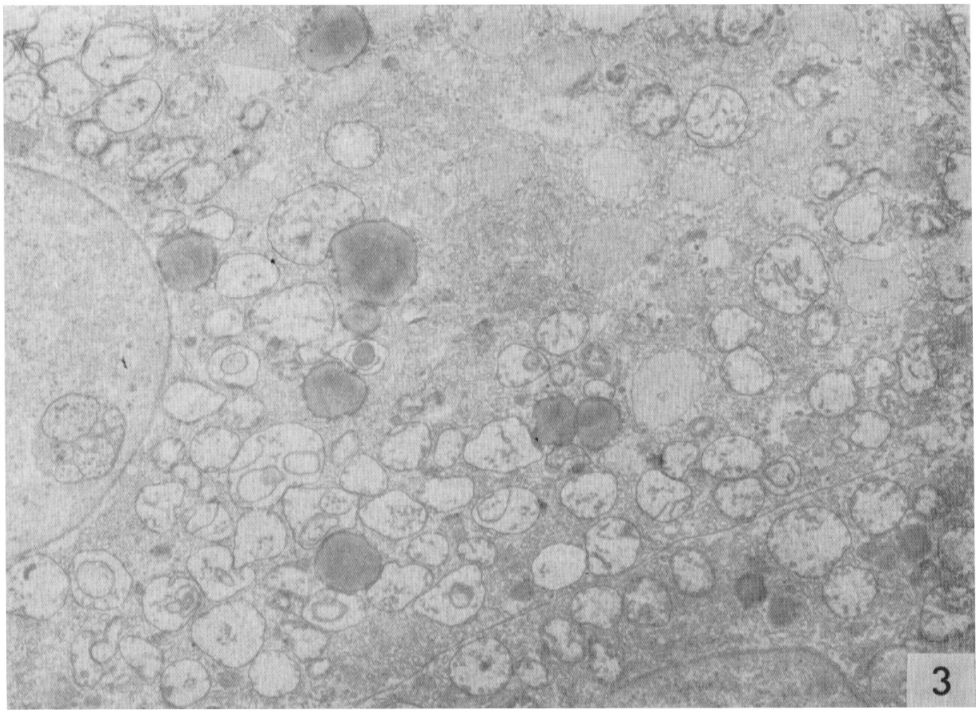
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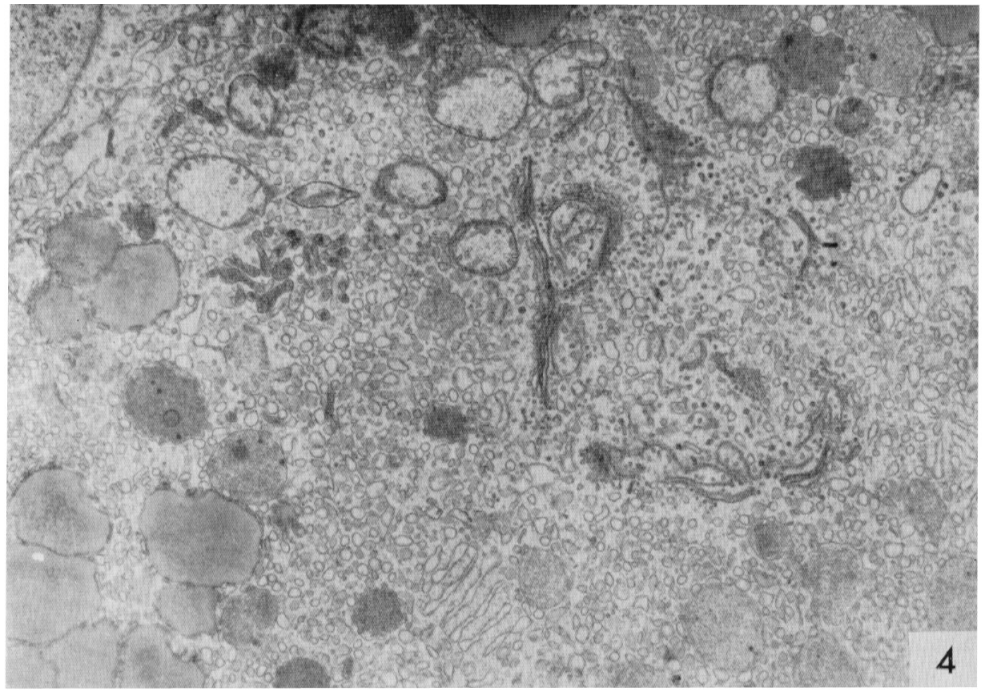

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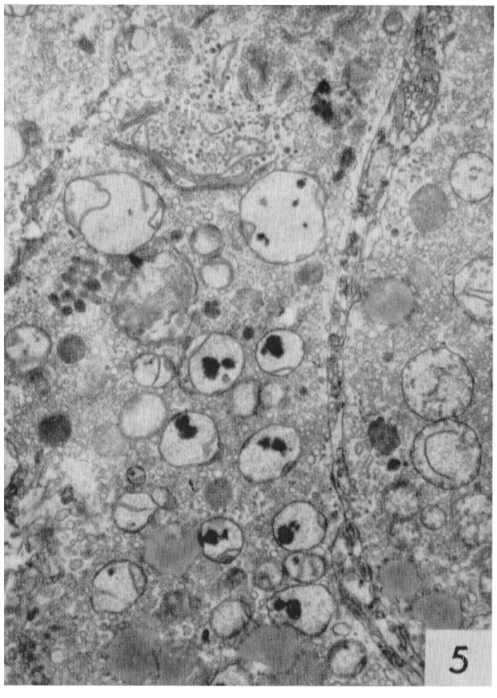

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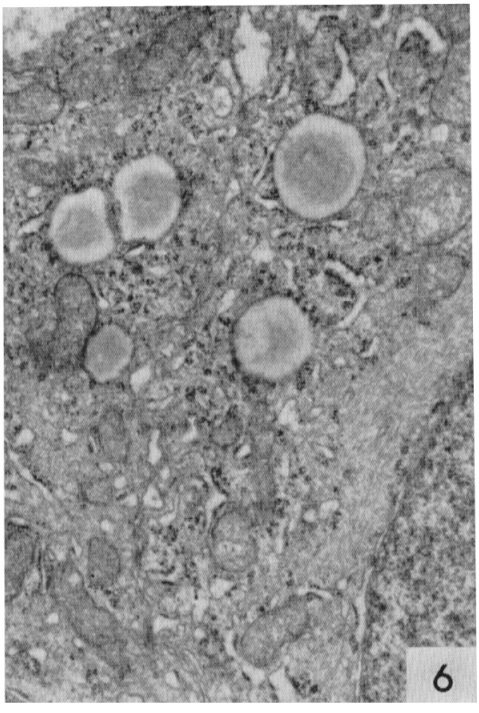

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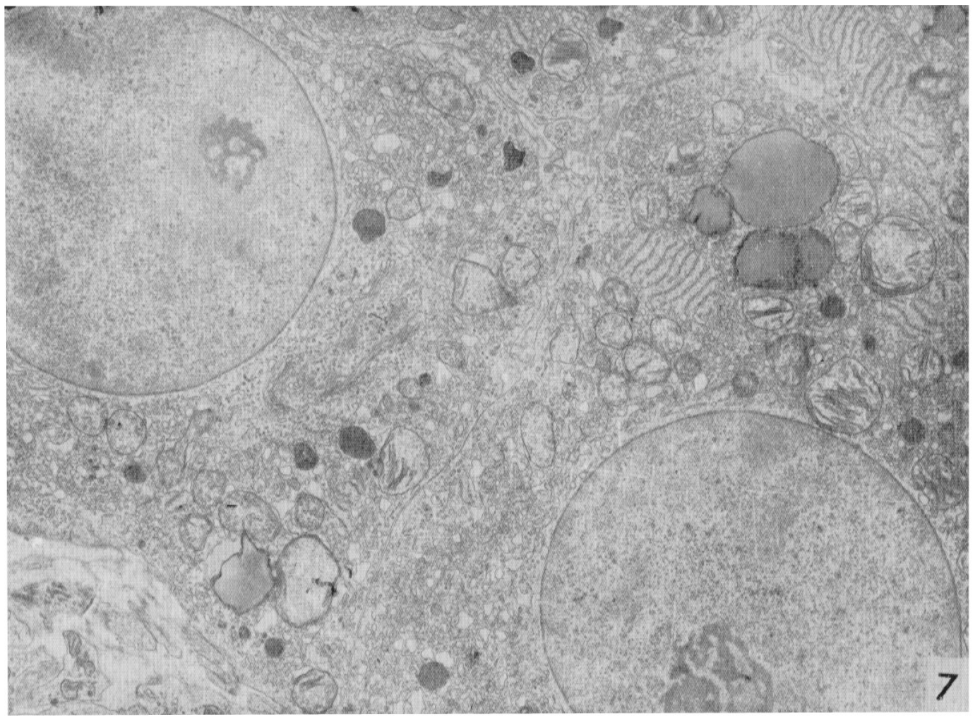

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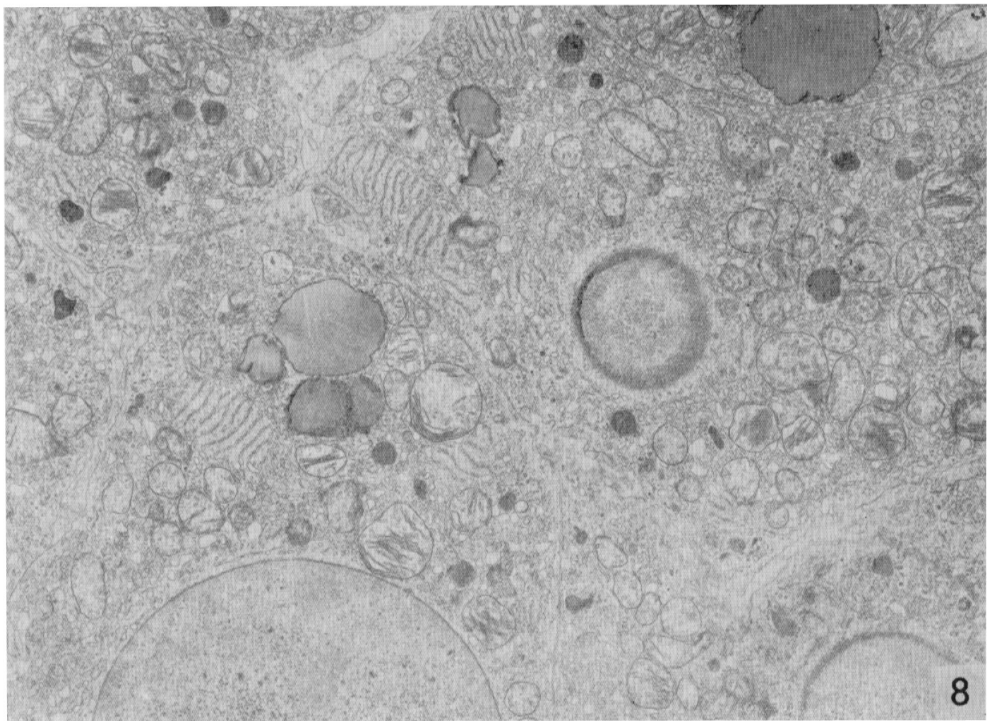

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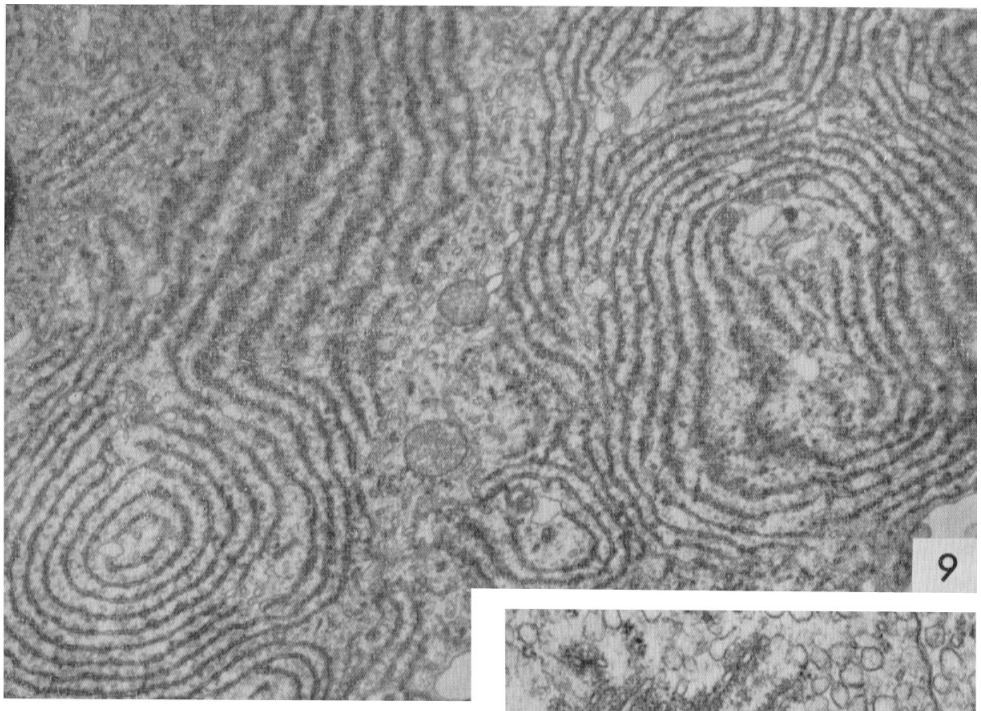
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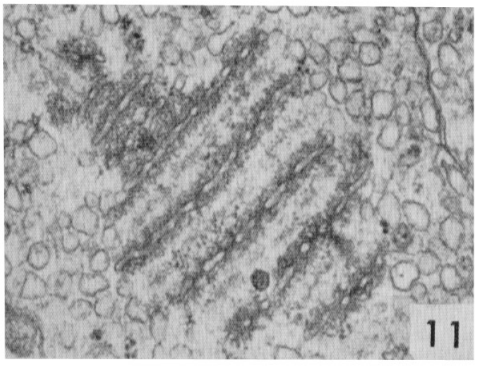
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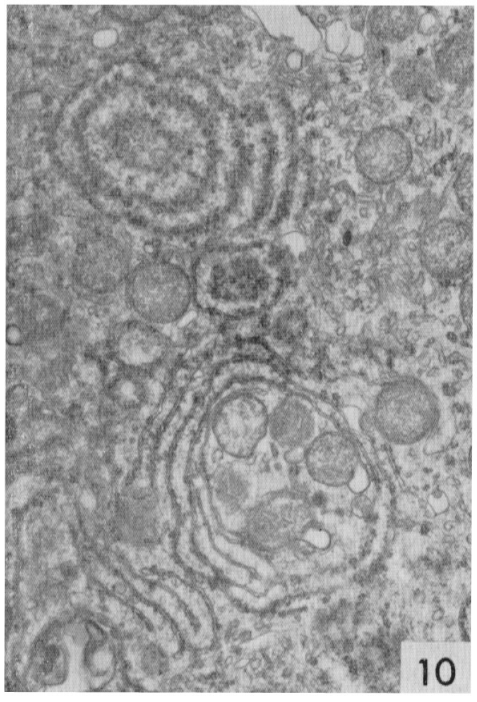
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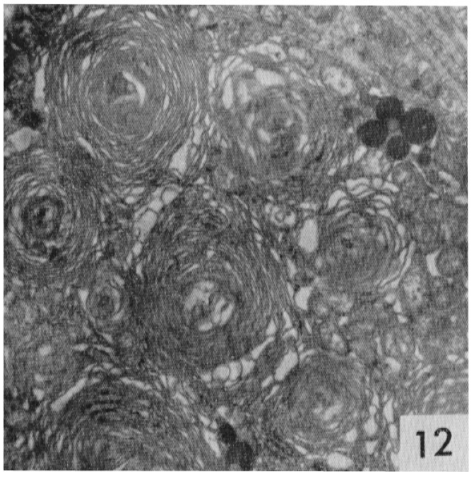
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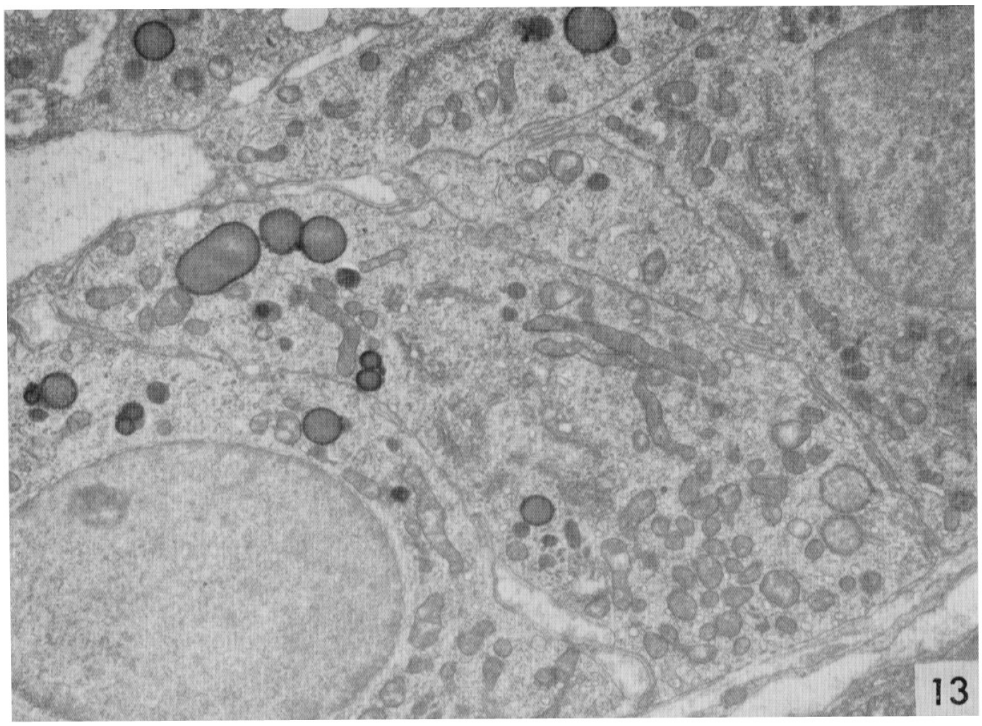

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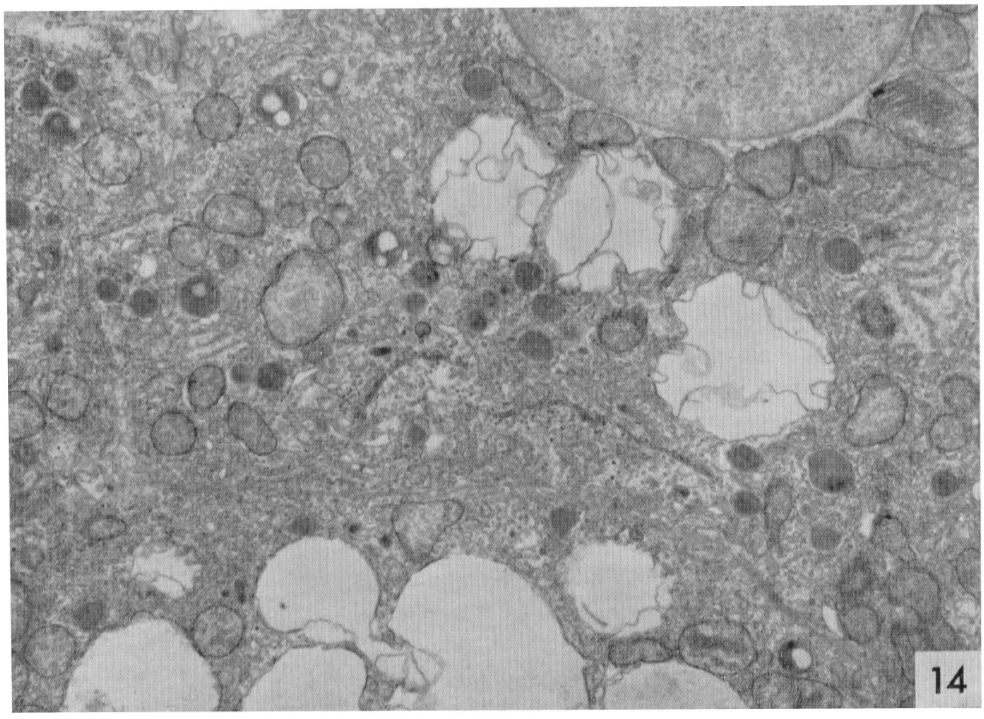

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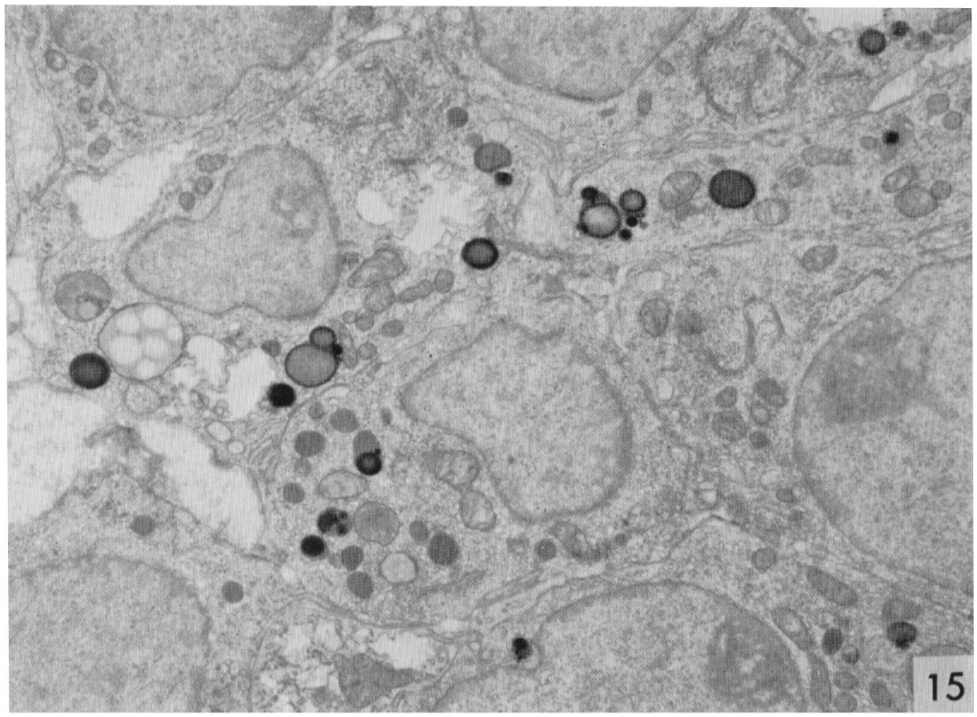

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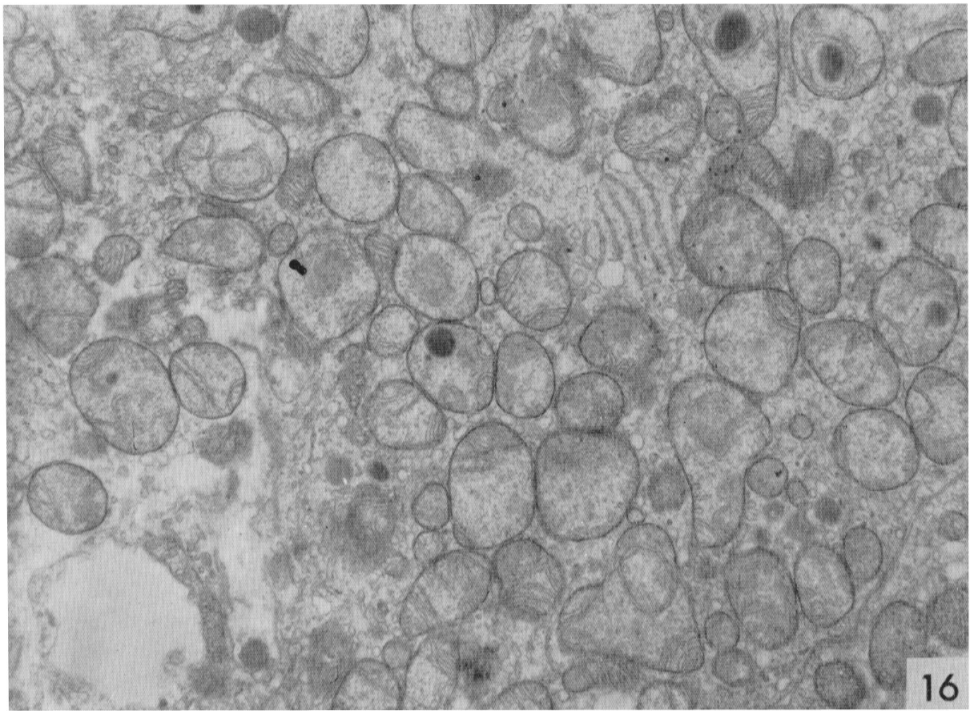

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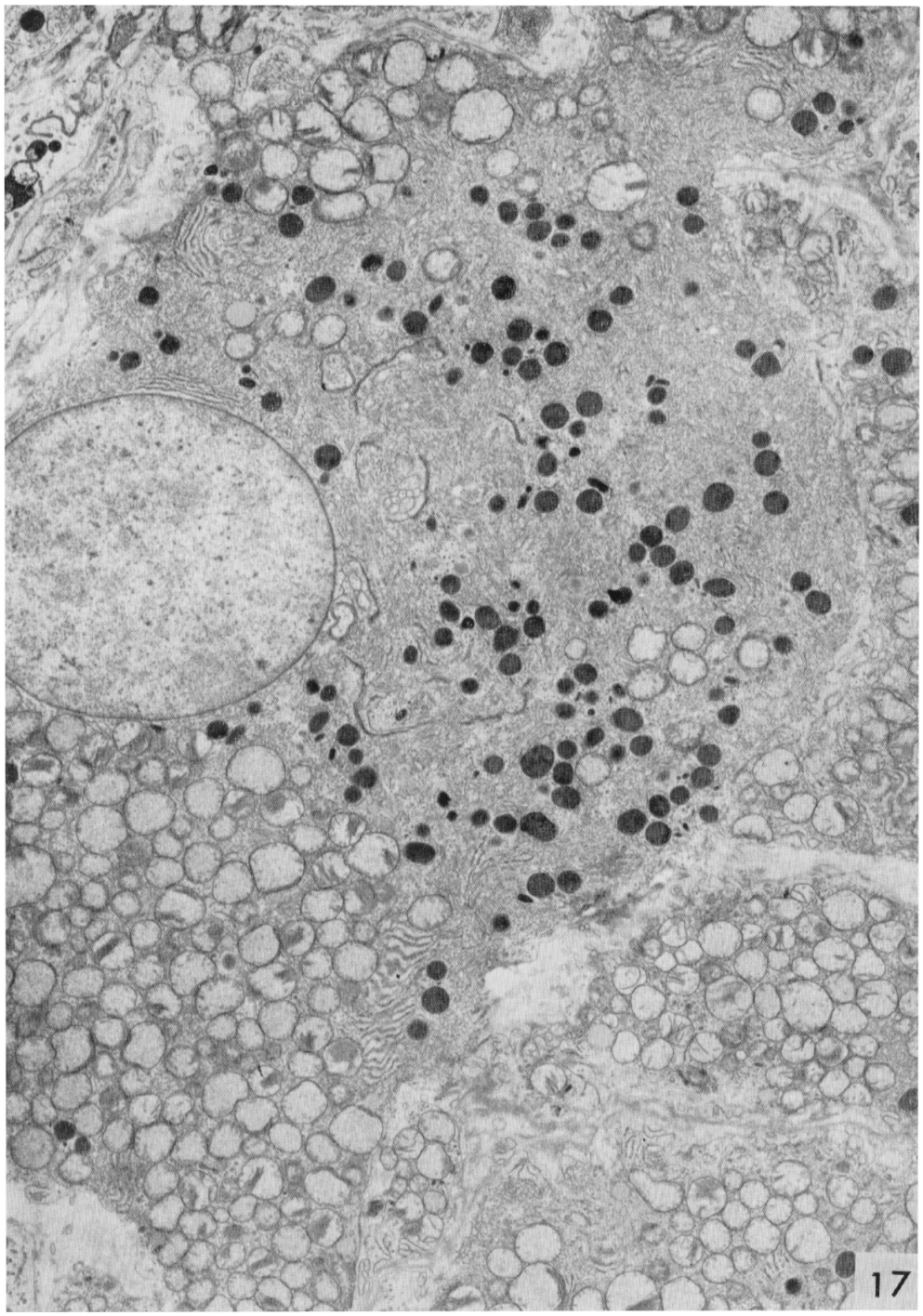
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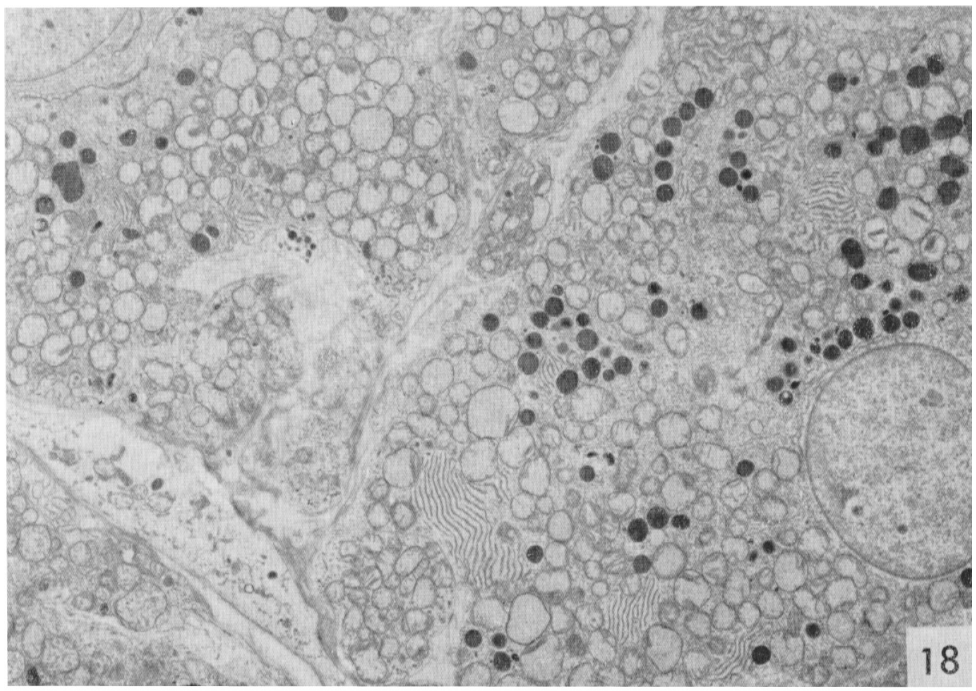
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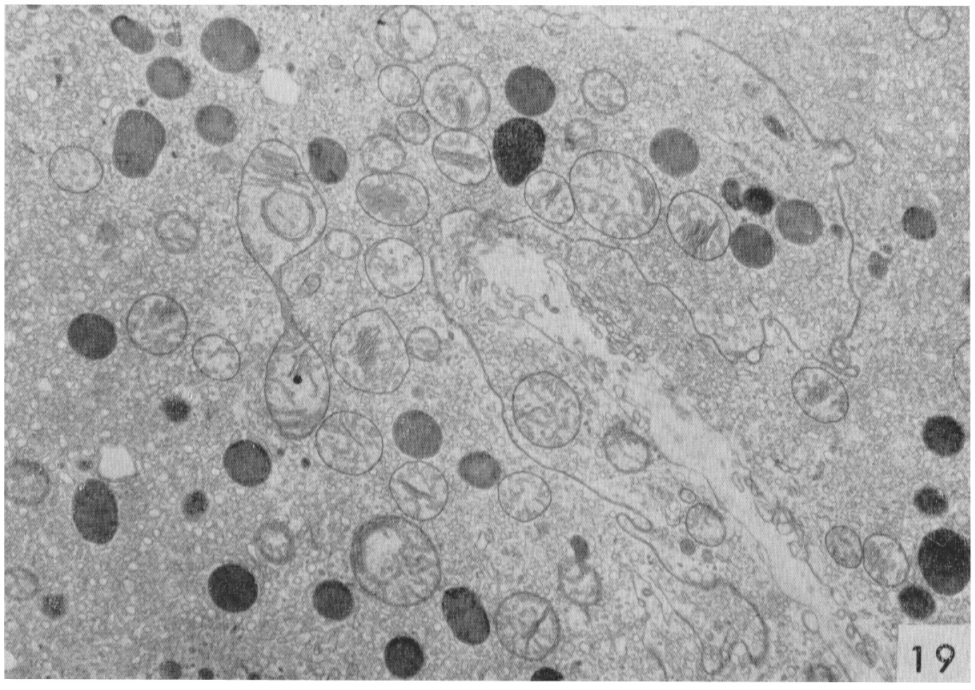
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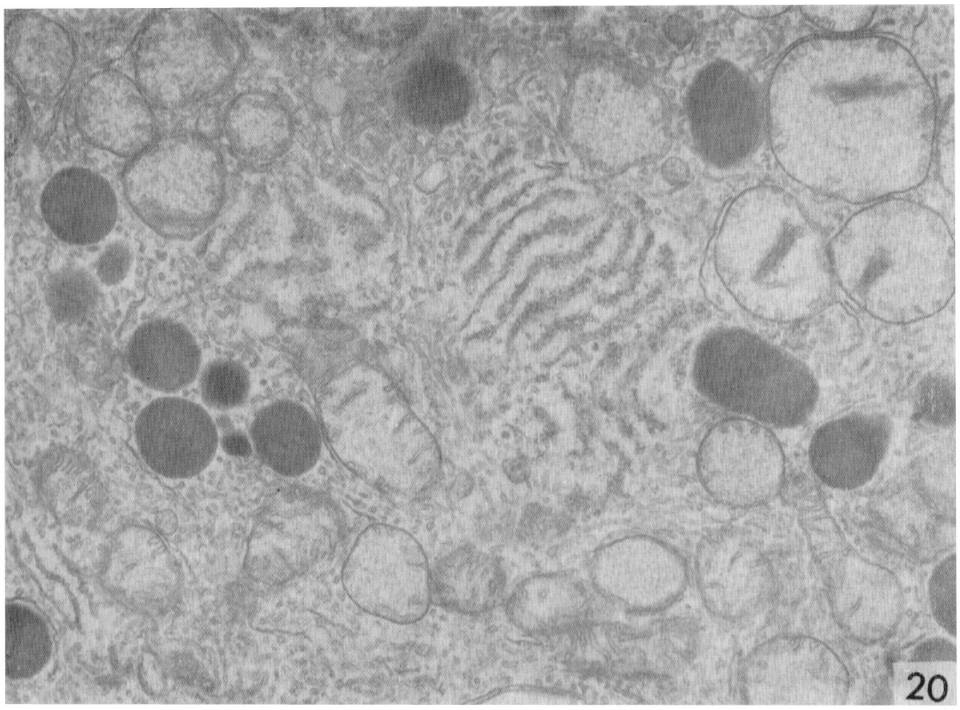
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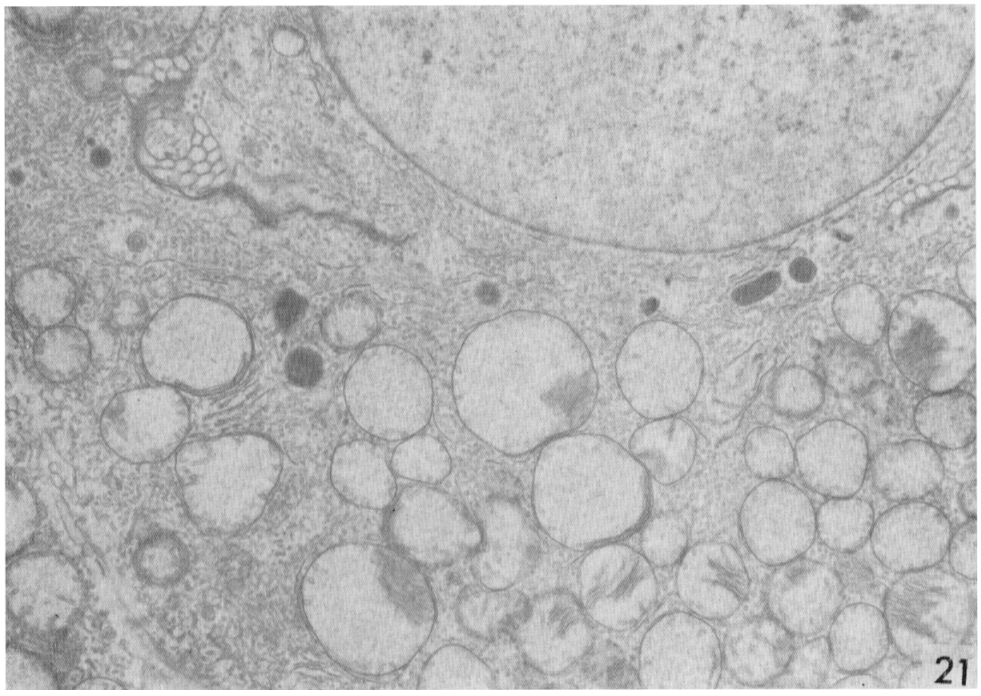
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