ELECTRON MICROSCOPIC OBSERVATIONS OF THE CENTRAL NERVOUS SYSTEM*

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PLATES 138 TO 147

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Study of the central nervous system by electron microscopy requires identification of the neural and glial cells and of their processes. Superficial inspection of electron micrographs reveals what first appears to be a bewildering array of components. Cells of varying sizes, shapes, and densities are recognizable by their nuclei, and in some instances, by the outline of their delimiting plasma membranes. Coursing among these cells are blood vessels, which may be identified by the morphology of their endothelial elements and by the presence of erythrocytes and leucocytes in their lumens. Between the cells and blood vessels, completely filling all available space, lies the neuropil. This component is a complexly interwoven meshwork of cellular processes derived from both neural and glial cells. It contains, in amounts which vary relative to one another in different locations, dendrites, axons (myelinated and unmyelinated), nerve endings, fibrous and protoplasmic processes of glial cells, and possibly an ill defined ground substance. By light microscopy, the relationships of these components of the neuropil have been poorly understood, since only the larger elements could be resolved. With electron microscopy, even the smallest of the cellular processes can be visualized, but the complexity of the structures revealed makes identification of the various elements difficult.

The problem of cellular identification has been approached by attempting, first, to correlate the characteristics of the neural and glial cells as observed by light microscopy with the electron microscopic appearance of the same cells. Much information concerning the structure and interrelationships of the neural and glial cells has been obtained from use of the silver and gold chloride procedures of Ramón y Cajal and of Del Rio-Hortega. In our interpretations, we have relied heavily on the accounts of Penfield (1) and Del Rio-Hortega (2). The nuclear differences which characterize the glial cells can be seen both

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in electron micrographs and by phase microscopy of thicker sections through the same cells. The characteristic distribution of oligodendroglia as neural satellite cells and their occurrence in rows in the white matter have been of value in their identification. The presence of fibrous processes has aided in recognition of astrocytes, as has the characteristic presence of many, rather than few processes. The well known acidophilia of astrocytic cytoplasm in contrast to the chromophobia of oligocytes has been correlated with the greater density of one cell type as compared with the other and used as a further index for identification. Finally, we have examined a few astrocytic tumors of the nervous system and have confirmed that the cell types we provisionally classified as astrocytes are similar to those involved in the tumorous condition; while in a single oligodendroglioma, the tumor cells were identical with those classified as oligocytes.

Neither the microglia nor the neurons have presented any particular problem in identification. Microglia are small, dense cells frequently found adjacent to capillaries but also located normally among the processes of the neuropil or as neural satellites. The frequent presence of phagocytosed particles or lipide also helps to identify these cells. The larger neurons are identifiable by their size alone; further, their distinctive cytoplasmic organization, once seen, permits recognition of other and smaller neurons.

Material and Methods

Small pieces of tissue from the spinal cord, cerebral cortex, aqueduct of Sylvius, wall of lateral ventricle, and choroid plexus of mice, guinea pigs, rabbits, and rats were removed and rapidly immersed in a 1 per cent solution of osmium tetroxide buffered at a pH of 7.4 with dichromate as recommended by Dalton (3). The tissue was fixed at room temperature for 2 hours, rinsed in distilled water, and dehydrated through a series of graded ethanol solutions. It was found that less fragmentation of the myelin occurred when the dehydration process was gradual. Following dehydration, the tissue was transferred to equal parts of absolute alcohol and methacrylate, and then through 3 changes of a mixture of 3 parts of butyl and 1 part of methyl methacrylate; after which it was embedded in this mixture. The methacrylate was polymerized at 60°C. this process having been catalyzed by benzoyl peroxide. Thin sections were cut with glass knives on a modified Minot rotary microtome (4) and examined in a RCA electron microscope (model EMU 2E) without removing the plastic. Adjacent thicker sections were mounted for phase microscopy.

Portions of tumors of the brain were obtained at the time of surgery and immediately placed in fixative. The tumor tissue was handled in a manner identical with that of tissue obtained from experimental animals.

Blunt probe wounds were made in the cerebral hemispheres of rabbits following the method described by Del Rio-Hortega and Penfield (5). The resulting

foci of gliosis were excised 2 and 3 weeks later and fixed in buffered osmium tetroxide as described previously.

OBSERVATIONS

Neurons

Nerve cells vary considerably in size and shape, but in the anterior horns of the spinal cord the large neurons are identifiable by their size alone. These cells contain large irregularly ovoid nuclei with an evenly dispersed finely granular chromatin. Nucleoli are prominent and occasionally multiple. Associated with the nucleolus, there is frequently a clump of dense chromatin particles. The nuclear membrane is distinct, and there is scant clumping or concentration of chromatin against its inner margin.

The plasma membrane of the anterior horn cells, is usually smooth and pursues a direct course with few invaginations or protuberances. It outlines the cell body and its branches or processes, the dendrites or axon. Dendrites are frequently encountered but the emergence of the axon from an anterior horn cell is only occasionally seen (Fig. 1). The cytoplasm, surrounding the nucleus and extending to the plasma membrane, is abundant and contains numerous finely divided granules of varying sizes and of moderate densities. In the cytoplasm, embedded in this granular or amorphous component, several formed elements can be recognized. These are the mitochondria, the Golgi components, and the ergastroplasmic structures. These have recently been described and illustrated by Palay and Palade (6) and so will receive only scant attention here. Mitochondria are variable in size, frequently appear elongated in sections, and are scattered throughout the cytoplasm. Their matrix is rather dense so that thin sections are required to reveal their internal membranous laminae. The Golgi components consist of vacuoles and tubules with walls made up of smooth membranes. These structures are of varying sizes, sometimes dilated with transparent lumina, but often collapsed and aggregated into either bundles of microtubules or laminar stacks of flattened sacs arranged in a coplanar fashion. These Golgi aggregates are usually multiple and arranged perinuclearly. Finally, the ergastoplasm of the anterior horn cells, as seen in sections, consists of membranous profiles associated with which is a dense, granular component. The granular component is not necessarily bound to the membranes, and frequently the granules are interspersed, singly or in clusters, among the cytoplasm which occupies the spaces between neighboring ergastroplasmic membranes. These associated granules and membranes often can be recognized in quite thick sections in which they are in the form of dense clumps, the sizes and shapes of which resemble the Nissl substance (Figs. 1 and 2).

It should be mentioned that Palay and Palade (6) designate as "agranular reticulum" the structures we have described as the Golgi components. They also

use the term "endoplasmic reticulum" in a fashion which is synonymous with ergastoplasm.

In addition to the structures enumerated above, occasional bodies of extreme density were observed. These were spheroidal and often exhibited the compression lines characteristic of fat droplets. They were sparsely and indiscriminately located in the cytoplasm, but were more frequent in neurons located in the human cerebral cortex than in the other material, possibly because of the older age of the individuals from which the specimens were obtained.

At their region of branching from the cell body dendrites have an internal structure identical with that of the perikaryon with prominent ergastoplasmic structures and with mitochondria (Fig. 3). However, this does not apply to the portions of dendrites distant from their cell body. In the neuropil, through which the dendritic branches pass in great number, they can be distinguished from glial processes only with difficulty, if at all. Moreover, as de Lorenzo (7) has shown, in regions of the olfactory brain in which bundles of dendritic processes are the predominant component, these elements contain only sparse small granules, and are less dense than in the other regions described. Caution is necessary, therefore, in the identification of dendrites and further study is required.

Myelinated fibers are easily recognized by their distinctive sheaths which vary in thickness depending on the size of the fiber and age of the animal. With high magnification the myelin of the central nervous system exhibits the same concentric lamellae which have been described previously in peripheral nerves (8–10). These lamellae are seen in Fig. 15. Unlike fibers in peripheral nerves, the myelinated fibers of the central nervous system lack a complete cellular or neurilemmal investment. Folded processes of astrocytes are most commonly encountered contiguous to the myelin, but in many places the medullated sheath appears to abut directly upon oligodendroglial processes, neuron plasma membranes, and even the basement membranes of blood vessels.

The axoplasm of myelinated fibers ordinarily has a delicately reticulated or fibrous appearance. In some fibers, bundles of delicate filaments or fibrillae are quite evident (Fig. 4). Mitochondria are abundant and in occasional fortunate sections they occur as greatly elongated structures lying along the long axis of the axon. These organelles vary somewhat in size depending on the size of the fiber. In some of the smallest fibers, however, the mitochondrion nearly fills the cross-sectional area of the axon. A definite axolemmal membrane delimits the axoplasm from its surrounding myelinated sheath.

Synapses are frequently observed on the surfaces of some cell bodies and of dendrites. Where they can be identified, they consist of terminal enlargements of the fiber, in which many mitochondria are closely packed. Microvesicles, of the type described by De Robertis and Bennett (11), are usually but not invariably evident. The plasma membrane of the termination is closely applied to

the limiting membrane of the postsynaptic element; thus, no glial structure is interposed between the presynaptic and postsynaptic neural structure. At the point of junction the plasma membrane is thickened and of increased osmiophilia, resembling the alteration present in the plasma membrane at the region of a terminal bar.

It is probable that types of synapses other than those described occur in the central nervous system. Neural processes or endings have been observed contiguous to one another, with no glial element interposed between them, but without the enlarged ending, the increased number of closely packed mitochondria, and the microvesicles which characterize the typical boutons, terminaux (Figs. 5 to 7). At the present time the significance of these neural interrelationships is problematical.

Glial Cells

Astrocytes.—Astrocytic cells are slightly less numerous than oligocytes. The nuclei are larger and less uniformly ovoid or round than those of the oligodendroglia, often being slightly reniform. The nuclear chromatin is finely and uniformly granular. Nucleoli are occasionally present in nuclei of normal astrocytes and are often multiple in those of neoplastic astrocytes. The astrocytic cytoplasm has a pattern conspicuously different from that of any of the other glial cells. In the perinuclear zone there is a scant finely granular cytoplasm, while the remainder of the cell is comprised of processes formed by a complexly folded, reduplicated plasma membrane surrounding small amounts of cytoplasm (Fig. 8). This complicated folded cytoplasm is more prominent in the protoplasmic than in the fibrous astrocytes, although in the latter unequivocal fibrils have been observed within the small processes formed by the much refolded plasma membrane (Fig. 10). Processes of other glial cells and of neurons are enclosed and surrounded by the astrocytic processes. In some of the astrocytes, both normal and abnormal, distinct fibrils are present. The fibrils of the fibrous astrocytes are more numerous in the distal processes where they present a grouped appearance not unlike that described by light microscopy. They are fine, rather dense, and closely placed together as is shown in Fig. 11. Rarely are these fibrils present in the more central portion of the cell. No characteristic banding of the glial fibrils can be seen with the resolution so far obtained. The Golgi apparatus was not identified in any of the normal astrocytic cells, but is distinct in some of the neoplastic astrocytes. Mitochrondria are relatively infrequent, and are usually not numerous in the folded processes.

In the cells of a low grade fibrous astrocytoma there are diffuse fine fibrils in most of the astrocytic processes as well as groups of more densely placed fibrils. In these cells fine fibrils occur in the perinuclear cytoplasm as well as in the distal processes. Neoplastic cells of other astrocytomas have irregular nuclei and the strikingly folded cytoplasm described in protoplasmic astrocytes (Fig. 9).

In experimentally produced gliosis in the cerebral hemispheres of rabbits, astrocytes are numerous and easily differentiated from the phagocytic microglial cells. These reactive astrocytes are similar in structure to the fibrous astrocytes, with numerous fine fibrils in their processes (Fig. 10).

The folded astrocytic cytoplasm is noted completely surrounding some of the small capillaries and attached to portions of the walls of larger vessels, as in Fig. 12. Occasionally a process containing fibrils is seen spreading out in contact with a vessel wall, as in Fig. 13. No Virchow-Robin space is present around these smaller vessels, but the vessels at the margin of the brain were not studied and no statement concerning the larger vessels can be made.

Oligodendroglia.—The oligodendroglial cells are arranged in the usual positions described by light microscopists, that is, in rows in the white matter of the cord and brain, and as perineuronal satellites (Fig. 16). The cells are of relatively smooth, round to oval outline with a distinct cytoplasmic membrane. The nuclei are centrally placed, round to ovoid, with nucleoli occasionally present in the plane of section. The cytoplasm, in contrast to that of the astrocytes, is abundant and pale with a sparse finely granular ergastoplasm and a distinct Golgi apparatus. Mitochondria are small and infrequent. Processes of the oligocyte are relatively few; occasionally a single stout process was sectioned as it emerged from the cell (Fig. 17). The cross sections of the oligondendroglial processes are of rounded outline with the same type of pale cytoplasm as that of the cell body. They are difficult to distinguish from those of the unmyelinated axons and from dendrites in the olfactory regions (7). Nevertheless, relatively thick processes with the characteristic pale cytoplasm and small frequently vacuolated mitochondria can be distinguished in most regions of the neuropil (Figs. 8, 12, and 14). Such processes are often distinguishable adjacent to the margins of capillary blood vessels (Fig. 12).

Microglia.—The microglia are arranged as satellites to both the neurons and the blood vessels, as well as appearing as single cells in the white and grey matter of the brain and spinal cord. Their nuclei are ovoid, large in relation to the size of the cells, and have a uniformly dense chromatin. Their cytoplasm is scant, moderately dense with one to three, rather short, blunt processes, often giving a somewhat triangular appearance to the cell. The mitochondria of microglial cells are distinct (Figs. 18 and 20). In an occasional cell in normal tissue, and more frequently in the margins of tumors, there are clumps of densely osmiophilic material in the cytoplasm of the microglial cells (Figs. 18 and 20). In areas of glial scars of recent origin, phagocytosed material distended the cytoplasm of these cells as is shown in Fig. 19.

Ependyma.—Ependymal cells comprising the membranes which line the cavities of the brain and the central canal of the cord show some variations. In the lateral ventricles they are flattened cells arranged in an imbricated pattern of one to two cell layers. Sparse microvilli and occasional cilia are present on the

free surface. In the central canal and in the aqueduct of Sylvius the ependymal cells are alike, being less flattened than in the lateral ventricles and arranged in several strata. The free surface of the cells presents a complicated appearance with numerous intertwined microvilli and varying numbers of cilia. The cells have an imbricated overlapping pattern with a distinct thickening of the plasma membrane at the upper portions of contact between adjacent cells, thus forming a type of terminal bar. In these regions a dense, finely granular material is present on each side of the plasma membrane. Farther from the surface of the ventricular space, the plasma membranes do not have terminal bars. Frequently the plasma membranes of cells are separated to form intercellular spaces, some of which are between two cells and some at the point of junction of three cells, the so called edge canals.

The cytoplasm is abundant and contains numerous small vesicles and occasionally a few fine osmiophilic granules. The mitochondria are numerous and large, with distinct internal double membranes. Dense granules are present in many mitochondria, as has been noted in mitochondria of other cells, such as those of the kidney and duodenum, but rarely in other cells of the brain. The mitochondria tend to be distributed in a perinuclear position and to be increased on the luminal aspect of the nucleus at the region of origin of the cilia (Fig. 21).

The nuclei are moderately large, ovoid, and slightly indented on their superior aspect. The nuclear chromatin is uniformly finely granular with occasional areas of clumping. A single small dense nucleolus is usually present.

The cilia of the ependymal cells are of the same structure as those described by Fawcett and Porter (12) in the oviduct of the mouse and of the human. They have a distinct arrangement of longitudinally oriented striae, or fibrils, which are situated as 9 evenly spaced groups around the margin and 2 centrally placed. Fawcett and Porter have pointed out that each of these peripheral fibrils actually is a pair. The basal bodies of the cilium are directly continuous with the cilium and its rootlets which extend into the apical portion of the cytoplasm of the cell. Mitochondria are somewhat increased in the region of the origin of the cilia. The microvilli of the ependyma are extensions of the cytoplasm covered by the plasma membrane and consistent with the cuticular surface described by Penfield (1) on the surface of ependymal cells.

Choroid Plexus

The choroid plexus has been examined in the rabbit and the guinea pig. The epithelium of the choroid plexus resembles that of ependyma with similar nuclei, mitochondria, microvillous surface, and cilia. However, the microvillous surface of the choroid plexus is more complicated than that of the ependyma, although as Dempsey and Wislocki (13) have pointed out, this may vary in different cells. The microvilli are intertwined, moderately long, and secondarily branched. The cilia are sparse. The cytoplasm immediately beneath the compli-

cated microvillous surface differs from that of the ependymal cells in that it has a more densely arranged ergastoplasm comprised of closely placed membrane-bounded profiles with a prominent adherent granular component. The mitochondria are moderately large, numerous, and have distinct internal laminar structure. The basal portion of the cell contains less closely arranged ergastoplasmic structures. The plasma membrane, particularly in that portion where two cells abut, is markedly tortuous and plicated in the basal portion of the cell, with a narrow space separating this portion of the cell from the underlying capillary. In some foci there are collagen fibrils present within the pericapillary space (Fig. 22).

Neuropil

The neuropil is a complicated arrangement of processes arising from the various cells of the nervous tissue, thus consisting of dendrites, axons, microglial, oligodendroglial, astrocytic, and possibly ependymal projections. The blood vessels are completely invested by this meshwork of cell processes. There is relatively little space between the component fibers that make up the neuropil, so that any type of intercellular material or ground substance is necessarily present in a very thin layer, rather than being a distinct substance in which the fibers are embedded. Actually, only in the ependyma are definite spaces present between cells in normal tissue. However, in brain tumors, there is more frequently evidence of a definite space between processes as well as between cell bodies. At the present time it is difficult to identify with certainty many of the cellular projections within the neuropil, since the individual differences between some of the fibers, in particular some of the dendrites, unmyelinated axons, and oligodendroglial fibers are subtle.

DISCUSSION

The identification of the various neural, glial, and vascular structures mentioned in the preceding section has not presented any unusual difficulties except in the case of the astrocytes and oligodendroglial cells. Two types of glial cells are readily distinguished in electron micrographs, one with pale cytoplasm containing only sparse granules and the other with much darker cytoplasm and with extensively refolded surface membranes, thus creating innumerable small protoplasmic processes. In this account the latter cell type has been identified as the astrocyte and the former is equated with the oligodendroglial cell.

In view of the difficulties in distinguishing between these two cell types it is necessary to discuss the criteria for identification used in this investigation.

The astrocyte classically is recognized by its elongated, indented nucleus, whereas the nucleus of the oligocyte is smaller and spheroidal. The cytoplasm of astrocytes stains moderately with acid dyes, whereas that of oligodendrocytes

is chromophobic. Oligodendroglia frequently are lined up in rows among the fibers in myelinated tracts, whereas astrocytes ordinarily are solitary. Likewise, oligodendrocytes occur as satellites to neurons, whereas astrocytes ordinarily do not. Only one variety of oligodendrocyte is recognized, whereas astrocytes are of two varieties, fibrous and protoplasmic. All of these characteristics accord well with the identification advanced here. In the illustrations accompanying this article, the elongated and indented nuclei occur in the dark cells, whereas the light cells have predominantly spherical nuclei. The dense cytoplasm of the dark cell accords well with the acidophilia of astrocytes, whereas the pale tenuous cytoplasm of the light cell is to be set against the chromophobic quality of the oligodendroglia. Rows of light cells disposed among columns of myelinated fibers have been observed; Fig. 17 is one cell from such a row. Light cells with spherical nuclei occur frequently as satellites to neurons as is shown in Fig. 16.

The contiguity of glial processes to capillary walls alone, is not of value in distinguishing these two cell types. The pale processes have been observed in association with capillary walls, but invariably it is found that the folded processes of the dark cells are in an association just as intimate (Figs. 12 and 13). It would seem therefore that either cell type can make contact with the walls of blood vessels; consequently it is not justified to identify either cell type on this criterion alone.

In addition to these observations, several others may be mentioned as being consonant with the view adopted here. Sections through tumors, classified as astrocytomas by light microscopy, reveal the predominant cell type to be the dark cell with refolded surface membranes (Fig. 9). Both protoplasmic and fibrous varieties have been observed in the astrocytic cells of these tumors. In experiments involving gliosis (healing of a surgically produced lesion) cells identified as fibrous astrocytes have been seen to form the glial scar. We have also observed that Mueller's cell, a specialized form of protoplasmic astrocyte forming the major glial component of the retina, has a fine structure similar to that described above (14). All of these facts, taken singly and collectively, constitute overwhelming evidence for the identification of the cell types of the two major glial elements.

The process of myelin formation in peripheral nerves has recently been studied by Geren (9) and Robertson (10) who have described the laminated structure of the myelin sheath as resulting from a helical wrapping of the Schwann cell mesaxon around the nerve fiber. This process is conceived as caused by a rotation of the Schwann cell, or of the axon, or of both. In the central nervous system, myelinated fibers also have laminated myelin (Fig. 15) quite comparable to that of peripheral nerves. Yet, these myelinated fibers sometimes are contiguous to nerve cells, to oligodendroglial processes, to astrocytic processes, or to capillary walls. They are rarely surrounded com-

pletely by the cytoplasm of a glial cell, and in this respect are different from peripheral fibers which are enveloped on all sides by the Schwann cells. The similarity in the myelin pattern of the peripheral and central fibers, and the dissimilarity of their relationships to their sheath cells make it imperative to investigate the mode of myelin formation in the central nervous system.

SUMMARY

In order to establish criteria for the identification of the neural and glial cells of the central nervous system, sections of the brains and spinal cords of mice, rabbits, guinea pigs, and rats; and portions of tumors of the human brain have been examined by electron microscopy.

Identification of neurons is made possible by the characteristic cytoplasmic picture, in which there is a distinct granular and less constant membranous ergastoplasmic pattern. In no other cell of the central nervous system is such a distinct granular component present in the ergastoplasm. The shape of the neuron in electron microscopic preparations is similar to that seen by light microscopy with several dendrites containing a similar cytoplasm arising from the perikaryon. Synapses are relatively common on the surface of the neuron and its dendrites.

Microglial cells are relatively small and dense with few processes, and are arranged as perineuronal and perivascular satellites for the most part. Occasionally phagocytized material is present in their cytoplasm. The oligodendroglial cells are identifiable by their position as perineuronal satellites and in the white matter as cells arranged in rows. They have a uniformly round to ovoid nucleus with a pale cytoplasm, which has a sparse, finely granular component and a few small mitochondria. The processes are few and relatively straight when cut in longitudinal section. The predominant cellular type in an oligodendroglioma was similar, with a pale cytoplasm. The astrocytes are variable in appearance. Their nuclei are moderately large, irregularly ovoid, and the cytoplasm adjacent to the nucleus is finely granular and scant. In the protoplasmic astrocytes the cytoplasm has a complicated infolded arrangement with reduplication of the plasma membrane, numerous processes extending radially from the cell and rebranching. To a certain extent this same folded plasma membrane was noted in the fibrous astrocytes. However, their more distant processes were narrowed, relatively straight, and filled with numerous dense fibrils. The processes of the astrocyte often surrounded axons, and other cellular processes, and surrounded some vessels, while attaching to a part of the wall of another vessel. Proliferating cells in experimentally produced gliosis and in astrocytic neoplasms were similar in structure.

The ependymal cells and the epithelium of the choroid plexus have a specialized surface with microvillous projections of the cytoplasm covered by the plasma membrane. Cilia in varying numbers are present in both epithelia.

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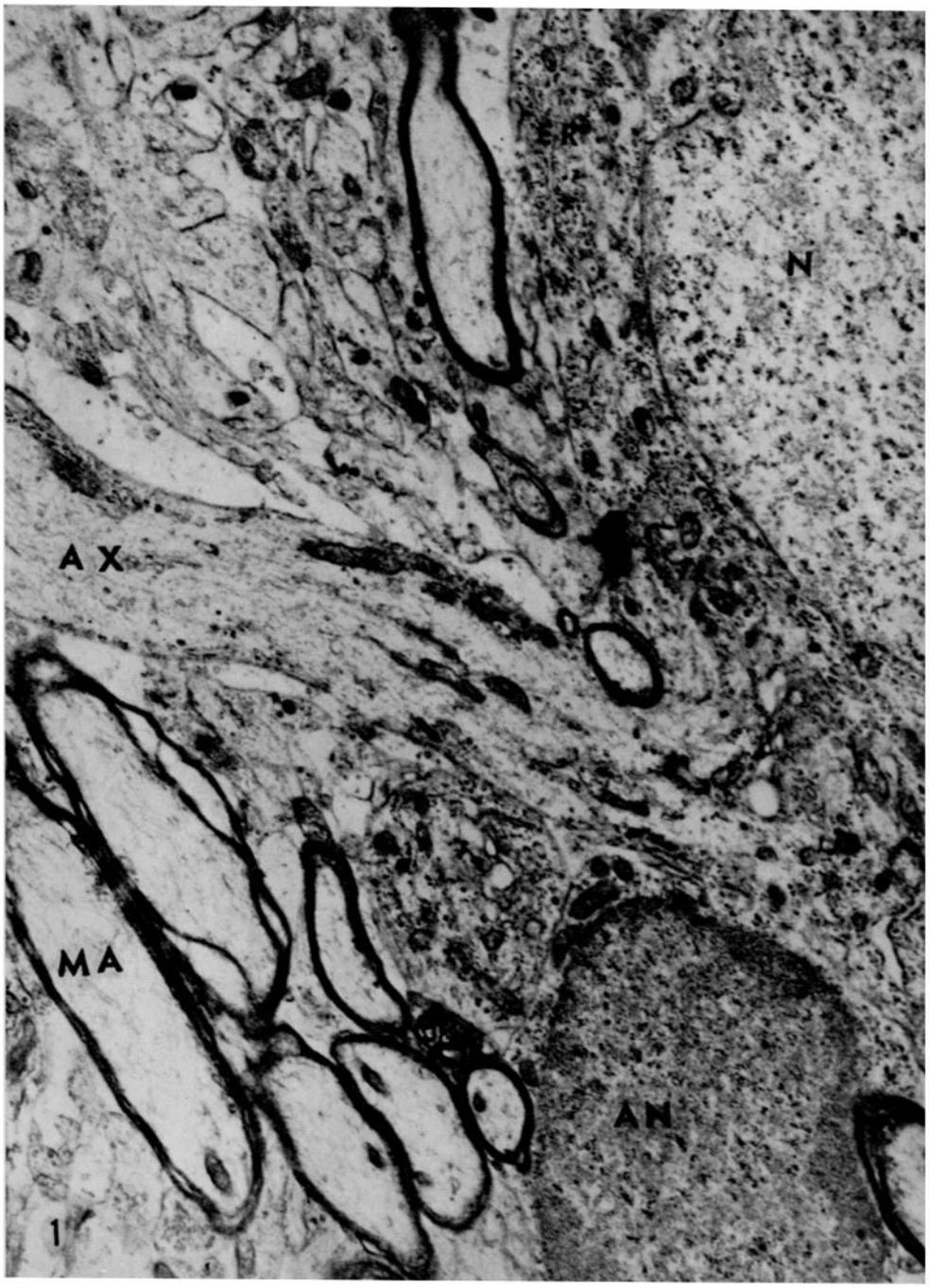
EXPLANATION OF PLATES

PLATE 138

FIG. 1. Electron micrograph of a section through an axon hillock in the spinal cord of a young rat. The nucleus of the neuron (*N*) is to the upper right of the field. The point of origin of the axon from the nerve cell cytoplasm is in the center of the field, as the axon (*AX*) extends across the micrograph to the left. Neurofilaments and mitochondria are present in the axon, but ergastoplasm, which is prominent in the cytoplasm of the neuron, is absent. The finely granular ergastoplasm (*ER*), the Nissl substance, extends to the origin of the axon. Several myelinated axons (*MA*) are present. An astrocytic nucleus (*AN*) is seen at the lower right. × 11,500.



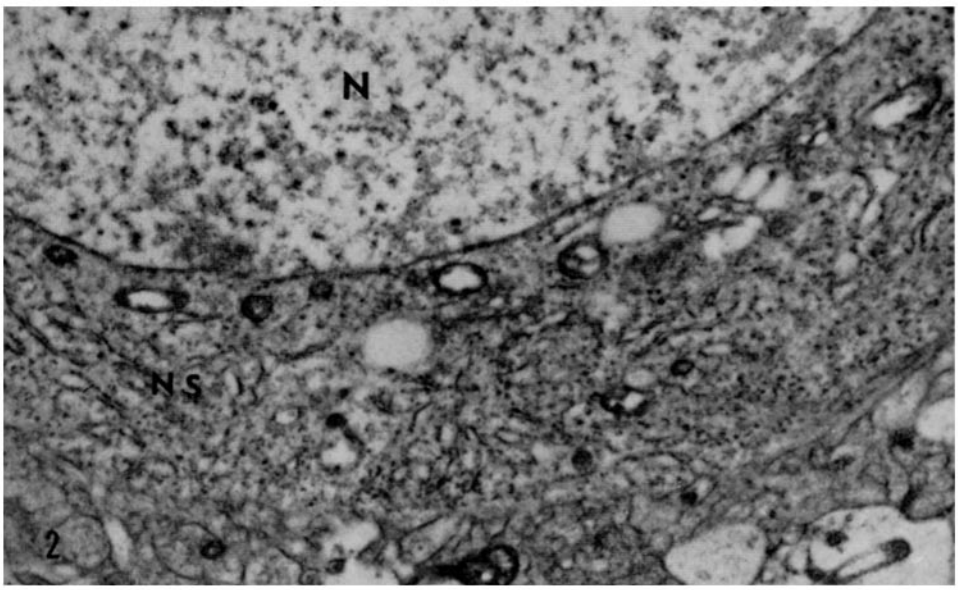
(Luse: Central nervous system)

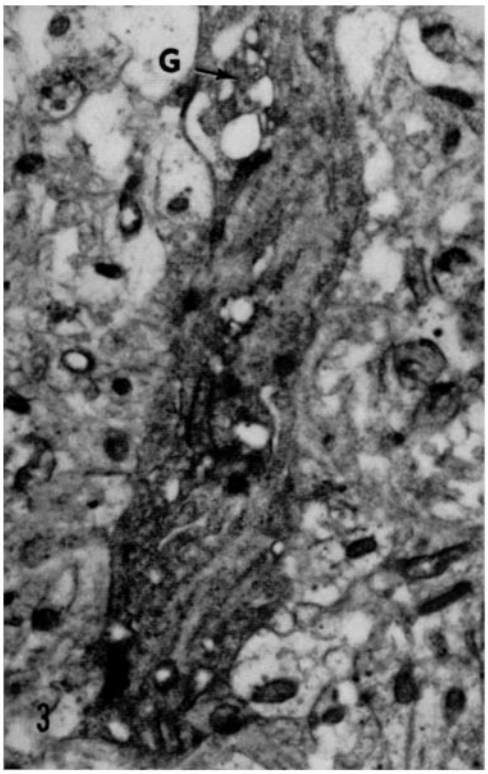
PLATE 139

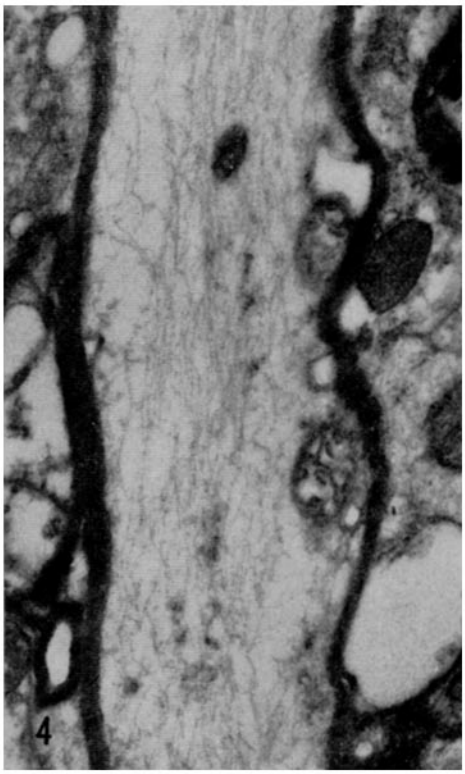
FIG. 2. Electron micrograph of a part of a neuron in the cerebral cortex of a rat. The nucleus (*N*) is at the upper part of the field. The Nissl substance of the cytoplasm (*NS*) is composed of ergastoplasmic membranous sacs and an associated finely granular component. The osmiophilic fine granules are interspersed in the interstices between the membrane-bounded spaces. Occasional small mitochondria are present. × 12,500.

FIG. 3. Electron micrograph of a portion of a dendrite rather close to its origin from the neuron. At the upper portion of the field a few Golgi membranes (*G*) are present. The dendrite has a fine but densely granular ergastoplasm, or Nissl substance. This is in contrast to the axon in Fig. 4, in which this granular material is absent. × 20,000.

FIG. 4. Electron micrograph of a section through a myelinated axon in the spinal cord of an adult mouse. Neurofilaments of the axon are evident as fine, moderately dense strands in the axoplasm. Two mitochondria are visible at the right margin of the axoplasm. × 25,000.







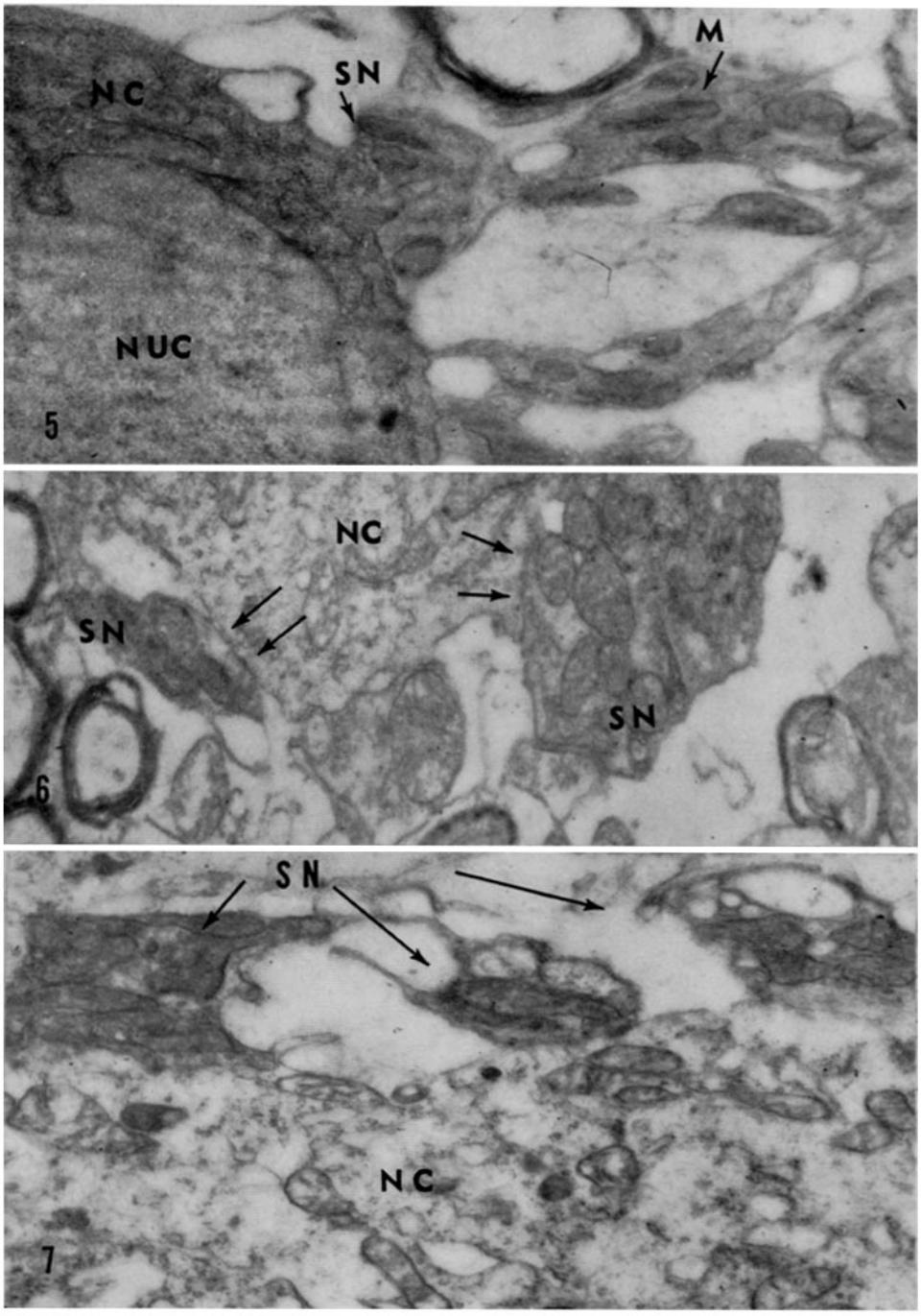
(Luse: Central nervous system)

PLATE 140

FIG. 5. Section through the spinal cord of an adult mouse. There is a portion of a neuron at the left of the field. A synapse is present at the right, indicated as (*SN*). The presynaptic fiber has expanded as a bouton terminal. There is an increased number of mitochondria in the synaptic ending. The plasma membranes are intact and distinctly separate at the site of synaptic junction. (*NUC*, nucleus; *M*, mitochondrion; *NC*, nerve cell cytoplasm.) × 25,000.

FIG. 6. Electron micrograph of part of the cytoplasm of a neuron (*NC*) and two synapses (*SN*) in the spinal cord of a mouse. The plasma membranes of both the synaptic endings and of the neuron are distinct (as is seen at the arrows) although they are closely apposed to each other. The synaptic endings are filled with numerous large dense mitochondria, and with microvesicles. Another synapse may be present in the lower central portion of the field. × 18,000.

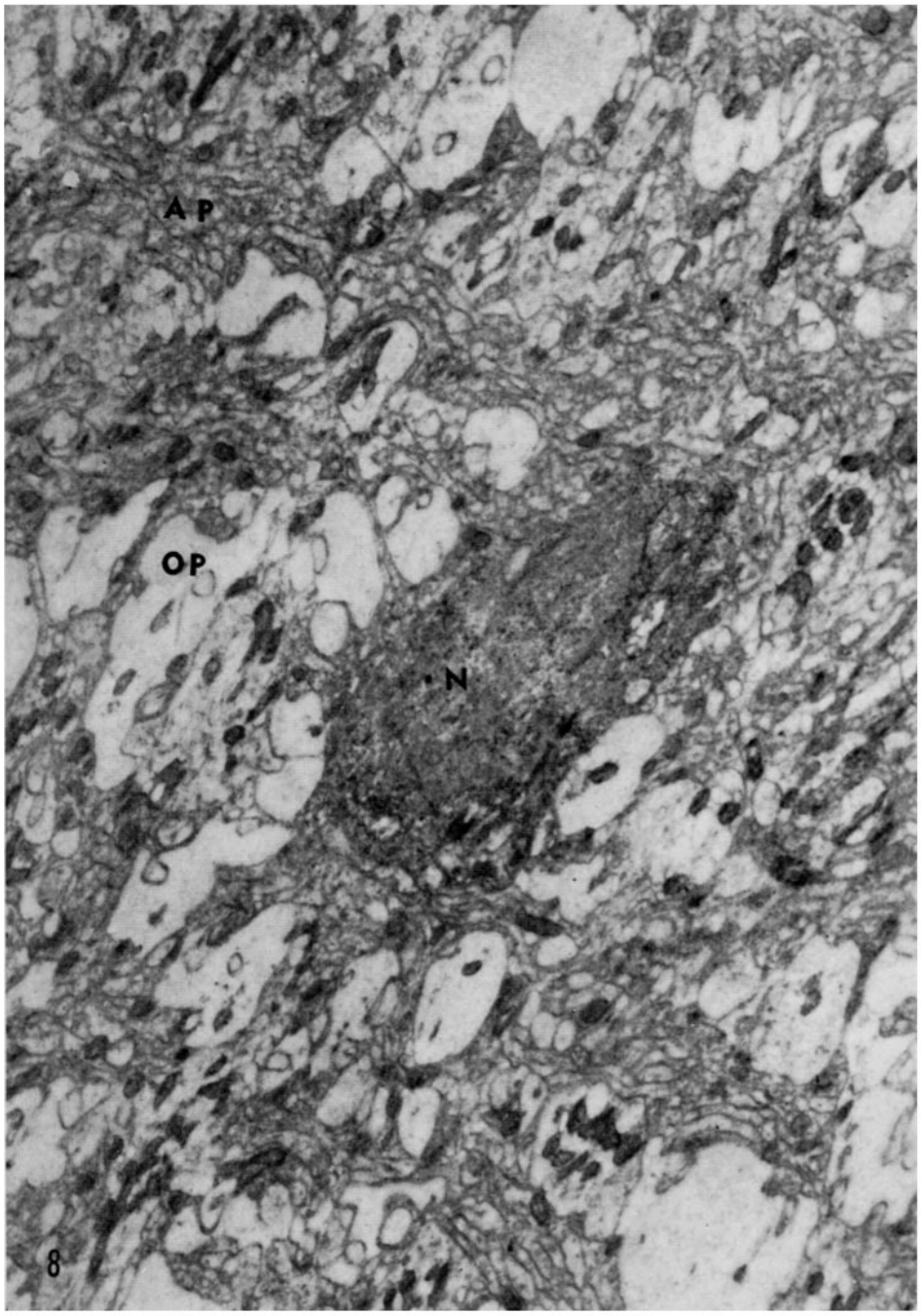
FIG. 7. Electron micrograph through part of the cytoplasm of a neuron (*NC*) in the spinal cord of a mouse. Three areas of synaptic contact are present. In all of the presynaptic neural endings (*SN*) there is a concentration of mitochondria and the mitochondria are more dense than those in the underlying neural cytoplasm. Microvesicles are also present in the endings. × 22,500.



(Luse: Central nervous system)

PLATE 141

FIG. 8. Protoplasmic astrocyte in the cerebrum of a mouse. The nucleus (*N*) is centrally located with a scant poorly defined perinuclear cytoplasm. Away from the nucleus, the cytoplasm becomes a thin extension bounded by complexly folded and refolded plasma membranes, extending as irregular protoplasmic processes in all directions from the nucleus. Interspersed between the folded astrocytic processes (*AP*) are pale oligocyte processes (*OP*). × 11,500.



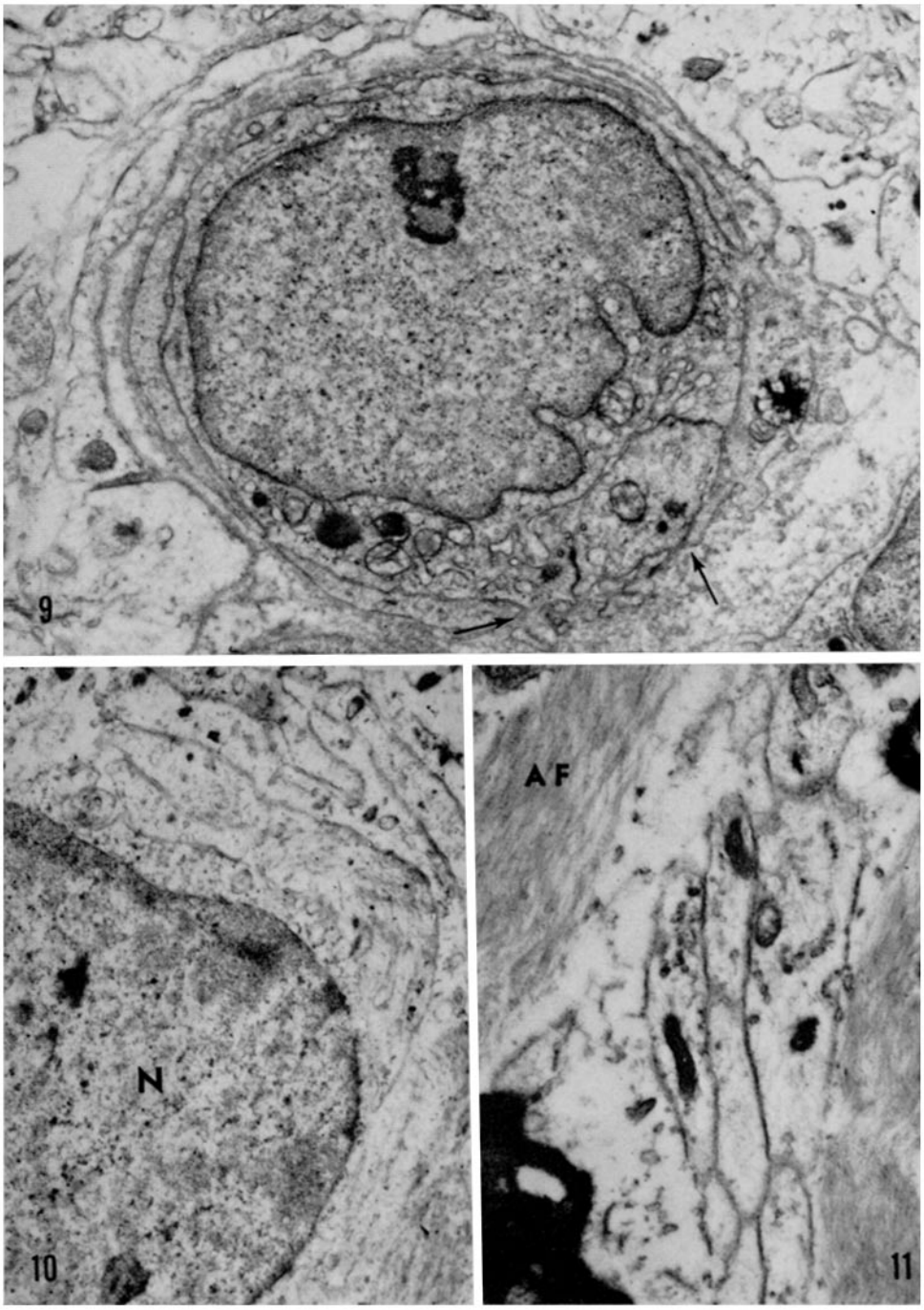
(Luse: Central nervous system)

PLATE 142

FIG. 9. Electron micrograph of a neoplastic protoplasmic astrocyte in an astrocytoma. The nucleus is more irregular in contour than those of normal astrocytes. The pattern of infolding of the plasma membrane in the formation of complex cystoplasmic folds is evident. At regions indicated by arrows, the folded inner membranes are continuous with the outer plasma membrane. × 11,500.

FIG. 10. Electron micrograph of a portion of an astrocyte from an area of experimentally produced gliosis. The nucleus (*N*) is to the right. The cystoplasm has a folded plasma membrane, which is similar to but less complicated than that of the astrocyte in Fig. 8. Astrocytic glial fibrils are present within the folded cytoplasmic processes. × 20,000.

FIG. 11. Electron micrograph of a portion of a fibrous astrocyte in the posterior column of the spinal cord of an adult rabbit. Dense groups of astrocytic fibrils (*AF*) are present in the cytoplasm. Reduplication of the plasma membrane similar to that of the protoplasmic astrocytes in Figs. 8 and 9 is present in the central part of the field. The dense masses of osmiophilic material are from the margins of the myelinated fibers adjacent to the astrocytic cytoplasm. × 13,000.

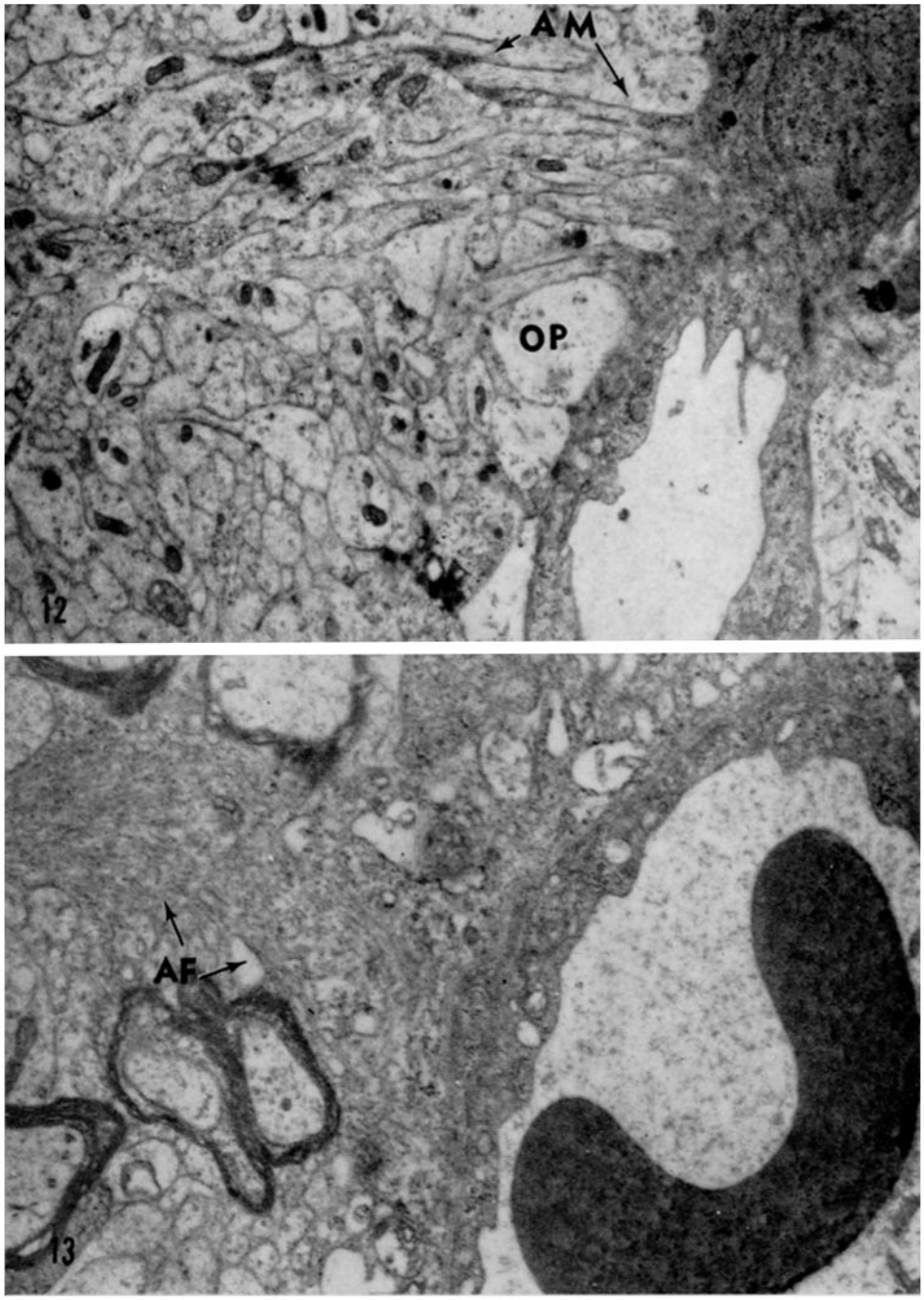


(Luse: Central nervous system)

PLATE 143

FIG. 12. Electron micrograph of a section of spinal cord of a 1-day-old mouse. A capillary lumen is at the lower right. Folded astrocytic membranes (*AM*) are attached to the vessel wall, forming a protoplasmic astrocytic foot at the central portion of the field. In addition to these astrocytic elements, light thicker processes (*OP*), identifiable as those of oligocytes, also touch the margin of the capillary. Cross-sections of small unmyelinated axons are present at the right margin of the field. × 9,500.

FIG. 13. Section of a capillary in the cerebral cortex of a 2½-week-old rat. At the center, extending to the left, is a fibrous astrocytic foot (*AF*) attached to the wall of the capillary. Astrocytic fibrils are present within the process. Within the lumen of the vessel is an erythrocyte. No Virchow-Robin space is evident around this small blood vessel. × 18,000.

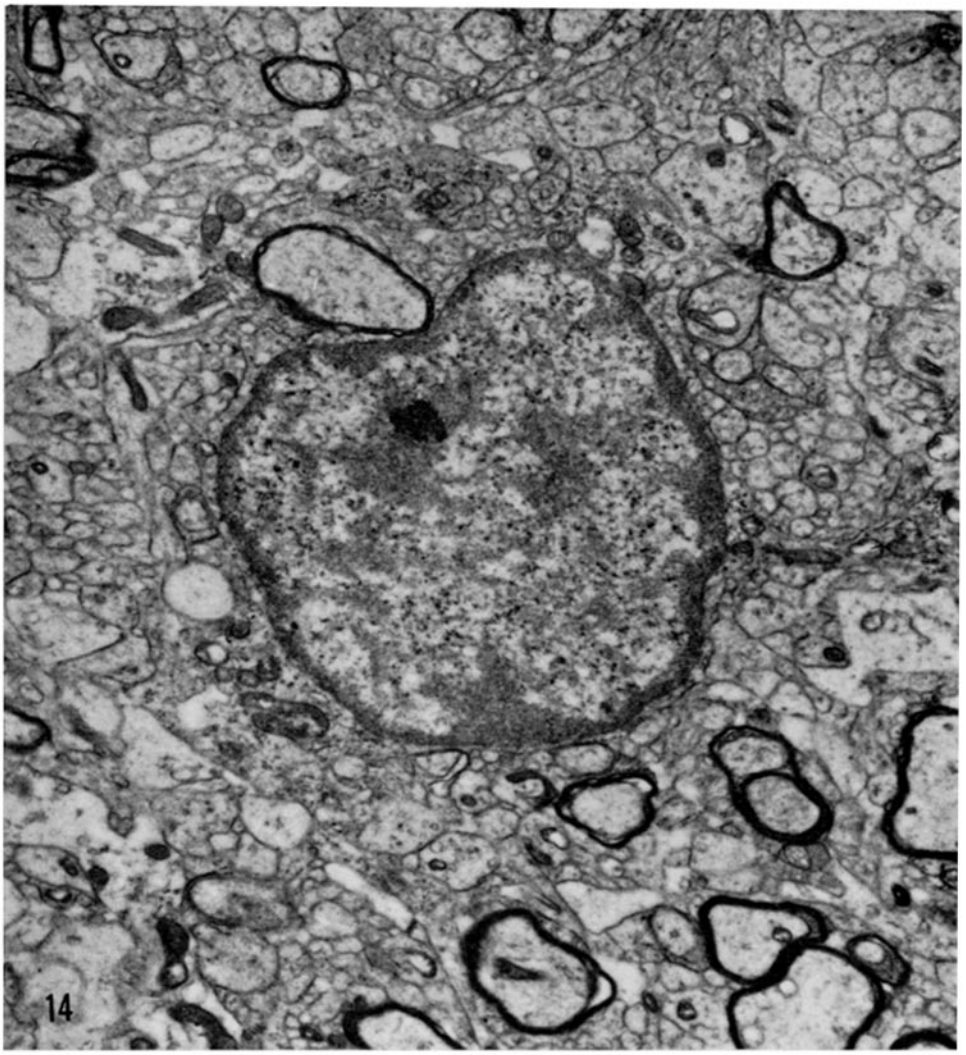


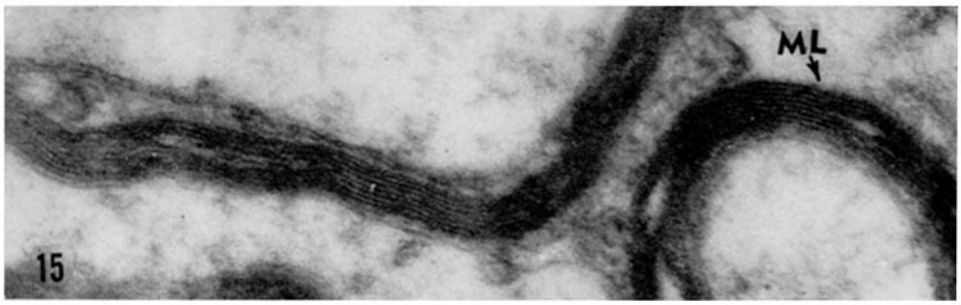
(Luse: Central nervous system)

PLATE 144

FIG. 14. Electron micrograph of a section through a protoplasmic astrocyte in the cerebral cortex of a young rat. The nucleus is irregular. The perinuclear cytoplasm is scant and finely granular. Completely intertwined and folded cytoplasmic processes extend out from the cell and surround the neural and other glial fibers of the neuropil. Note the myelinated fibers in the lower portion of the micrograph. × 11,500.

FIG. 15. Electron micrograph of myelinated fibers in the spinal cord of a mouse, demonstrating the laminated structure of the myelin sheath (*ML*) in the central nervous system. × 55,000.



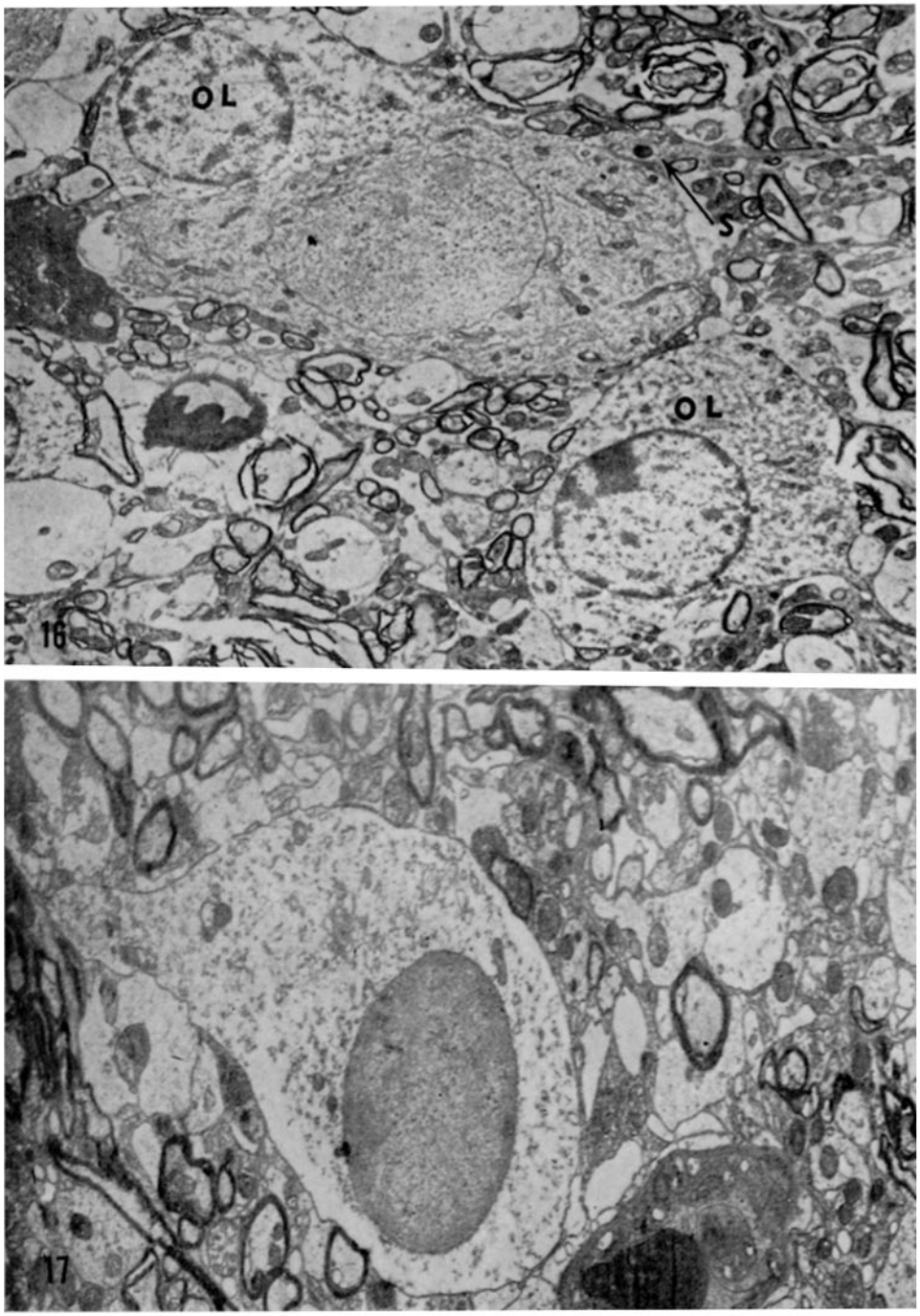


(Luse: Central nervous system)

PLATE 145

FIG. 16. Section through the spinal cord of an adult mouse. In the center of the field is a small neuron with two satellite oligodendroglial cells (*OL*). The oligocytes have round nuclei and pale cytoplasm as contrasted with the cytoplasm of the neuron. The neural cytoplasm contains granular ergastoplasm. At the upper right margin of the neuron there is a synapse (*S*), indicated by an arrow. Surrounding the cells is the neuropil. A small capillary is present at the lower left. × 4000.

FIG. 17. Section through the spinal cord of an adult mouse. An oligodendrocyte, one of several which were lined up in a row, is in the center of the field. The nucleus is ovoid. The cytoplasmic outline is smooth with a single stout process. The cytoplasm is pale with a scant, finely granular component and a few Golgi membranes. Neuropil surrounds the oligocyte. A small vessel is present at the lower right. × 8,500.



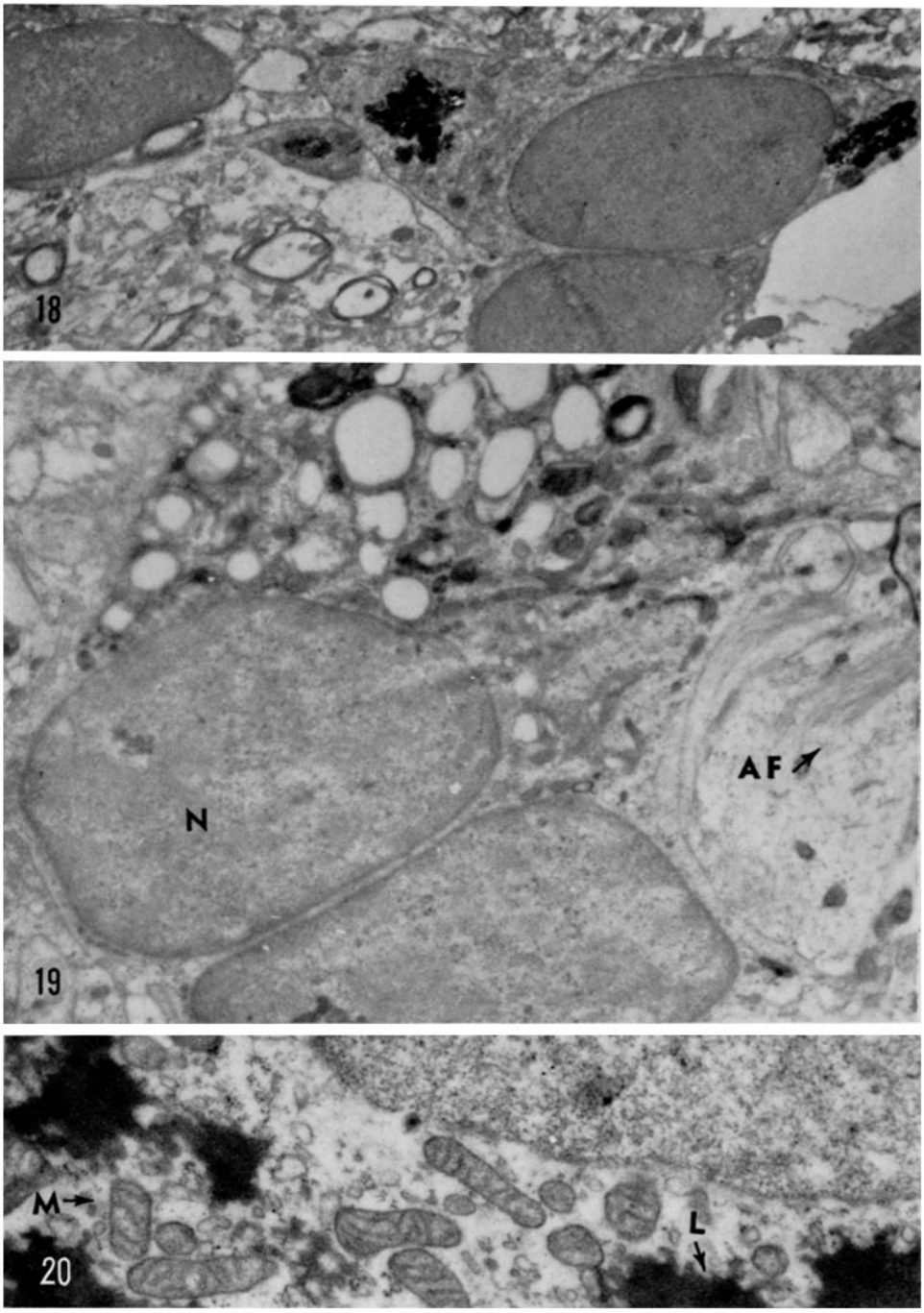
(Luse: Central nervous system)

PLATE 146

FIG. 18. Section through microglial cells in a human brain. The central cell has a characteristic ovoid densely osmiophilic nucleus. The cytoplasm is prominent because of ingested osmiophilic debris. Mitochondria are evident. The cellular outline is smooth. Neuropil containing glial processes and myelinated axons surrounds the cells. × 11,500.

FIG. 19. Section through a glial scar three weeks following a surgical lesion in the cerebral hemisphere of a rabbit. To the right are fine glial fibrils (*AF*) in the process of a reactive fibrous astrocyte. The cell, the nucleus of which (*N*) is at the lower left, is a phagocytic cell containing osmiophilic material, cellular debris, and vacuoles; its swollen cytoplasm occupies most of the upper portion of the field. Mitochondria and Golgi vacuoles are present. × 18,000.

FIG. 20. Section through part of an altered phagocytic microglial cell, (compound granular corpuscle) in the margin of a brain tumor. Lipide material (*L*) and debris are present in the cytoplasm, as are numerous mitochondria (*M*). × 18,000.

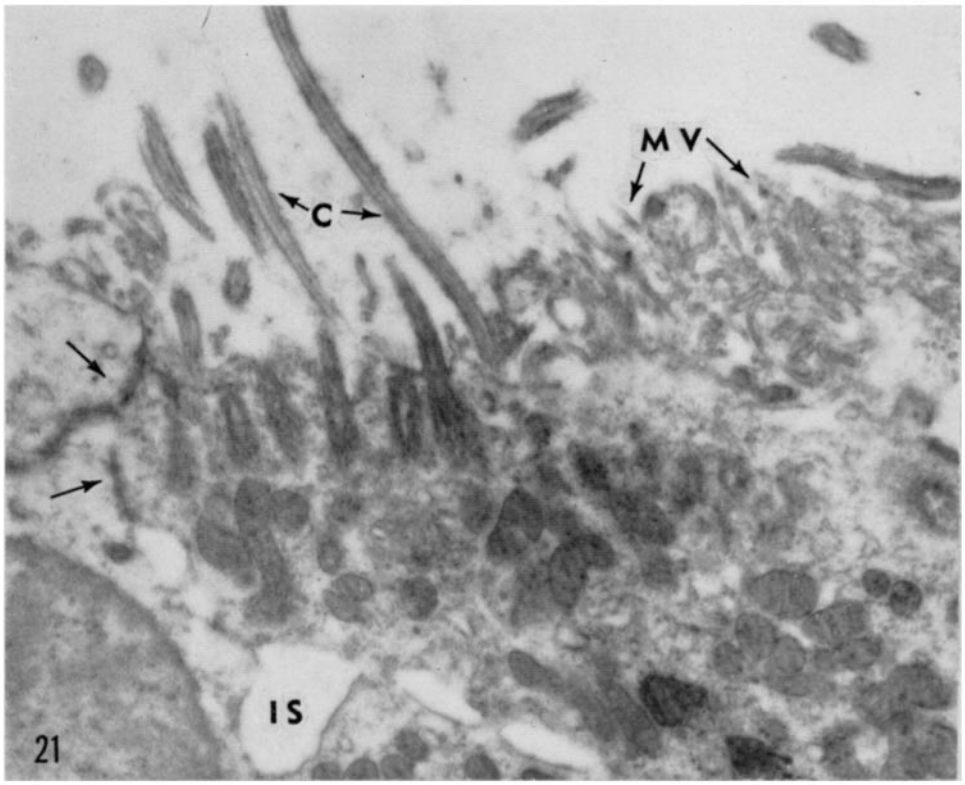


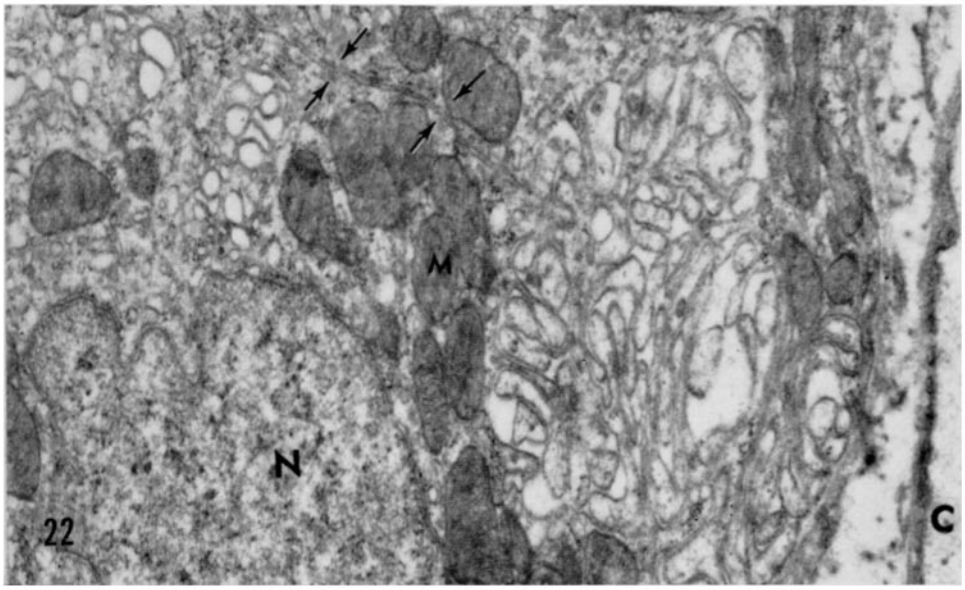
(Luse: Central nervous system)

PLATE 147

FIG. 21. Section through the superficial surface of an ependymal cell from the aqueduct of an adult mouse. The white space at the top of the figure represents the cavity of the aqueduct of Sylvius. Projecting into it are cilia (*C*) and tangled microvilli (*MV*). The rootlets of the cilia are clearly evident extending downward into the cytoplasm. Mitochondria are numerous. At the left of the field, indicated by arrows, are two regions in which the plasma membrane has an associated osmiophilic granular material forming terminal bars. At the lower left are several intercellular spaces (*IS*). × 11,500.

FIG. 22. Electron micrograph of the choroid plexus from an adult mouse. The nucleus (*N*) of one cell is present at the lower left. At the upper margin of the field (indicated by arrows) are the plasma membranes of two adjacent cells. As the apposed plasma membranes approach the capillary they become extremely plicated as the cells dovetail into one another. A connective tissue space separates the capillary wall (*C*) from the choroid plexus. Many mitochondria (*M*) are present in the cytoplasm. × 18,000.





(Luse: Central nervous system)