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ELECTRON MICROSCOPY OF THE SOMATIC SENSORY CORTEX OF THE CAT

II. THE FINE STRUCTURE OF LAYERS I AND II

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[Plates 11 to 20]

CONTENTS

Layers I and II of the somatic sensory cortex are clearly distinguishable with the electron microscope because of characteristic differences in the number, type and orientation of neurons and dendritic and axonal ramifications. Layer I may be subdivided into: (i) a subpial astrocytic layer immediately deep to the basement membrane of the cerebral surface; (ii) a superficial quarter consisting of bundles of small myelinated axons and large numbers of small axon terminals which contain spherical vesicles and end in asymmetrical synaptic complexes mainly on large dendritic spines. Most of these terminals are derived from a dense feltwork of fine unmyelinated axons which are especially concentrated at the junction of the superficial and deep parts of layer I; (iii) a deeper three quarters with similar features to the above but with the additional characteristic of many obliquely orientated large dendrites which are the diverging branches of apical dendrites ascending from deeper layers.

Small pyramidal neurons dominate layer II, but among them are a small number of non-pyramidal neurons whose beaded dendrites are covered with axon terminals. Large apical dendrites traverse this layer, and in addition to the typical asymmetrical synapse on dendritic spines, a few symmetrical types appear. These are derived from thin unmyelinated axons orientated horizontally within the layer, and the terminals contain many small flattened or pleomorphic synaptic vesicles.

Introduction

Although experimental studies will be required to elucidate the problem of the internal organization of the cerebral cortex, a knowledge of the normal structure is necessary as a basis for such experimental investigations. Many electron microscopic studies have already been made on the cortex but to a large extent they have been concerned with some specific aspect of its structure—either the main synaptic types (Gray 1959; Colonnier 1968), the dendritic spine (Gray 1959) or the different types of neuroglial cell (Maxwell & Kruger 1965; Kruger & Maxwell 1966). In this and the succeeding paper certain of the features which have enabled the various

laminae of the somatic sensory cortex to be distinguished at the electron microscopic level will be described as an essential prerequisite for experimental investigations on the laminar pattern and mode of termination of the extrinsic afferent pathways to this area (Jones & Powell 1970*a*).

Material and methods

The material is the same as that described in the preceding paper (Jones & Powell 1970*b*), all the brains being fixed by perfusion under hypothermia with a buffered mixture of paraformaldehyde and glutaraldehyde. The blocks of tissue were removed and embedded so that in a thick section taken from the long face of the block and stained for light microscopy (Richardson, Jarett & Finke 1960), all six cortical layers were aligned parallel to the pial surface (figure 1, plate 11). The block was trimmed appropriately so that thin sections could be obtained from one or more known laminae; in some cases all six were included in single, long sections which were mounted on coated grids containing a single hole 2 mm × 1 mm. In a number of instances blocks were embedded so that thin sections for electron microscopy could be obtained which passed through the cortex parallel to the pia mater, while still enabling the block to be turned around so that thick sections for light microscopy could be cut perpendicular to the surface. By cutting a thick perpendicular section after each successive group of thin tangential ones, an indication of the cortical layer sampled electron microscopically could be obtained.

Results

Light microscopy

Recognition of the classical six laminae of the cerebral cortex is dependent upon the form and arrangement of the constituent neurons usually as seen in relatively thick sections stained by the Nissl method and viewed with the light microscope. These cellular layers become more distinct the thicker the section, but all are clearly recognizable in the $\frac{1}{2}$ to 1 μm thick section stained by the method of Richardson *et al.* (1960). A brief description of a representative section (figure 1, plate 11) will be given as these sections have been of considerable importance in defining the cortical laminae in this and the experimental studies.

Layer I, the molecular layer, is obvious in that usually no neuronal perikarya are present. Apart from this lack of neuronal cell bodies, two main zones are seen. The superficial one quarter or so of the layer, extending up to the pia mater, is characterized by large numbers of dendrites cut in cross-section and a few small myelinated axons, while in the deeper three quarters the dendrites are cut mainly in horizontal or oblique section and are frequently arrayed in vertical rows, in which individual dendrites may branch. Layer II is also distinct as a densely cellular layer, one to three cells thick, most of the constituent neurons appearing as small pyramids with their apices directed towards the molecular layer. Deep to this is layer III, the thickest layer, and it is characterized by loosely arranged pyramidal cells of small and medium size, many of the more superficially placed cells obviously sending their dendrites into the molecular layer through layer II. In these $\frac{1}{2}$ μm sections layer IV, the inner granular layer, is also a loosely arranged cellular layer in which the constituent neurons are variable in size and their somata angular or rounded rather than pyramidal. Deep to this, layer V is distinguished by the appearance of some very large pyramidal cells and many large myelinated fibres. Layer VI which merges insensibly with both layer V and the subjacent white matter contains a few

obviously pyramidal cells, but in general the cells, although larger, resemble those of layer IV. Its main distinguishing feature is the presence of very large numbers of myelinated axons, many of them arranged in radiate fasciculi. Many other features of the cortex are visible in such thick sections, but only the above simple criteria were necessary for identifying the cortical laminae from which tissue was being investigated electron microscopically.

The fine structure of layer I

Under the electron microscope layer I is probably the most readily recognized of the six layers and has the most clear-cut boundaries. It is bordered superficially by the pia mater and deeply by the rows of neuronal perikarya forming layer II. The two zones, superficial and deep, visible in light microscopy and in each of which there is a characteristic arrangement of dendrites, are clearly seen. In addition, a third zone, consisting of the pia mater and a number of subjacent glial lamellae becomes obvious.

The pia mater and subpial glia

The actual surface of the brain is a basement membrane beneath which there is usually a thin lucent layer (figures 2 to 4 plates 11 and 12). The cerebral substance immediately deep to this consists of a variable number of stacked astroglial lamellae, while lying on the surface of the basement membrane are the cells of the pia mater. The basement membrane is so intimately related to the astroglial processes as to suggest that it should be considered a part of the brain rather than as a component of the overlying pia mater. The cells of the latter are rarely in intimate contact with the basement membrane, often being separated by a considerable gap. At times, probably as the result of mechanical interference during processing of the blocks, the pial cells have been lost, but the basement membrane always remains intact.

The cells of the pia mater consist of a flattened soma containing an oval or irregular nucleus in which the chromatin material is dense and clumped peripherally; from the soma long, very attenuated cytoplasmic processes spread over the basement membrane of the brain (figure 4, plate 12). Many of these processes may overlap one another; junctional complexes have not been observed between points of contact of adjacent pial cells. Superficial to this layer, and separated by a small gap, there is commonly a second layer of similarly attenuated cells, which are identical in appearance but are not associated with a basement membrane; this layer may be reduplicated several times. Within the gap between the two layers, small bundles of collagen fibres are usually present, and occasionally irregular, vacuolated cells resembling macrophages are present. It seems probable that the two layers of cells and the intervening collagen-containing space should be together considered as the pia-arachnoid (figure 4, plate 12). The glial layer (figures 2 to 5, plates 11 and 12) lying beneath, and closely applied to, the basement membrane, consists exclusively of astroglial processes and is of variable thickness. Large astrocytic somata, usually more flattened than in other parts of the cortex, occur at intervals in this part of layer I, and give off long processes which pass upwards at an obtuse angle towards the basement membrane. These processes commonly branch and usually expand as they reach the surface. Several of these processes may be seen lying parallel to one another in any one section. It is probable that they spread out in all planes, because it is common to see bundles of them cut in transverse section and lying among the obliquely orientated ones cut in longitudinal section. Especially prominent in the subpial astrocytic processes are large bundles of thin fibrils running from the soma in the long axis of the lamellae, and there is usually a heavy concentration of

these filaments immediately deep to the surface basement membrane. Glycogen granules are seen only occasionally. The plasma membranes of most of the astrocytic lamellae forming the subpial glia are separated from one another by an extracellular cleft which is narrowed at certain points, and the centre of the narrow gap may contain a thin line of electron dense material so that the whole resembles a pentalaminar junctional complex (figure 3, plate 11). Junctional complexes of this type are relatively common, but frequently the cleft separating adjoining astroglial processes in immediate apposition to the basement membrane is no less wide than the extracellular space of the rest of the brain and no junctional complexes are seen. In some instances, the cleft may be filled by electron dense material resembling that of the basement membrane but more frequently it is clear.

The neural elements of layer I

Just beneath the astrocytic lamellae, a constant feature is the presence of a loose aggregation of small myelinated axons, their total diameter measuring between 0.5 and 1.0 μm (figures 2, 4, 6 plates 11 to 13). These small fibres run parallel to the surface of the brain and probably spread out in all directions because they are cut both longitudinally and transversely in sections perpendicular to the surface; in sections cut tangential to the surface, they are invariably cut longitudinally and cross one another at all angles. Below this level in layer I myelinated axons are far less common, are small, and in perpendicular sections may be cut in transverse section, but are more commonly seen passing up vertically from deeper layers. Apart from the axons beneath the subpial glia, the superficial one quarter to one half of layer I contains a dense mass of small dendrites, large dendritic spines and axon terminals. Among these are interwoven very large numbers of small unmyelinated axons and astroglial processes (figures 6 to 8, plates 13 to 15). The majority of the dendrites present are cut in transverse section irrespective of whether the sections are made in the long axis or in the transverse axis of a gyrus. As this superficial part of layer I lacks neuronal perikarya, these dendrites must arise from cells in deeper levels. Among the small dendrites are scattered approximately equal numbers of dendritic spines and small axon terminals. The spines may be recognized by their characteristic shape and especially by the common presence of the 'spine apparatus' (Gray 1959). Even when this is not present, the absence of neurotubules, ribosomes and usually mitochondria serves to distinguish them from dendrites. These spines are large, frequently being of the same diameter as the parent dendrites (figure 7, plate 14). The vast majority of the axon terminals present are small, contain a high complement of spherical synaptic vesicles and have a relatively dense background cytoplasm. They terminate by means of asymmetrical synaptic thickenings (Type 1 of Gray 1959), with approximately equal frequency on dendritic spines and shafts (figures 6, 7

DESCRIPTION OF PLATE 11

FIGURE 1. Photomicrograph of a 'thick' section stained by the method of Richardson *et al.* (1960) showing the cellular laminae (I to VI) of the somatic sensory cortex. × 100.

FIGURE 2. Electron micrograph showing the surface basement membrane (arrows), the subpial glial lamellae (line) and the superficial aspect of layer I. Note the numerous small myelinated axons (M) immediately beneath the glia. × 9000.

FIGURE 3. The attenuated cells of the pia mater (P) lying on the surface basement membrane (BM) beneath which are three astroglial processes (G) one of which contains filaments (F). The large arrows indicate the extracellular clefts only one of which (small arrows) is closed by a tight junction. × 52000.

All the electron micrographs are of material stained with lead citrate or with lead citrate and uranyl acetate.

(*Facing p.* 16)

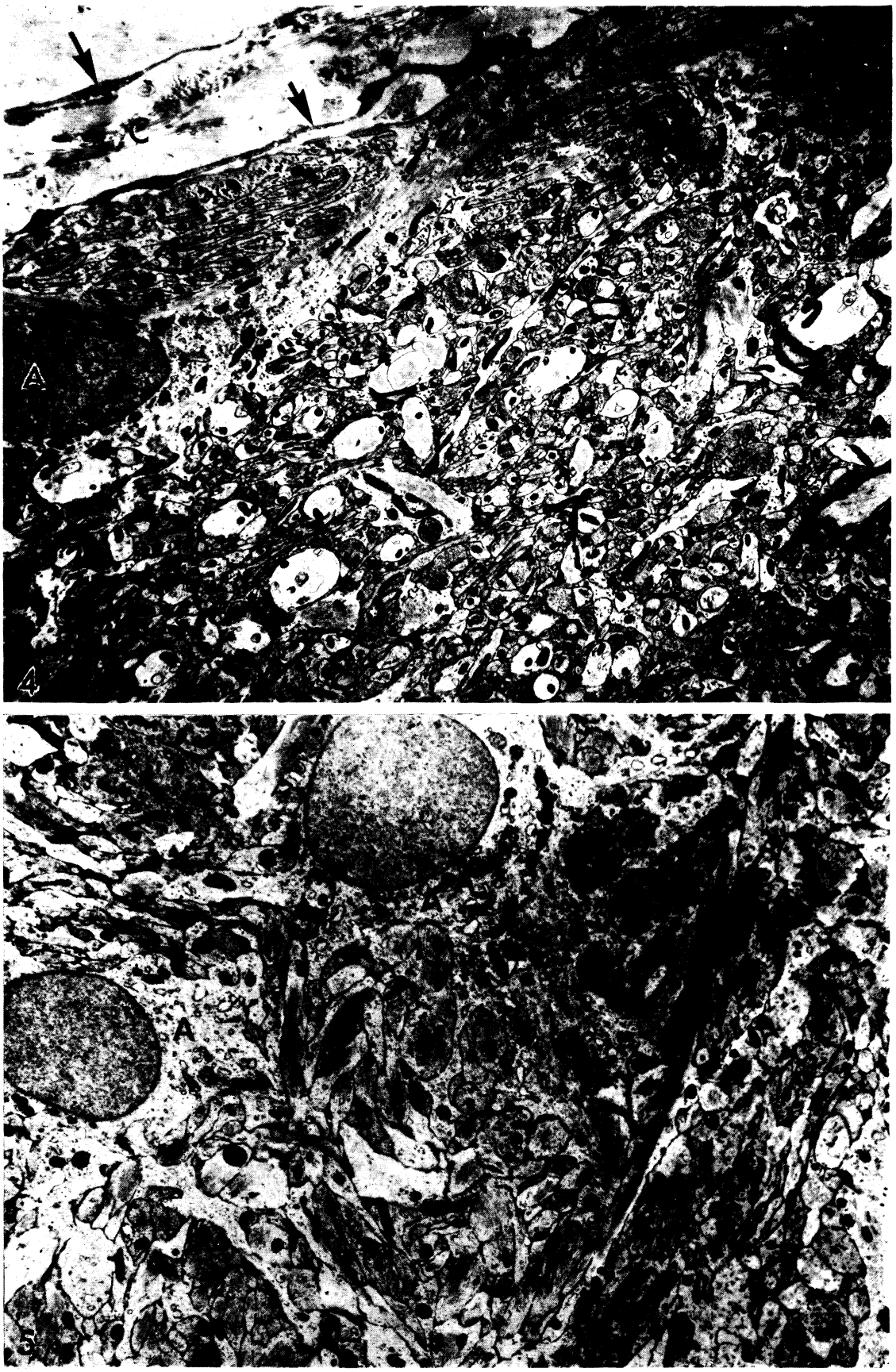

FIGURE 4. The superficial aspect of layer I showing the subpial astrocyte (A) giving rise to processes many of which contain filaments (F) and which spread out beneath the surface. Note the thin attenuated cells of the pia-arachnoid (arrows) separated by the sub-arachnoid space containing collagen bundles (C). × 5000.

FIGURE 5. The subpial zone as seen in a section cut tangential to the surface. The somata of two astrocytes (A) are seen and the remainder is made up of interlacing astroglial processes. × 5000.

FIGURE 6. The superficial aspect of layer I in a section cut perpendicular to the surface. Apart from a small aggregation of myelinated fibres, the layer consists of small dendrites (D), dendritic spines (S) receiving small dense axon terminals and small unmyelinated axons some of which (arrow) are seen to be the parent axons of the terminals. A, astrocyte. × 17000.

FIGURE 7. The superficial aspect of layer I showing a dendrite (D) giving rise to two small branches, one of which ends as a typical spine containing spine apparatus (SA), and the other is shown by arrow head. This and the other spines present in the micrograph (S) receive small axon terminals. The terminal segment of the parent axon of one of these terminals is shown (arrows), while throughout the neuropil there are numerous other similar small unmyelinated axons and a few astroglial processes (A) containing glycogen granules. × 31 000.

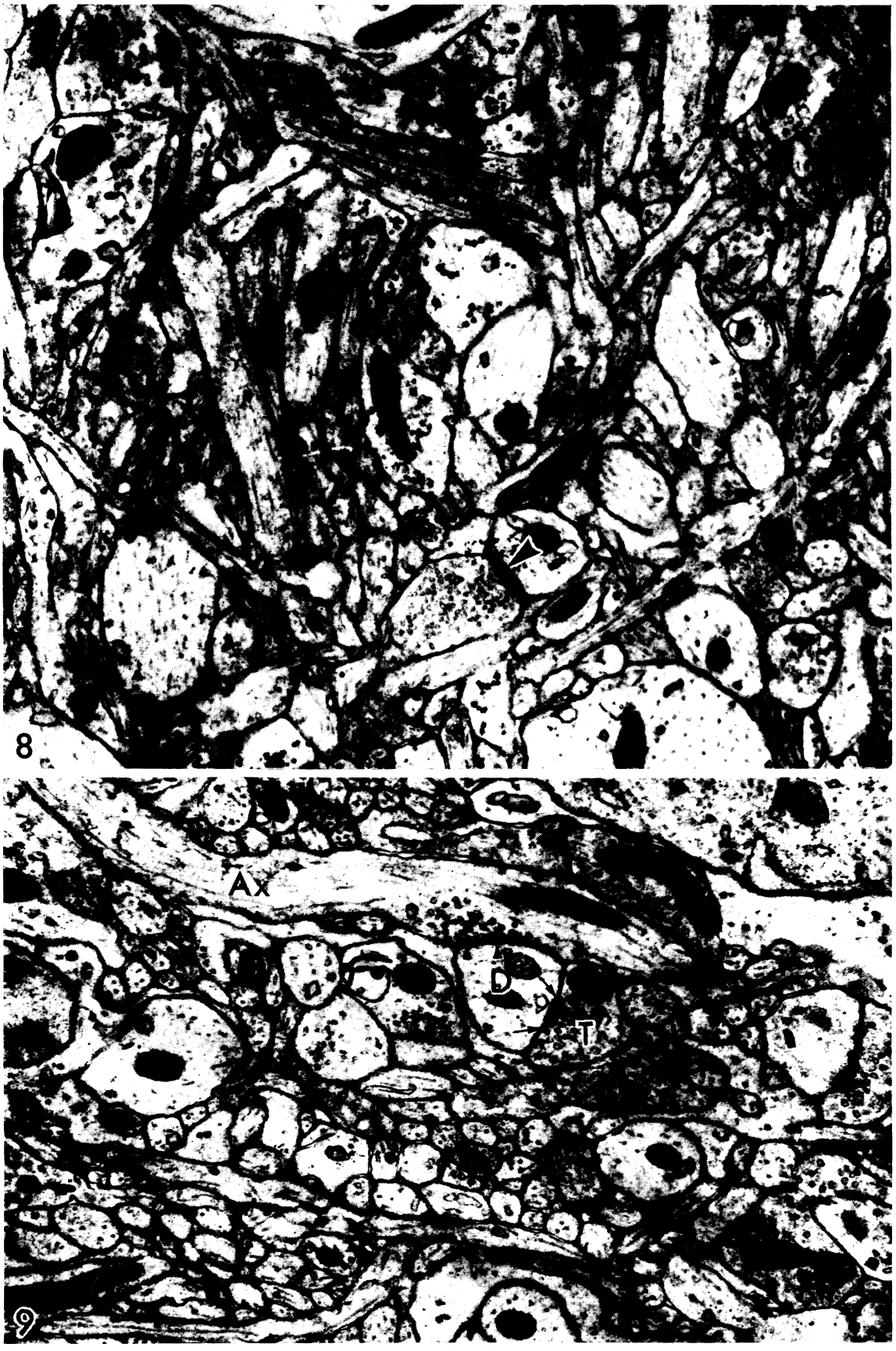

FIGURE 8. The small unmyelinated axonal plexus present at the junction of the superficial and deep aspects of layer I. Few axon terminals are present (arrow head). Tangential section; × 26 000.

FIGURE 9. A part of layer II showing the fine unmyelinated fibre plexus with interspersed dendrites and axon terminals. Note the unmyelinated axon (Ax) ending as an *en passant* terminal upon the dendrite (D). The contact (arrow heads) is a symmetrical one in contrast to the asymmetrical contact (arrows) made by the other terminal (T) ending upon the same dendrite. × 29 000.

FIGURE 10. The deeper aspect of layer I showing large dendrites some of which are seen to be the branching apical dendrites (AD) of cells in deeper layers. Also present are many dendritic spines (S) which receive small axon terminals and which may be seen to arise from the apical dendritic branches (arrow head). An occasional small myelinated axon (arrow) is present. The remainder of the neuropil consists largely of very small unmyelinated axons. × 12000.

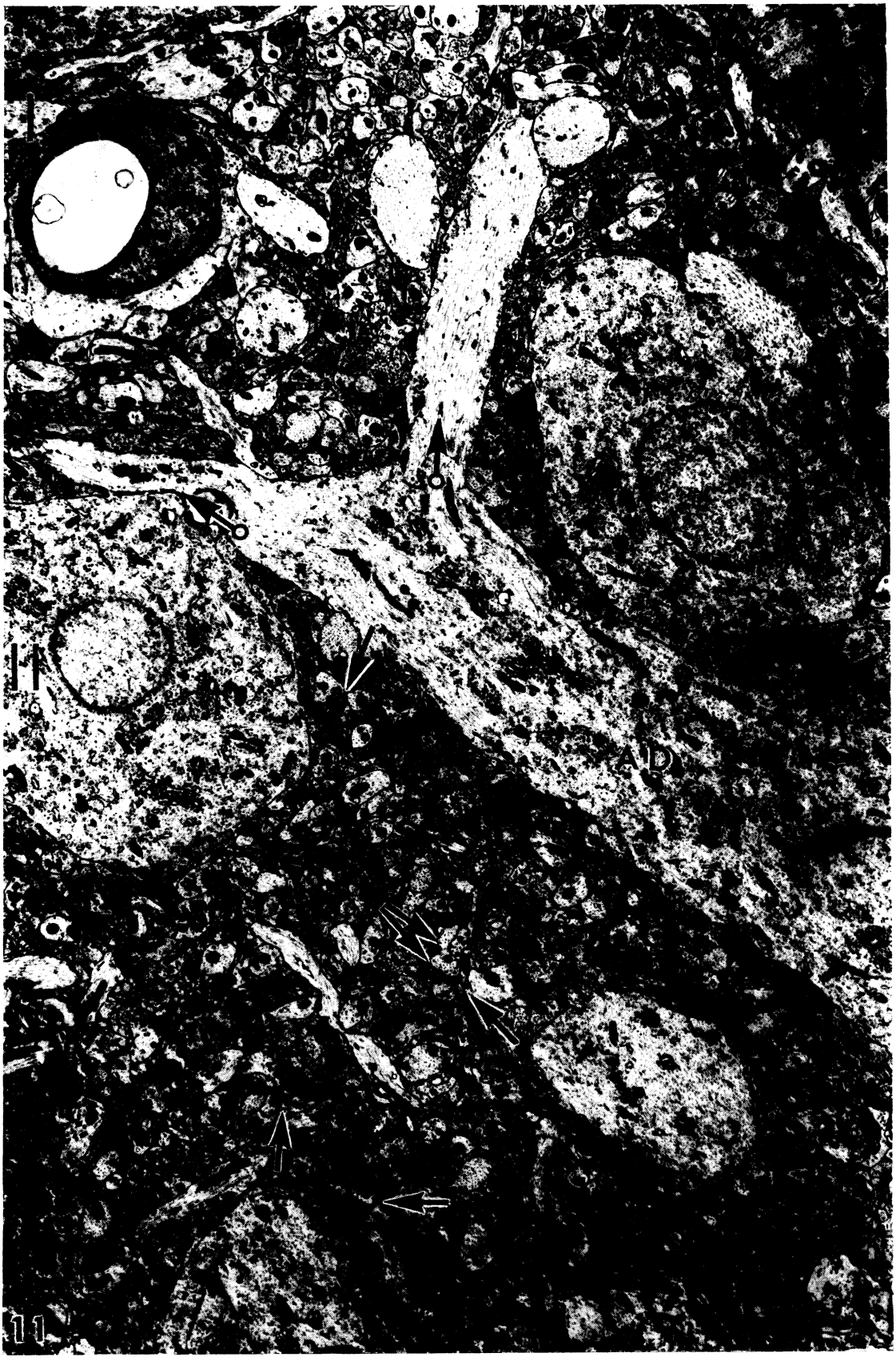

FIGURE 11. Layers I (above) and II (below) showing the bifurcating (ringed arrows) apical dendrite of a pyramidal neuron passing between two other cells to reach layer I. Note the densely packed neuropil of layer II with many small axon terminals, dendrites and dendritic spines; many of the spines can be seen to be derived from the small dendrites of the layer (arrows). × 5000.

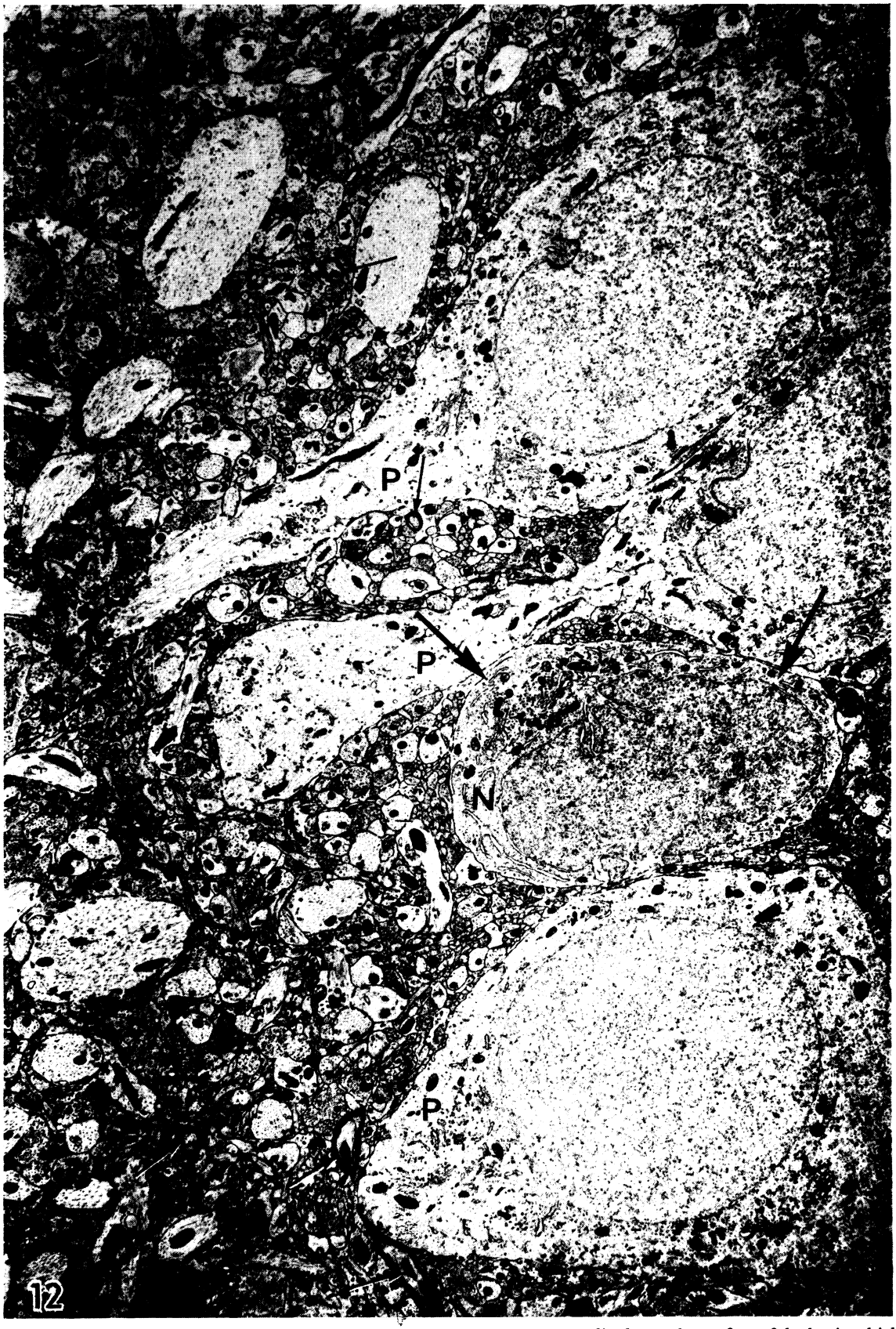

FIGURE 12. Layer II and the adjacent part of layer I in a section cut perpendicular to the surface of the brain which is to the left. Note that the cells of layer II are largely pyramidal (P) in shape with the exception of the one (N) indicated by the arrows which is smaller, rounder and has a denser nucleus and greater complement of cytoplasmic inclusions, notably elongated cisternae of rough-surfaced endoplasmic reticulum. A few transversely orientated myelinated axons are also present (small arrows). × 6000.

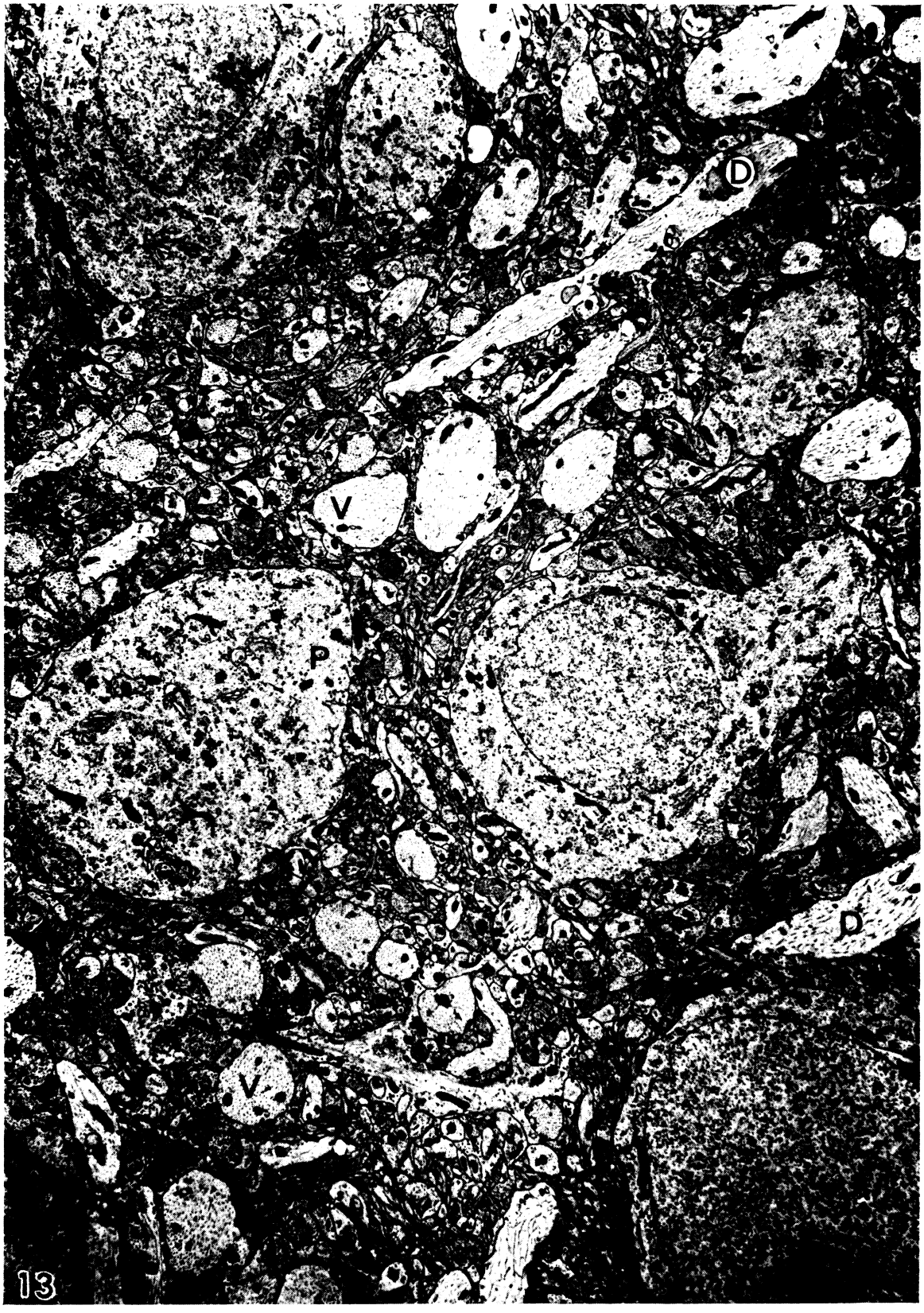

FIGURE 13. Layer II as seen in a section cut parallel to the surface. The most obvious features are the neurons (P) and vertically orientated dendrites. Some smaller dendrites, however, (D) are disposed horizontally and there are large numbers of dendritic spines and axon terminals in the neuropil. × 6000.

FIGURE 14. Layer II in a section cut parallel to the brain surface. Note the large pyramidal cell with only a few axon terminals on its soma (arrow heads), the large apical dendrites (D) which have few or no axon terminals upon them, and the smaller dendrites (arrow) which may be surrounded by terminals. × 9000.

FIGURE 15. A small, beaded dendrite (D) from layer II receiving many axon terminals (arrow heads) which end both symmetrically and asymmetrically. × 16000.

plates 13 and 14). The spines usually receive only one axon terminal, but individual small dendritic profiles may receive several, some being surrounded by terminals. Lying among the dendrites, spines and axon terminals, are large numbers of very thin unmyelinated axons which often contain a few synaptic vesicles and at times may be seen to expand as the small dense terminals. Very occasionally present are some larger axon terminals containing relatively fewer synaptic vesicles and a much less dense background axoplasm than the other terminals. These terminals also have asymmetrical membrane thickenings on dendritic spines. Terminals ending with symmetrical membrane thickenings (Type 2 of Gray 1959) are not seen in this part of layer I.

In the deeper three-quarters or so of layer I the same elements are present, but interspersed among them are considerable numbers of dendrites of medium to large diameter. In sections cut perpendicular to the surface these are commonly arranged in rows lying just above the cells of layer II. Almost invariably they are cut obliquely suggesting some degree of divergence from the perpendicular, and in favourable sections it may be seen that many are the diverging branches of dendrites passing up through layer II from below (figures 10 to 12, plates 16 to 18). In sections cut parallel to the surface these dendrites are cut in cross-section giving this part of layer I a very characteristic appearance. Many possess spines which receive the small dense axon terminals characteristic of the layer, but the main shafts do so but rarely. Throughout the neuropil, large numbers of small unmyelinated axons persist and at the junction of the superficial and deep parts of layer I (figure 8, plate 15) may appear, especially in tangential sections, as a dense meshwork with few interspersed elements. The larger, less dense terminals, which end asymmetrically on dendritic spines are a little more common than in superficial parts of layer I, and some may end on dendritic shafts as well as on spines. In a single section covering this deeper aspect of layer I, 111 axon terminals of all types ended axo-spinously and 50 axo-dendritically.

Neurons are rarely present in this part of the cortex, but a small rounded perikaryon is occasionally seen. These perikarya are rich in organelles, have many small dendrites and may receive axon terminals ending both symmetrically and asymmetrically. A few small myelinated axons are also present and are orientated both transversely and vertically.

The fine structure of layer II

This layer is clearly distinguishable mainly because of the close packing of many of the neurons. However, in addition to the neurons, the layer also contains large numbers of apical dendrites and smaller numbers of myelinated axons passing through it towards layer I.

The neuronal perikarya are the most obvious component of this lamina and appear in two or three irregular and loosely arranged rows which are at intervals incompletely merged (figures 11 to 14, plates 17 to 20). Within each row three or more perikarya may lie in intimate relation to one another, their plasma membranes being separated only by the usual extracellular space, but elsewhere in a row the perikarya may be separated by other profiles. Two main types of neuron are present in layer II (figure 12, plate 18). In the majority, by far, is a cell which has the appearance of a typical small pyramid having a roughly triangular soma with a large dendrite forming the apex and passing up into layer I and one or more smaller basal dendrites entering layer III. A few axon terminals may end on the cell soma and on the proximal parts of the apical and basal dendrites, but these sites are, in general, relatively free of synapses. A second type of neuron, though much less common than the pyramidal neuron, is seen quite regularly in layer II.

It may be about the same size or smaller than the pyramidal cell, but it is oval rather than triangular in shape, and does not have an apical dendrite. Dendrites, which may arise at any point on its surface, are small, occasionally slightly beaded, and are commonly covered in axon terminals, even quite close to the perikaryon. Apart from the differences in their dendrites, these neurons also show the differences in their perikarya which have been interpreted as being typical of non-pyramidal neurons (Colonnier 1968; Jones & Powell 1970*b*). So characteristic is the appearance of these cells that they stand out from the pyramidal neurons even at relatively low magnifications. A distinctive feature of the perikaryon is that, unlike that of the pyramidal cell, it may receive very large numbers of axon terminals.

Glial cells are relatively uncommon in layer II, and of particular note is the relative absence of oligodendrocytes. One or more of these cells are commonly seen as satellites of neuronal perikarya in deeper layers, but are rare in this position or in any other part of layer II. When glial cells are seen they are usually astrocytes.

In between the neuronal perikarya, the neuropil of layer II is dominated by dendrites of large and medium size, most ascending through it to reach layer I. These dendrites are especially obvious in sections cut parallel to the pial surface. Sometimes, in perpendicular sections, the dendrites are seen to arise from the apices of pyramidal cells in the superficial parts of layer III, while in others they can be traced down into even deeper layers of the cortex. These vertical dendrites have spines which receive axon terminals, but they themselves receive only an occasional terminal. In among them, on the other hand, are large numbers of much smaller dendrites which have less regular outlines and are transversely or obliquely disposed. They appear to lack dendritic spines but may be completely surrounded by axon terminals which end upon them (figure 15, plate 20). Considerable numbers of dendritic spines, isolated in the plane of section and receiving axon terminals, lie scattered throughout the neuropil. In cases in which spines are seen attached to their parent dendrite, the dendrite can be large, medium or small in size but usually it has a regular outline.

Most of the axon terminals in layer II are of a small, dark variety similar to those forming the majority in layer I. These terminals end on the small dendrites or upon dendritic spines in asymmetrical synaptic complexes. Some also end on perikarya of both types or directly upon the larger dendritic shafts, but most of the terminals in these positions, while relatively small, are less dense, have fewer and smaller vesicles and terminate in symmetrical complexes. A few, on the perikarya of non-pyramidal cells only, may end asymmetrically. The origins of the two types of axon terminal are difficult to ascertain. A few thin myelinated axons traverse this layer (figure 12, plate 18) and considerable numbers of small unmyelinated profiles similar to the unmyelinated axons of layer I are also present, but they are relatively less common and never appear as a dense network as is seen at the junction of the two parts of layer I. In a single section of layer II, out of a total of 160 terminals which ended in definite synaptic contacts on positively identifiable postsynaptic profiles, 117 ended axo-spinously, 35 axo-dendritically and 8 axo-somatically. Of the 35 ending axo-dendritically, 30 terminated on dendrites of small diameter.

Discussion

This study has shown that the superficial two laminae of the cerebral cortex show obvious differences at the electron microscopical level and that layer I can be further subdivided into superficial and deep parts. That layers I and II differ from one another in being relatively

acellular and cellular respectively is apparent from light microscopy, but there are more subtle differences, particularly in their synaptic organization, which become visible only with the electron microscope.

The electron microscopic appearance of the meninges and cerebral surface have been described by several workers (Ramsay 1965; Pease & Schultz 1958; Nelson, Blinzinger & Hager 1961), and as the present results confirm these in all respects only a few points require discussion. As the pia mater does not appear to form a continuous layer, the cerebral substance is separated from the cerebrospinal fluid by only the basement membrane on the surface and the stacked astroglial lamellae. There is little evidence for the presence or absence of a definite 'C.S.F.-brain barrier' at this point, and it is not known whether or not the C.S.F. and extracellular fluid of the brain are in equilibrium (Kuffler & Nicholls 1966). Recent work (Reese & Karnovsky 1967; Bodenheimer & Brightman 1968) is tending to show that astrocytic perivascular foot processes are not involved in the formation of the 'blood-brain barrier', and there is evidence that ferritin injected into the cerebral ventricles can bypass tight junctions between ependymal cells (Brightman 1965). Astrocytes and their widely ramifying processes are present in large numbers throughout layer I, but their numbers progressively diminish in deeper layers; conversely, oligodendrocytes are virtually absent in layer I and increase as the white matter is approached. In the absence of information regarding the nature of the relationship between the C.S.F. and cerebral extracellular fluid (Kuffler & Nicholls 1966), it is not certain whether this concentration of astrocytes beneath the surface of the brain has any more than a purely mechanical significance.

There are good grounds for dividing layer I into two parts on both light and electron microscopic criteria. The aggregation of small myelinated axons which lie immediately beneath the glia and which radiate out in all directions have been shown to degenerate up to a distance of a few millimetres from a lesion in the cortex, and it has been suggested (Jones & Powell 1968) that they could mediate the initial surface negative response when the cortex is stimulated by surface electrodes (Adrian 1936; Burns 1951). These fibres are intrinsic to the cortex because they do not degenerate following lesions in the thalamus or in the cortex of the opposite hemisphere (Jones & Powell 1970*a*), but their origin and termination are unknown. The remainder of the superficial quarter of layer I contains many small dendritic profiles, the majority of which, from a comparison with Golgi studies, must be derived from dendrites ascending from pyramidal cells in deeper layers. In a perpendicular section, irrespective of whether it is transverse or longitudinal with respect to a gyrus, most of these small dendrites are cut in cross section, suggesting that the terminal tips of the apical dendritic tree do not bend and run beneath the surface for any great distance. Presumably, therefore, the diameter of the apical dendritic arborization (see Globus & Schiebel 1967) is determined by the extent of primary branching of the apical dendrite. These small terminal branches of the apical dendrites tend to possess the largest spines in the cortex.

Apart from astroglial processes, the remainder of this superficial part of layer I is filled by small unmyelinated axons which form a very dense plexus especially at the junction of the two parts of layer I. According to Ramón y Cajal (1911) and Lorente de Nó (1949) many axons in this region should be derived from the 'horizontal cells' of layer I, although the number of these axons relative to the extremely small number of neurons in layer I seems excessive and suggests that some at least are derived from other sources. The deeper three quarters of layer I contains the same small dense terminals, although the unmyelinated plexus is less distinct. In

both the superficial and deep parts these terminals end in asymmetrical synaptic contacts on dendrites and dendritic spines, and if current speculation is correct (see Walberg 1968) such synapses may be excitatory. Experimental studies (Jones 1968; Jones & Powell 1970*a*) have shown that a small number of commissural and association fibres terminate in this manner in layer I, but the numbers are too few to account for all the small dense terminals. There are good grounds for considering that the small number of thalamo-cortical axons which end in layer I end as the larger, less dense terminals which occasionally appear in both parts of layer I, but more particularly in its deeper part. A large proportion of the small dense terminals are, therefore, probably derived from axons intrinsic to the cortex.

Unlike layer II and many other layers of the cortex, the superficial part of layer I lacks the long, unmyelinated intrinsic axons which terminate as *en passant* terminals in symmetrical contacts and contain flattened or pleomorphic vesicles. Such synapses have been considered to be inhibitory in nature, and if this is so, the superficial part of layer I would be unique in apparently not being subjected to local inhibition. To some extent this may be true of the whole of layer I, for the long unmyelinated axons with flattened vesicles are not present in its deeper part either; the only symmetrical synapses with flattened vesicles are those on the somata of the rare neurons which occur there and on the dendrites of the small proportion of non-pyramidal cells whose somata lie in layer II. Two cortical laminae only receive the terminals of *all* extrinsic afferent fibres—laminae I and IV (Jones 1968; Jones & Powell 1970*a*). In contrast to layer I, however, layer IV contains large numbers of short axon stellate cells and many more of the unmyelinated axons containing flattened vesicles and symmetrical synaptic contacts. In view of this difference between layers I and IV, it is of interest that in layer II there are two types of neuron, the typical pyramidal cell and a less common smaller neuron which, unlike the pyramidal cell, receives large numbers of terminals upon it and these synapses may be asymmetrical as well as symmetrical. The non-pyramidal cells in layer II are morphologically similar to the short axon stellate cells of layer IV and are also like them in receiving the terminals of some of the thalamo-cortical fibres upon their dendrites. It is possible, therefore, that these two groups of non-pyramidal cells which lie close to the sites of termination of thalamo-cortical fibres serve a similar function in the integration of sensory information within the sensory cortex.

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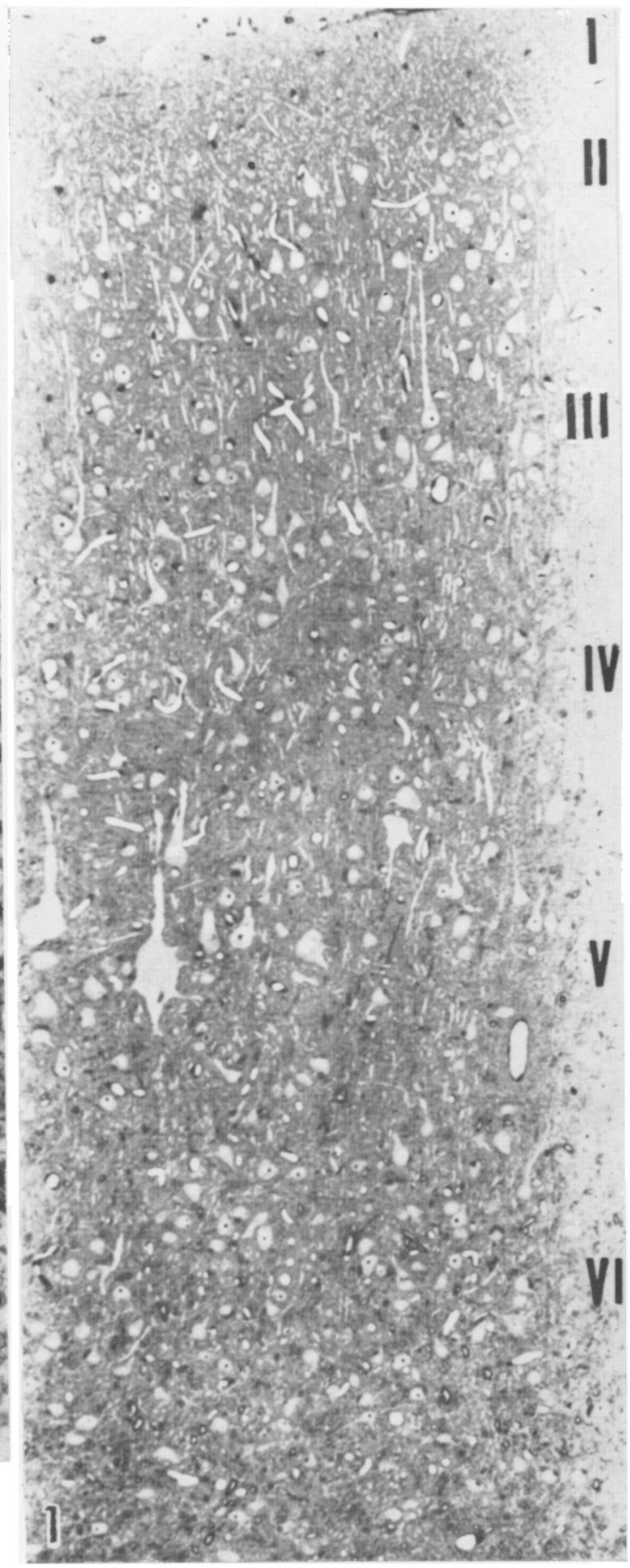
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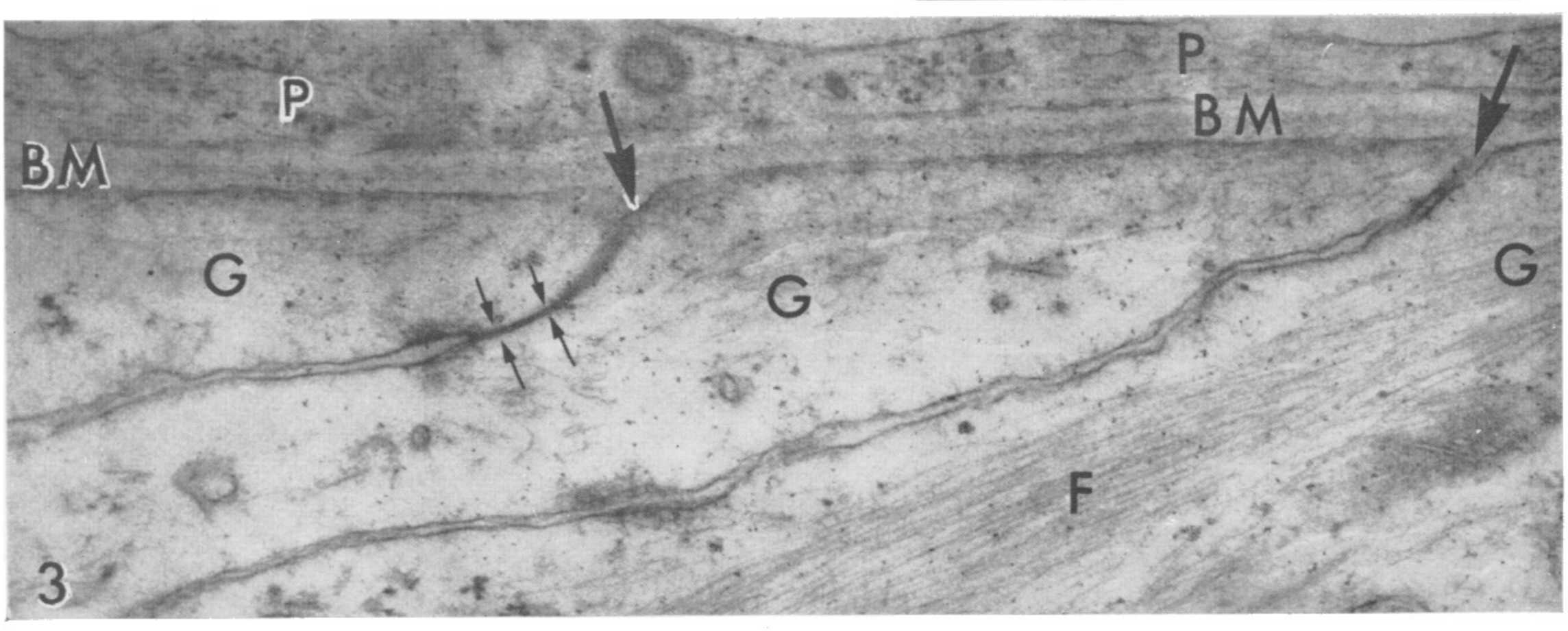
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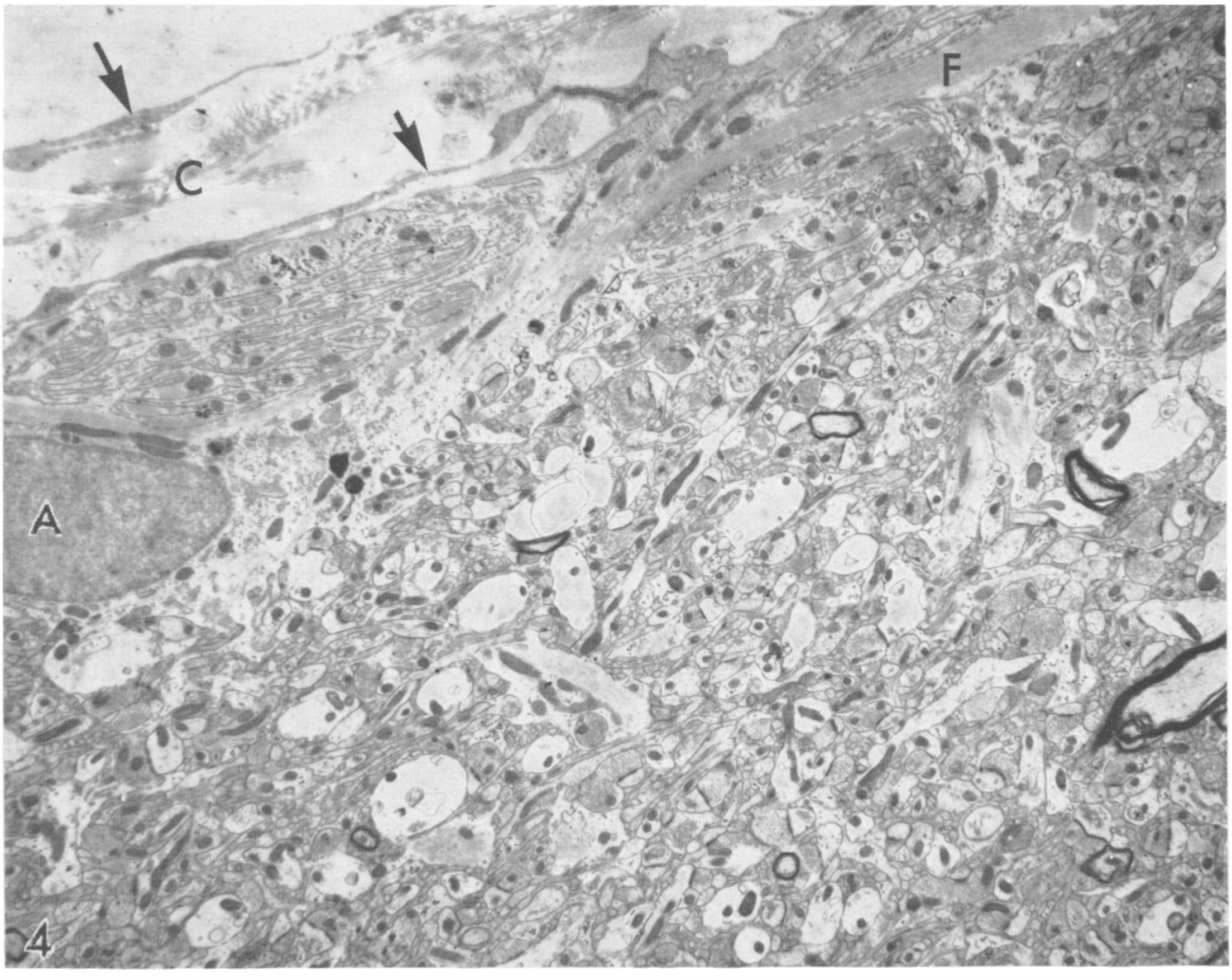


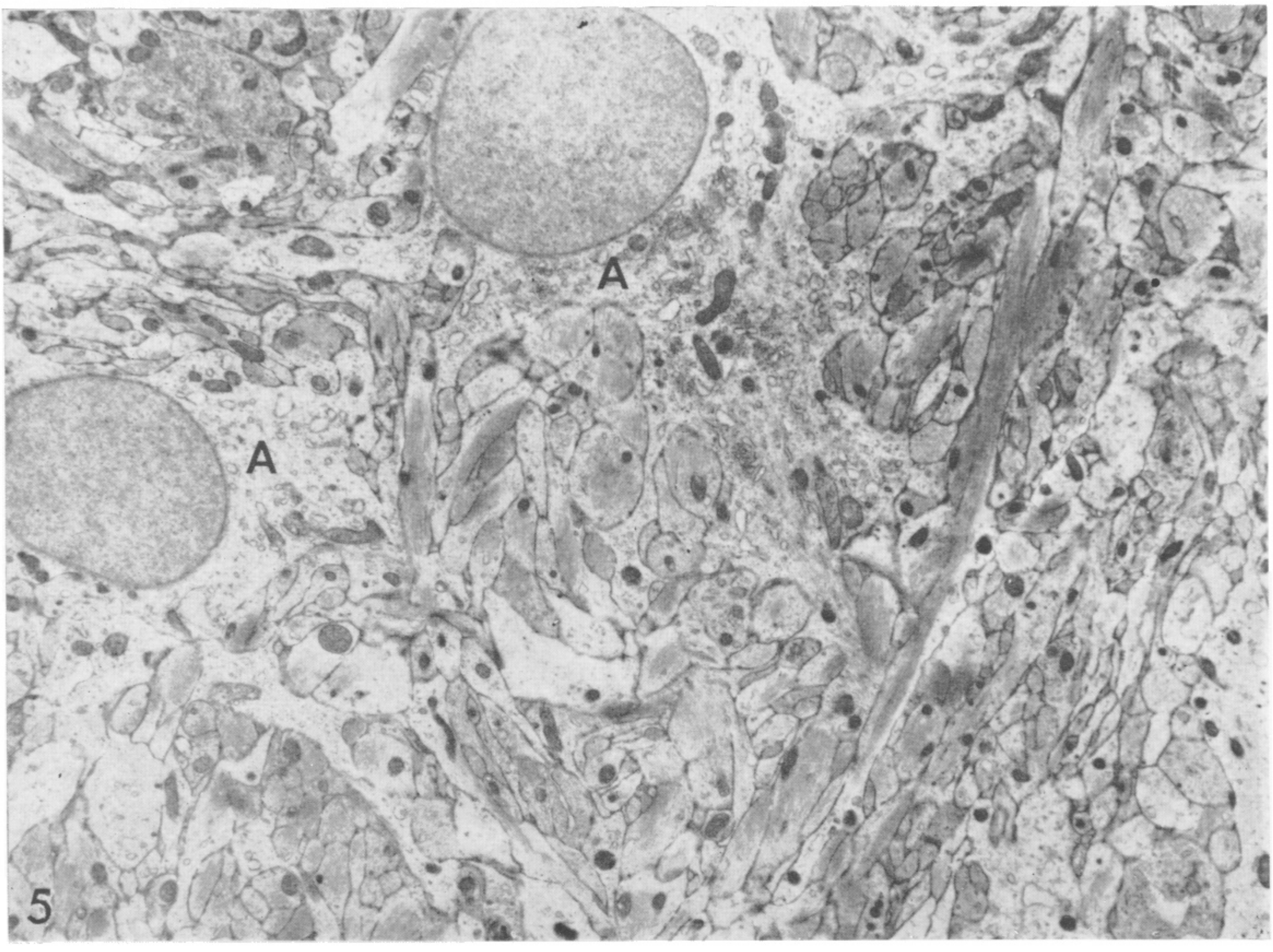


FIGURE 4. The superficial aspect of layer I showing the subpial astrocyte (A) giving rise to processes many of which contain filaments (F) and which spread out beneath the surface. Note the thin attenuated cells of the pia-arachnoid (arrows) separated by the sub-arachnoid space containing collagen bundles (C). × 5000.

FIGURE 5. The subpial zone as seen in a section cut tangential to the surface. The somata of two astrocytes (A) are seen and the remainder is made up of interlacing astroglial processes. × 5000.

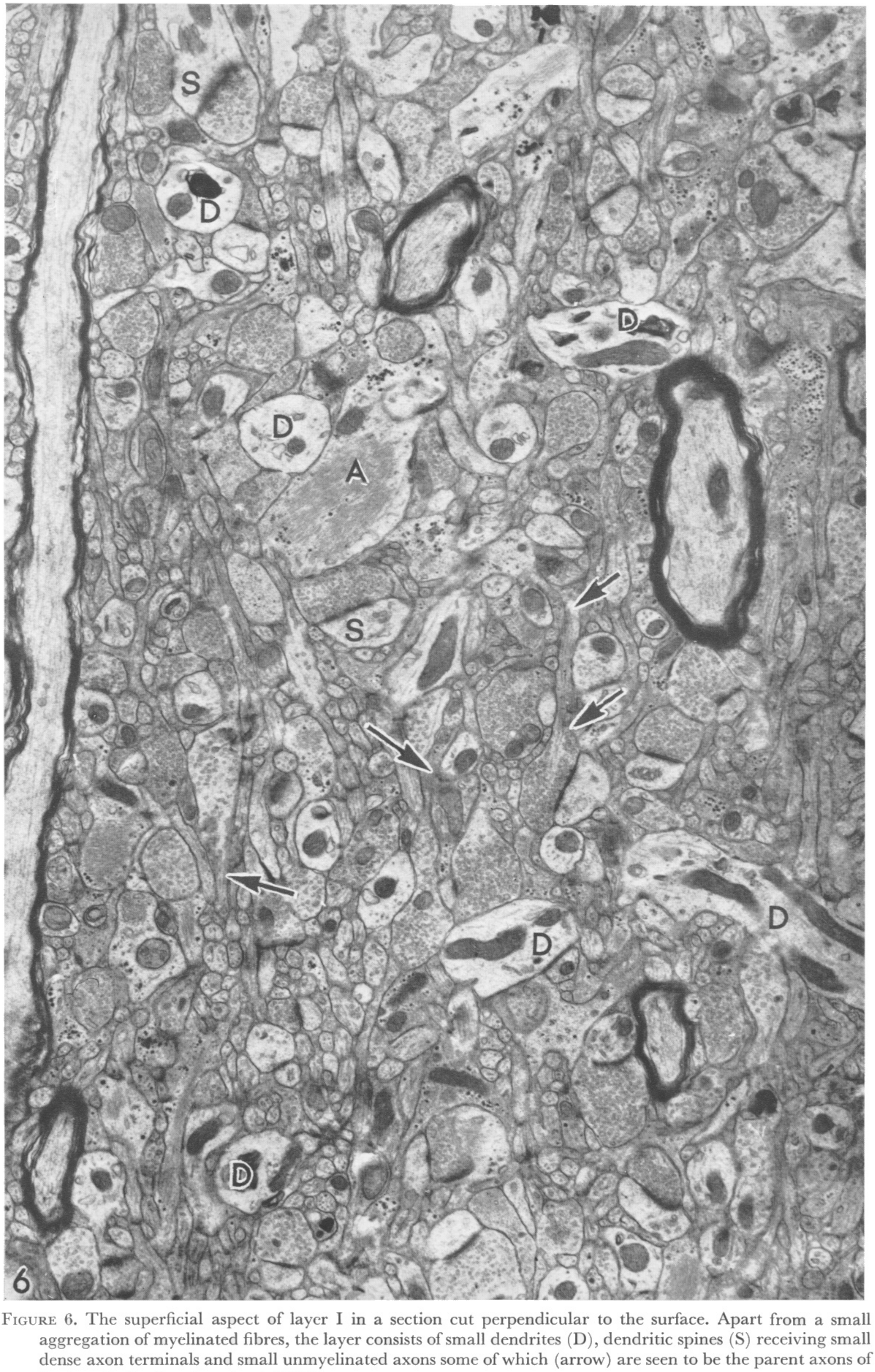


FIGURE 6. The superficial aspect of layer I in a section cut perpendicular to the surface. Apart from a small aggregation of myelinated fibres, the layer consists of small dendrites (D), dendritic spines (S) receiving small dense axon terminals and small unmyelinated axons some of which (arrow) are seen to be the parent axons of the terminals. A, astrocyte. × 17 000.

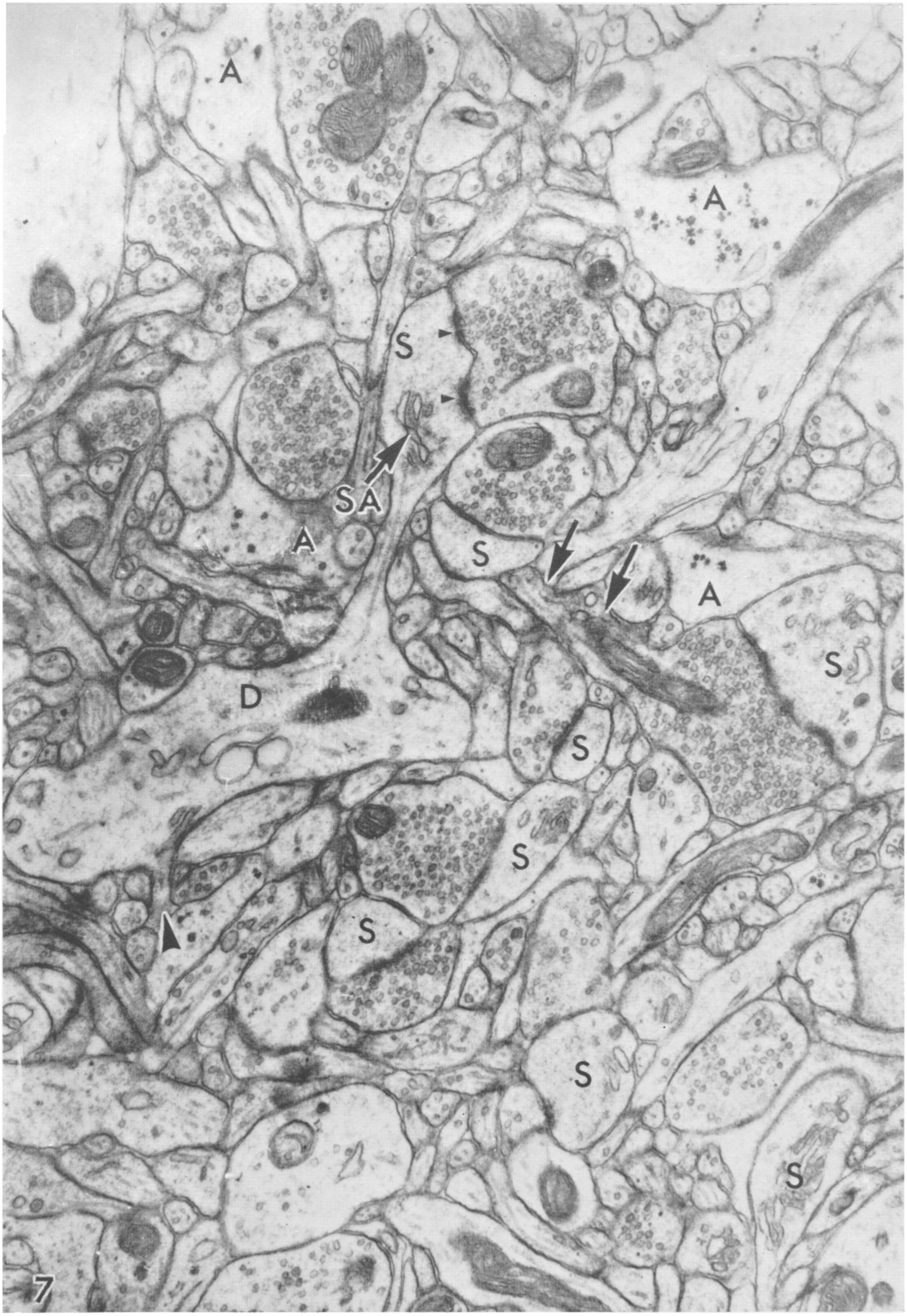
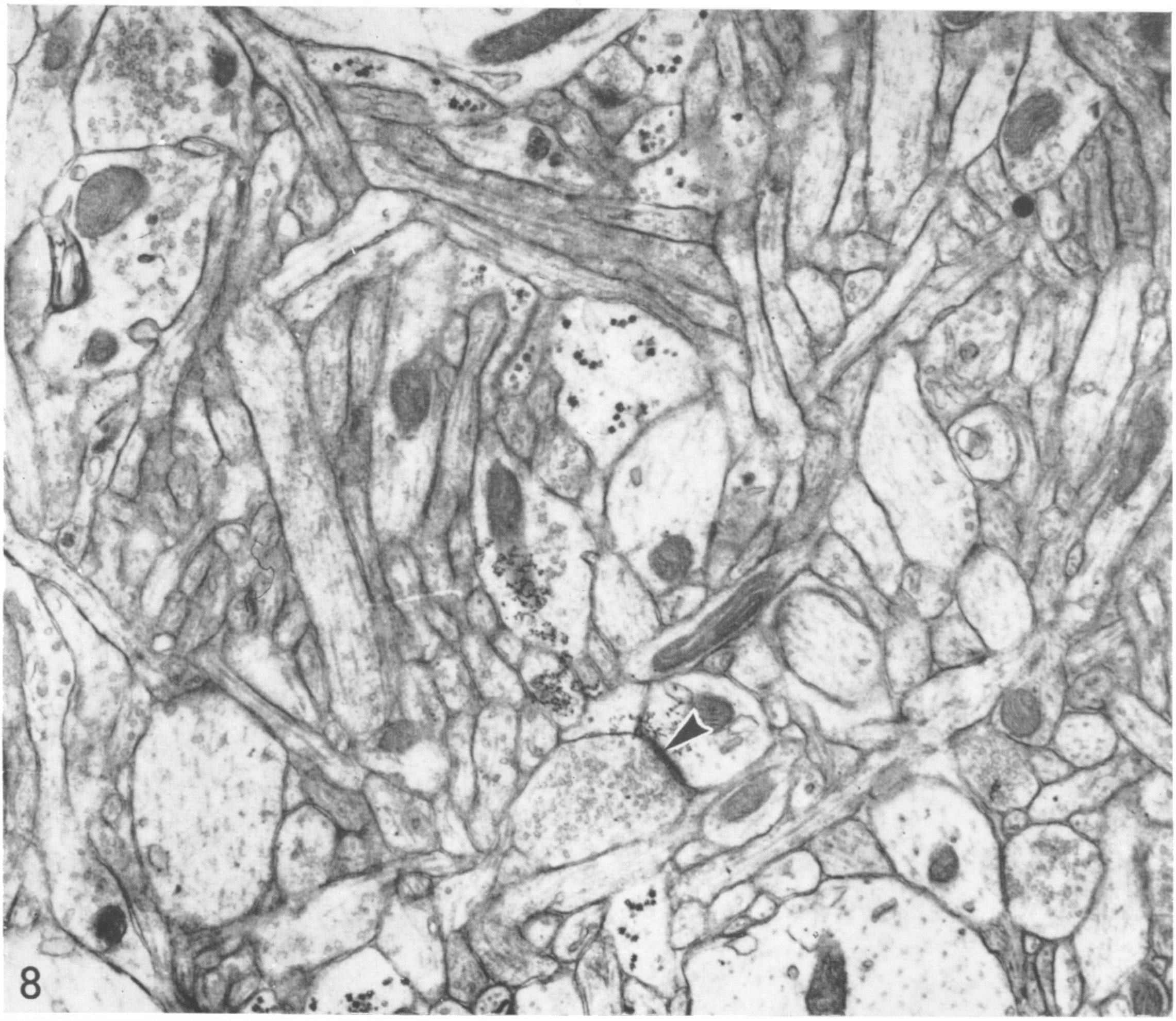


FIGURE 7. The superficial aspect of layer I showing a dendrite (D) giving rise to two small branches, one of which ends as a typical spine containing spine apparatus (SA), and the other is shown by arrow head. This and the other spines present in the micrograph (S) receive small axon terminals. The terminal segment of the parent axon of one of these terminals is shown (arrows), while throughout the neuropil there are numerous other similar small unmyelinated axons and a few astroglial processes (A) containing glycogen granules. × 31 000.



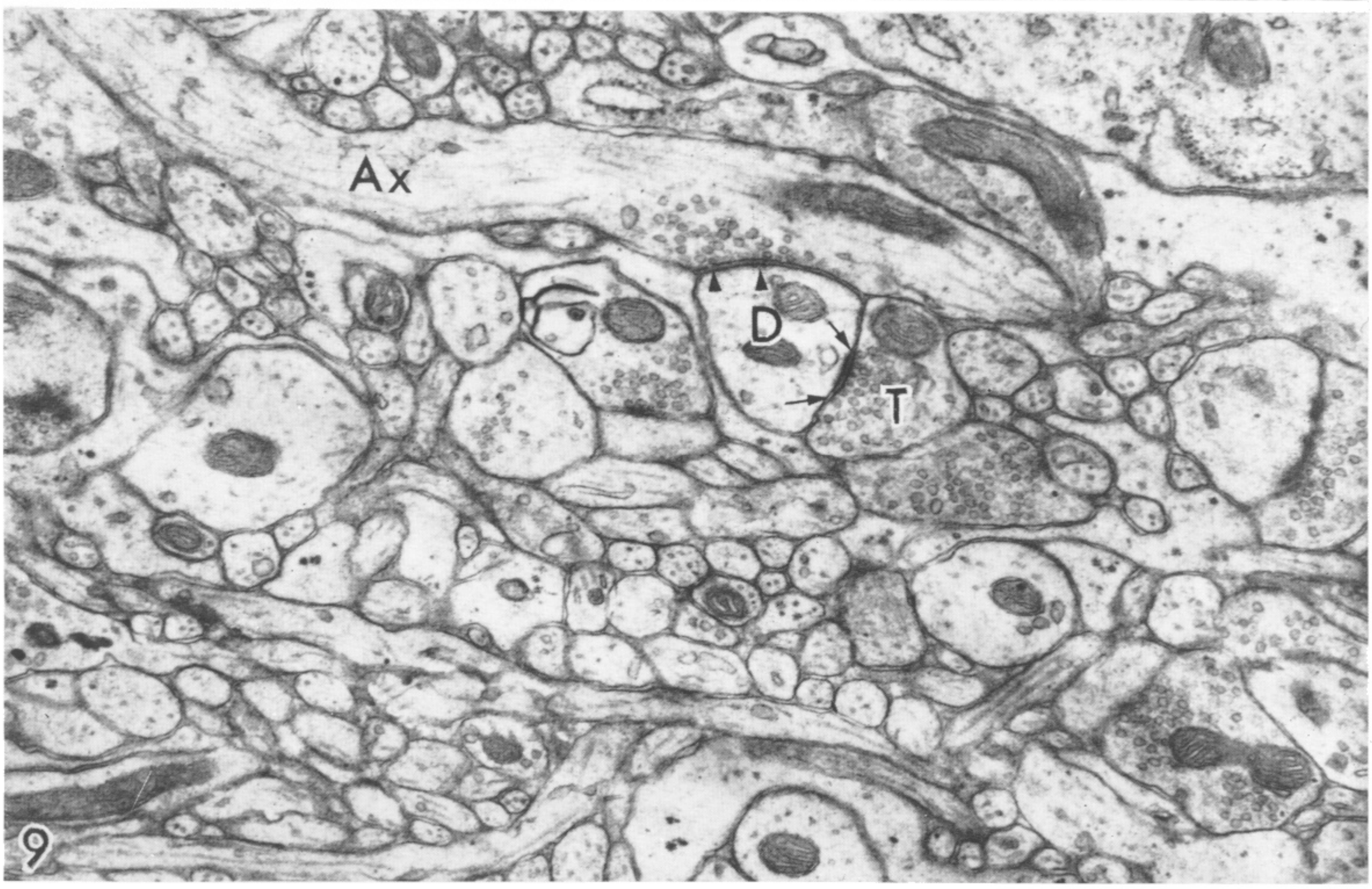


FIGURE 8. The small unmyelinated axonal plexus present at the junction of the superficial and deep aspects of layer I. Few axon terminals are present (arrow head). Tangential section; × 26 000.

FIGURE 9. A part of layer II showing the fine unmyelinated fibre plexus with interspersed dendrites and axon terminals. Note the unmyelinated axon (Ax) ending as an *en passant* terminal upon the dendrite (D). The contact (arrow heads) is a symmetrical one in contrast to the asymmetrical contact (arrows) made by the other terminal (T) ending upon the same dendrite. × 29 000.

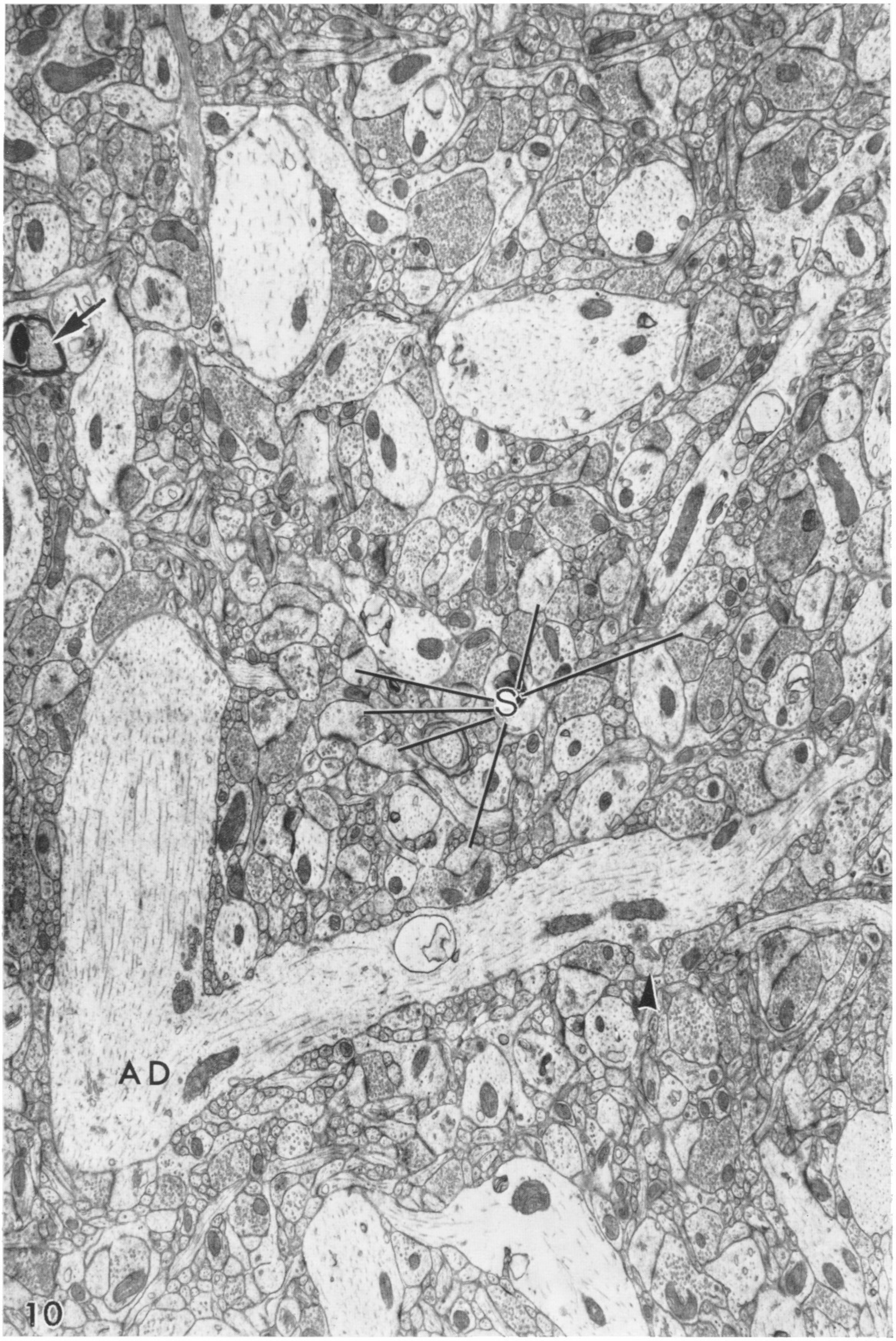


FIGURE 10. The deeper aspect of layer I showing large dendrites some of which are seen to be the branching apical dendrites (AD) of cells in deeper layers. Also present are many dendritic spines (S) which receive small axon terminals and which may be seen to arise from the apical dendritic branches (arrow head). An occasional small myelinated axon (arrow) is present. The remainder of the neuropil consists largely of very small unmyelinated axons. × 12000.

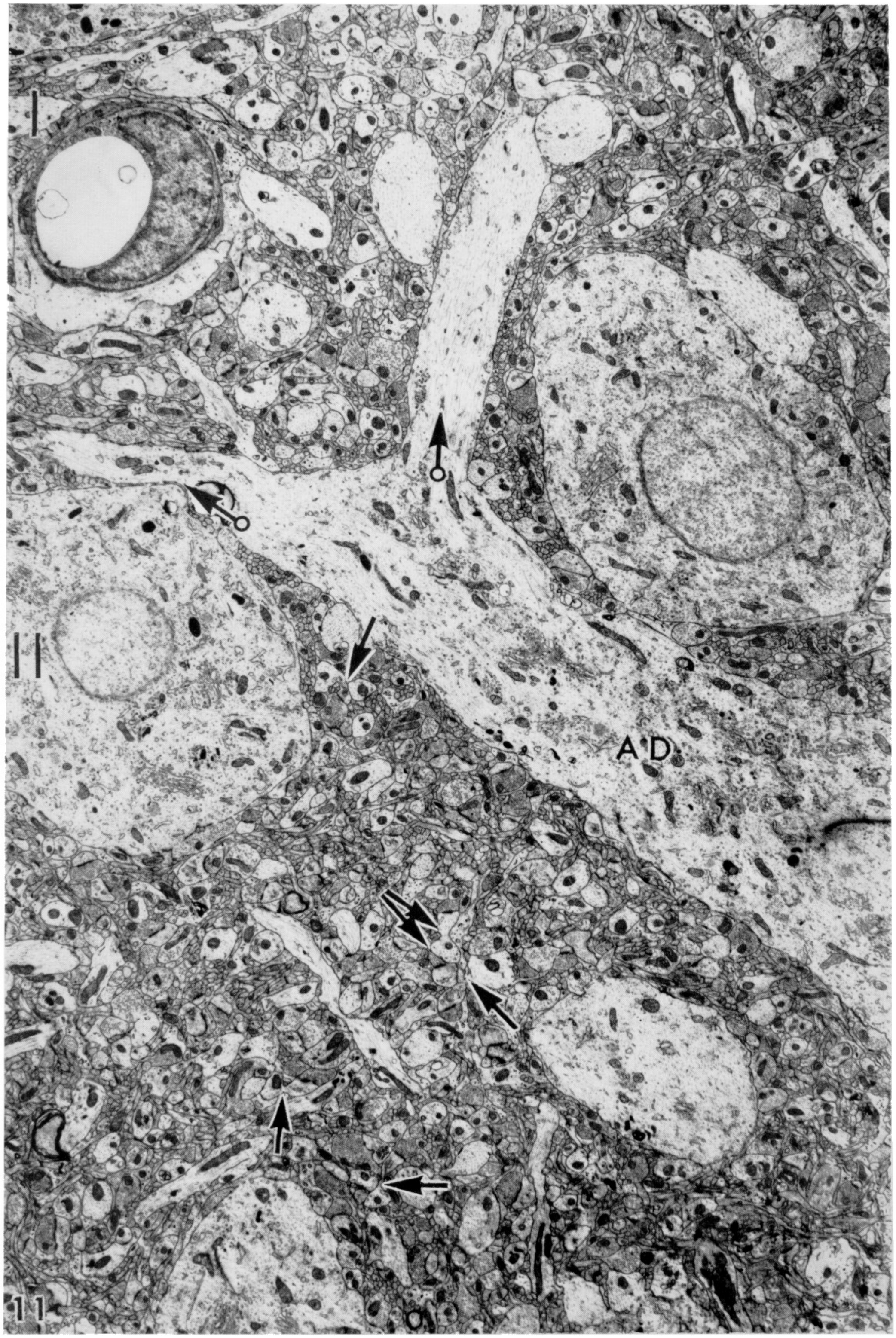


FIGURE 11. Layers I (above) and II (below) showing the bifurcating (ringed arrows) apical dendrite of a pyramidal neuron passing between two other cells to reach layer I. Note the densely packed neuropil of layer II with many small axon terminals, dendrites and dendritic spines; many of the spines can be seen to be derived from the small dendrites of the layer (arrows). $\times 5000$.

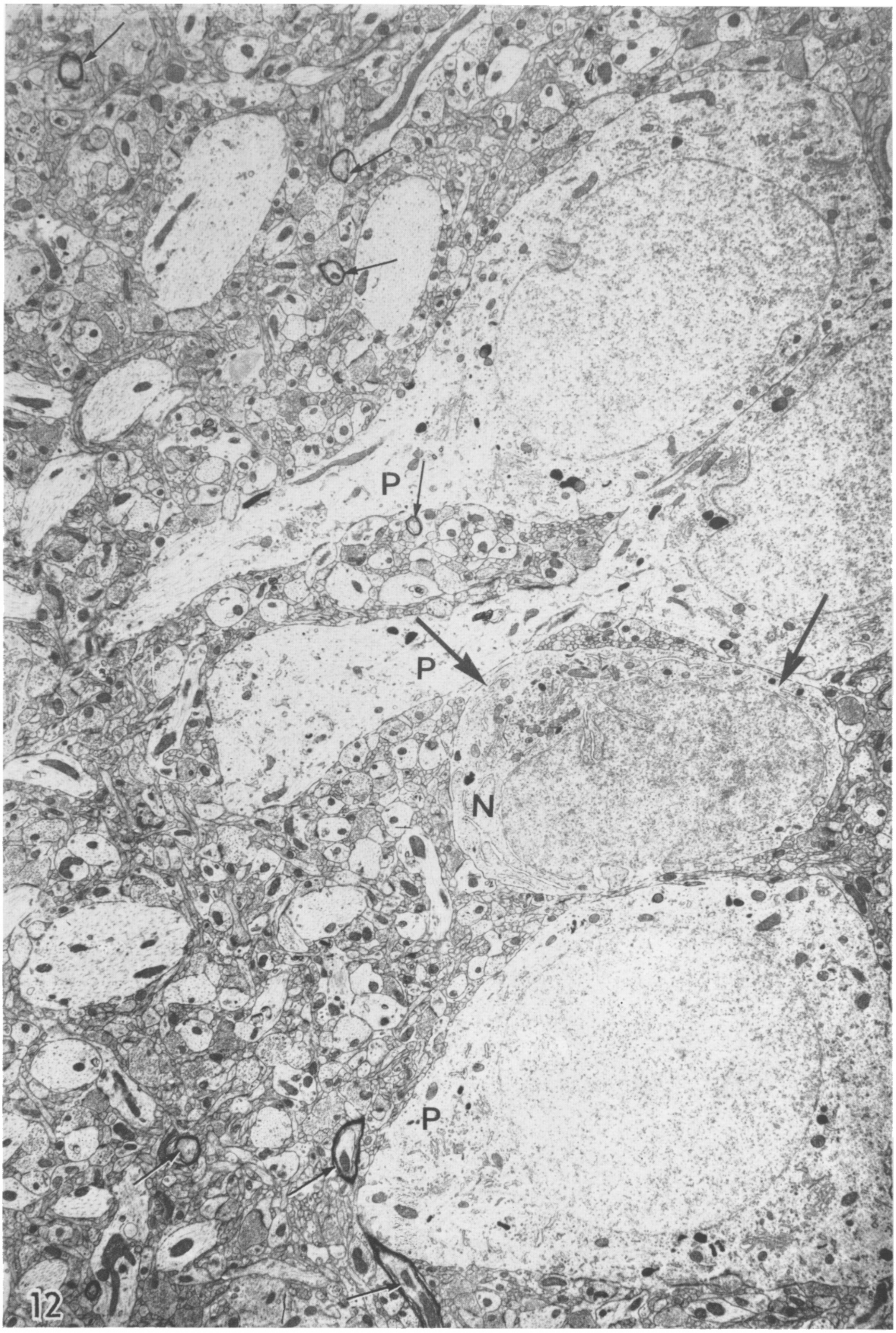


FIGURE 12. Layer II and the adjacent part of layer I in a section cut perpendicular to the surface of the brain which is to the left. Note that the cells of layer II are largely pyramidal (P) in shape with the exception of the one (N) indicated by the arrows which is smaller, rounder and has a denser nucleus and greater complement of cytoplasmic inclusions, notably elongated cisternae of rough-surfaced endoplasmic reticulum. A few transversely orientated myelinated axons are also present (small arrows). × 6000.

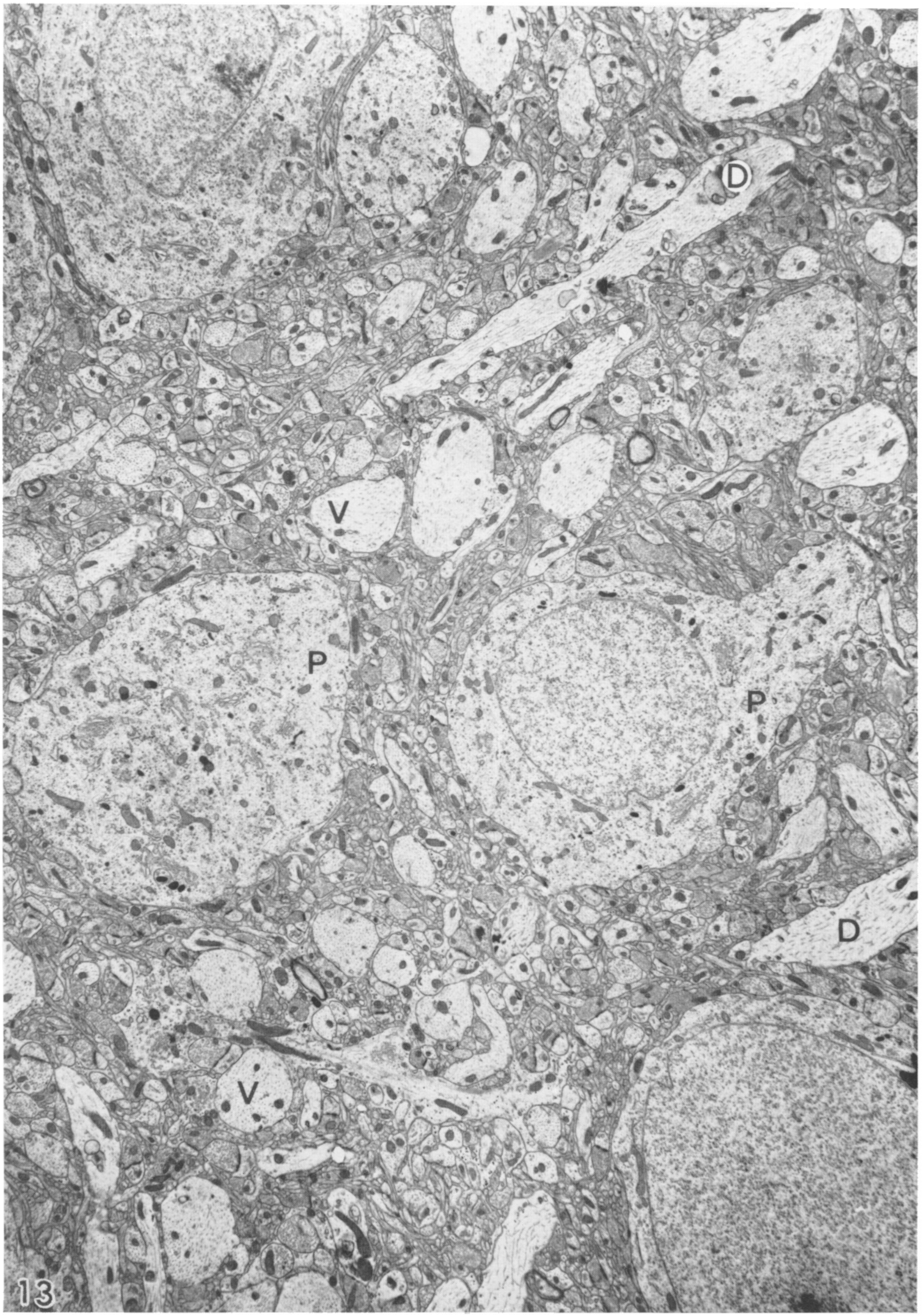


FIGURE 13. Layer II as seen in a section cut parallel to the surface. The most obvious features are the neurons (P) and vertically orientated dendrites. Some smaller dendrites, however, (D) are disposed horizontally and there are large numbers of dendritic spines and axon terminals in the neuropil. × 6000.

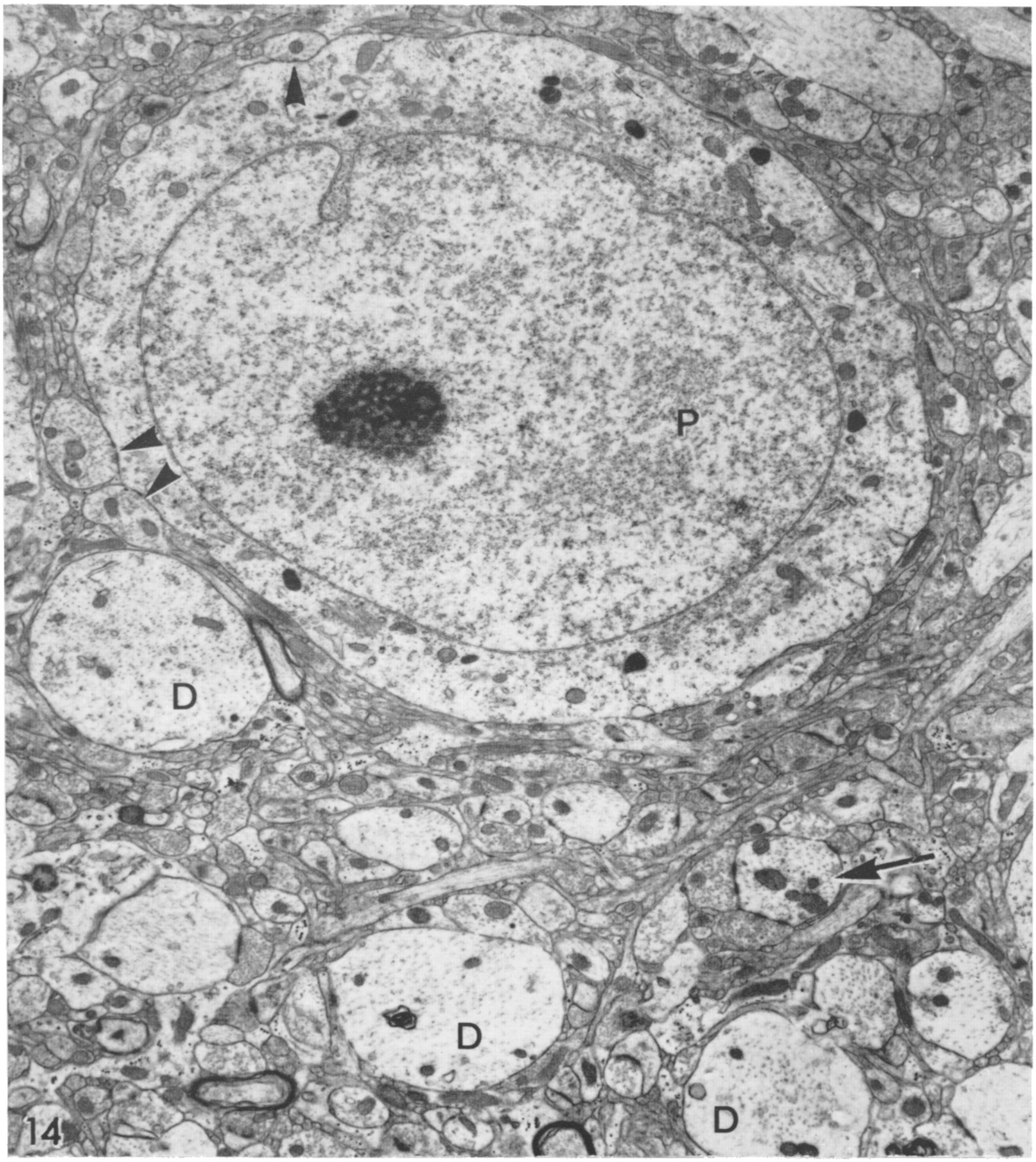


FIGURE 14. Layer II in a section cut parallel to the brain surface. Note the large pyramidal cell with only a few axon terminals on its soma (arrow heads), the large apical dendrites (D) which have few or no axon terminals upon them, and the smaller dendrites (arrow) which may be surrounded by terminals. × 9000.

FIGURE 15. A small, beaded dendrite (D) from layer II receiving many axon terminals (arrow heads) which end both symmetrically and asymmetrically. × 16000.