THE YEAR BOOK *of* NEUROLOGY, PSYCHIATRY *and* NEUROSURGERY

(1961-1962 YEAR BOOK *Series)*

NEUROLOGY

EDITED BY

ROLAND P. MACKAY, M.D.

Professor of Neurology, Northwestern University; Attending Neurologist, Chicago Wesley Memorial Hospital; Consultant, Veterans Administration Hospital, Hines, Illinois

PSYCHIATRY

EDITED BY

SAM BERNARD WORTIS, M.D.

Dean, New York University Schools of Medicine; Professor and Chairman, Department of Psychiatry and Neurology, and Director, Psychiatric and Neurologic Services, New York University Hospital

NEUROSURGERY

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OSCAR SUGAR, M.D.

Professor of Neurological Surgery, University of Illinois

YEAR BOOK MEDICAL PUBLISHERS

INCORPORATED

35 EAST WACKER DRIVE CHICAGO 1

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NEUROLOGY

ROLAND P. MACKAY, M.D.

INTRODUCTION

The great loom on which the fabric of neurology is woven never ceases its clang and clatter. The patterns emerging today had their foreshadowing in previous designs and flow uninterruptedly into the forms of the future. As the shuttle flies to and fro, what are the strands that catch one's eye as warp and woof interlace?

Anatomy and physiology now seem to be inseparably united. The revelations of ultramicroscopic anatomy invariably imply function, and histochemistry adds its quota. In recent years we have been impressed with the intimate anatomic relationship between the glia and neurons, just as we had already known of the close connections between astroglia and vascular structures. As this work in electron microscopy has progressed, we have noted the role of oligoglia in the formation of myelin and, by inference, in its upkeep and also the essential absence of extracellular space and consequently the nonexistence of cerebral edema as formerly envisioned as extracellular fluid. Further, the close relationship of the glia to blood vessels and to neurons strongly suggests that the glia performs an important role in the metabolic sustenance of neurons—almost as though the highly specialized neurons could not obtain their metabolites directly from blood but only through the aid of the glia. Articles on this subject in this YEAR BOOK by Luse and by Cammermeyer are worthy of note.

Ultimate microscopy combined with histochemistry promises further important anatomicophysiologic facts, such as exemplified in the work of Darin de Lorenzo, who found chemical differences between axosomatic and axodendritic synapses, and in that of Klatzo and Miguel, who observed "pinocytosis" as evidence for the role of glia in transport.

The physiology of muscle tone, its regulation and its abnormalities (hypotonia, spasticity and rigidity) continue to be of paramount interest. The gamma system is in the center of modern work in this field and offers much for the future, not only in the elucidation of abnormal clinical states but

also, it is to be hoped, in their treatment. The fashion now, in constantly increasing degree, is the stereotaxic approach to parkinsonism. Its effectiveness is not to be denied, and its dangers are remarkably few (with a modicum of skill); but the details of its applicability, especially in other hyperkinesias, such as spasmodic torticollis and tremors of cerebellar origin, are not yet demarcated. Much of value in our concepts of the pathophysiology of these states should come from these "experiments" on human material, since lower animals do not lend themselves to this work. Fortunately for our patients, but not for anatomic control, autopsy material is scarce.

The increased interest in circulation in the spinal cord continued in 1961, at both anatomicophysiologic and clinical levels. An important event was the publication of an admirable book in French, which approaches this subject fundamentally (Corbin, J. L.: *Anatomie et Pathologie Artérielle de la Moelle* [Paris: Masson & Cie, 1961]). Corbin begins with the embryologic and phylogenetic development of the circulation of the spinal cord and continues to detailed anatomic and pathologic features. The book should be available to, and read by, every neurologist.

As for cerebral circulation, the chief emphasis in 1961, as in previous years, was on the treatment of arterial occlusions and aneurysms. As one who has always had skepticism about the wisdom of anticoagulative therapy, this editor watches with interest the shifting fortunes of this method of treatment. Certainly in 1961 the dangers were well documented. The problem has been usefully subdivided by separating "strokes" into ingravescent and completed forms, as well as threatened types, as typified by repeated "little strokes." The impression is that the tide of opinion is swinging away from anticoagulative therapy in all but threatened occlusion, and even here it seems of minor value and of considerable danger. The great problem, of course, is the opportune recognition of the "threatened occlusion."

The reader will find valuable, detailed and extensive discussions of this whole problem in a volume presenting the transactions of the Third Conference on Cerebrovascular Disease held at Princeton, New Jersey, in January, 1961, under the chairmanship of Clark H. Millikan and jointly

sponsored by the American Neurological and American Heart Associations (*Cerebral Vascular Diseases,* Robert G. Siekert and Jack P. Whisnant (eds.) [New York: Grune & Stratton, Inc., 1961]). Refrigeration in the treatment of severe cerebrovascular episodes and as a technic permitting surgical attack on extracranial atherosclerotic plaques and thromboses is in the forefront of clinical study. The method seems to offer tremendous promise, but its value cannot be accurately appraised as yet, and its application is restricted to a few large centers where equipment and skill are at hand. The method warrants close attention.

Valuable clinical research of considerable importance continues in several other fields. Important studies include those on the course and duration of multiple sclerosis by Kay Hyllested, reported in this YEAR BOOK, and by H. R. Müller, mentioned in an editorial comment following the abstract of Hyllested's article. Estimates of the duration of life in this disease continue to increase. Careful studies on the geographical distribution of multiple sclerosis are to be found in the report of the Geomedical Conference held in Copenhagen (Studies in multiple sclerosis III, Kay Hyllested [ed.], Acta psychiat. et neurol. scandinav., vol. 35, supp. 147, 1960). Such studies will eventually play a large part in our concepts of the etiology of this disease. Already, cosmic rays have been suspected. See the article by Barlow in this YEAR BOOK.

Mention should be made of a careful monograph in English on myasthenia gravis in Norway, with attention to its prevalence, distribution, course, prognosis and treatment (Storm-Mathison, A.: *Myasthenia Gravis* [Oslo: H. Aschehong & Co., 1961]).

The importance of combined clinical and laboratory research is further emphasized by the continuing reports on neurologic disorders occurring "at a distance" from malignant tumors and by those describing the neurologic results of macroglobulinemia and other disturbances of

Illustrative articles are present in this YEAR BOOK. Again, interest in the neurologic consequences of disturbances in continues to result in a spate of articles. Advances in this field promise further revelations of great importance on the complex physiology of muscle.

The intimate relationships between neurology, general

physiology and medicine are strongly reflected in the current revelations on autoimmune or hyperergic factors in neurologic disease. These revelations bear acutely on the problems of multiple sclerosis, rheumatoid neuropathy, periarteritis, the Guillain-Barré syndrome, histiocytic granuloma, etc., and many are reported in this YEAR BOOK.

In the field of the convulsive disorders no great new discoveries are currently appearing. Slowly the progress of electroclinical correlation advances, but it is to be doubted from present appearances whether such correlation is ever to become sharp. Electroencephalography still seems to be a method of value only in concert with, and as illuminated by, clinical phenomena. Interesting articles record cases of photic stimulation by television flicker, of reading epilepsy and of other unusual trigger mechanisms in the production of seizures.

As a conclusion to this introduction, one may emphasize that the neurologist of today must be conversant with advances in the great body of medical, general biologic and biophysical science. A great and wise clinician, whose discernment and skill are the admiration of all, recently complained, "Neurology is getting too complex for me!" How much more applicable is this remark to the rest of us!

ROLAND P. MACKAY

ANATOMY AND PHYSIOLOGY

Electron Microscopy of Cerebral Cortex: I. Ultrastructure and Histochemistry of Synaptic Junctions. According to A. J. Darin de Lorenzo[1] (Johns Hopkins Univ.), the past difficulty in demonstrating synapses in the cortex is attributable partly to the limited resolving power of the light microscope. Consequently, sections of the visual and auditory cortex were removed from animals, fixed, cut and studied with the electron microscope. Some sections were stained for cholinesterase.

Examination with the electron microscope revealed the general ultrastructure of the cortex to be a complex network of cells, neuroglia and their processes in intimate contiguity. The cells and their processes occupied most of the space available, and the extracellular space, if any, was quite small. A glial sheath separated most of the vascular bed from the nerve cells. Axons, dendrites and neurons were closely applied to one another.

The ultrastructure of the synapses was characterized by closely applied pre- and postsynaptic processes separated by a synaptic cleft about 200 Å wide (Fig. 1). Presynaptic processes contained accumulations of mitochondria and "synaptic vesicles." Localized thickenings were seen in one or both synaptic membranes. Two types of synapses were seen, axodendritic and axosomatic. Dendrites were characterized by endoplasmic reticulum. Synaptic vesicles were usually clustered at the regions of synaptic thickenings. In areas where the axons terminate on the main dendritic trunk, both the terminal axons and the dendrites contained mitochondria; but the more numerous endings on dendritic spines usually lacked mitochondria. Since many axon terminals show no membrane specialization, it is not certain that all axodendritic synapses must be associated with membrane thickening. The axosomatic synapses differed in fine structural detail. The presynaptic process contained vesicles and

(1) Bull. Johns Hopkins Hosp. 108:258-279, April, 1961.

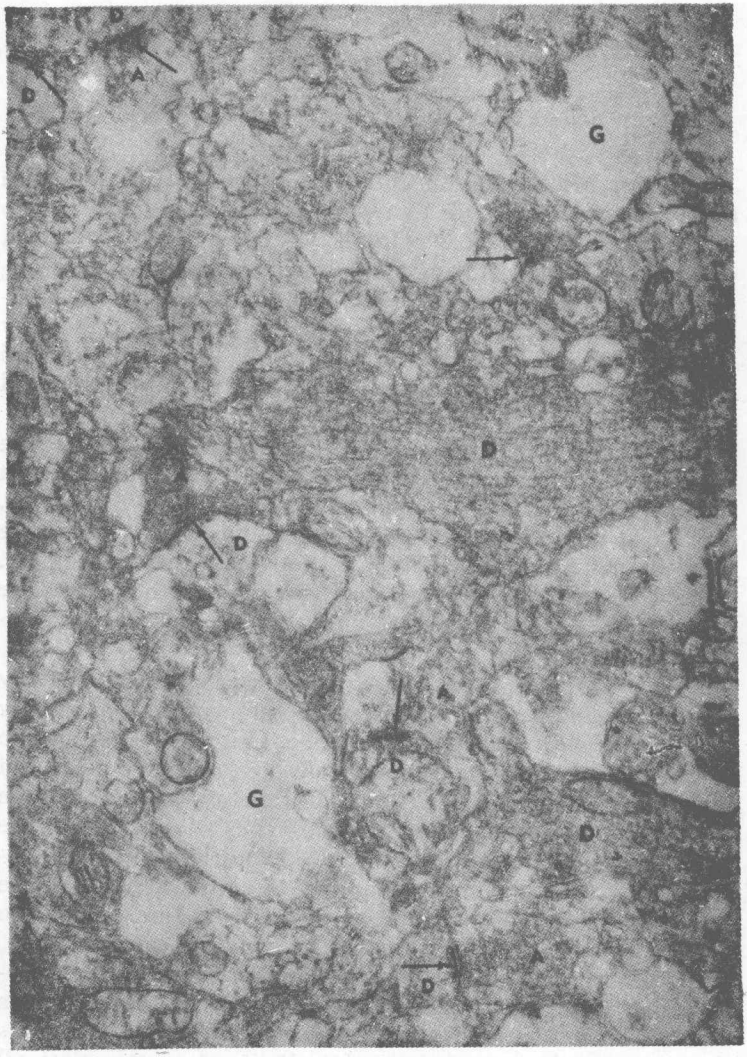

Fig. 1.—Section through region of apical dendrites (*D*) demonstrating at least 6 axodendritic synapses (*arrows*). Presynaptic axons (*A*) contain clusters of synaptic vesicles and dendrites contain components of endoplasmic reticulum. Appositional synaptic membranes demonstrate characteristic thickening seen in this type of synapse. Pale neuroglial processes (*G*) are apparent but are never seen in or between synaptic membranes. Reduced from ×16,200. (Courtesy of de Lorenzo, A. J. D.: Bull. Johns Hopkins Hosp. 108:258-279, April, 1961.)

mitochondria, but the thickened regions were conspicuously absent.

Acetylcholinesterase staining technics were used to elucidate further any relation of fine structure to function. The axodendritic synapses showed heavy deposits of staining in the region of the synaptic membrane. The vesicles and mitochondria appeared denser than in the unstained sections. The stain was located in both the pre- and postsynaptic membranes. In contrast, the axosomatic synapses remained relatively unstained. These data support the interpretation that cholinesterase is differentially located. Further studies are needed to assist in correlating fine structure with function.

► [The most important anatomic work in neurology today is being done with the electron microscope, with findings significant also for the understanding of function and disease. Thus, the relative absence of cholinesterase at axosomatic as compared with axodendritic synapses suggests different functions of the two types of synapses.—Ed.]

Histochemical Implications of Electron Microscopy of Central Nervous System are discussed by Sarah A. Luse[2] (Washington Univ.). One of the significant contributions made by electron microscopy has been the demonstration of the paucity of extracellular space in the brain and spinal cord. The ultrastructure of the central nervous system is unique in that cell touches cell and the cell processes of neurons and glia occupy the entire neuropil.

Edema and dehydration of the brain have demonstrated that the cellular changes associated with water transport reside in the oligodendroglia. The oligodendroglia are satellites of both the capillary and the neuron (Fig. 2). Either the oligodendroglial cell body or its processes touch the capillary wall to form a zone of contact tenuous in comparison to the stout, firmly adherent, astrocytic feet which insert into the capillary wall. Whether edema occurs spontaneously, as in man, or as the result of experimental procedures, the changes observed are the same. Sections of normal rabbit cortex exhibit the usual picture of astrocytic feet and oligodendroglial cytoplasmic processes surrounding the capillary. In edema, there is no increase in extracellular space but rather a massive increase in volume of oligodendroglial cytoplasm, both in the processes and in the cell body proper.

(2) J. Histochem. 8:398-411, November, 1960.

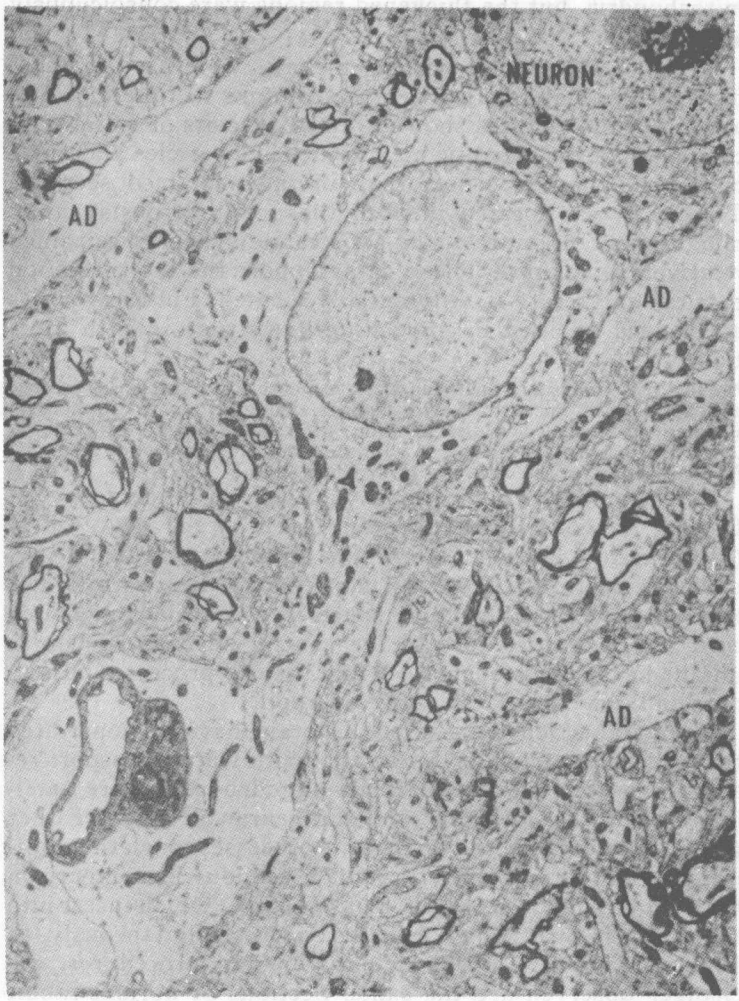

Fig. 2.—Section from cerebral cortex of adult rabbit, showing oligodendroglial position between neuron and capillary. Here an oligodendroglial cell is a satellite to a neuron (upper right) and has a foot process contacting the capillary (lower left). Another oligodendroglial process encircles the rest of the capillary; no astrocytic foot is present at this level. The brain of this rabbit had been made edematous by intravenous water and then partially shrunken by intravenous 50% sorbitol. Three apical dendrites (*AD*) are present. They differ from oligodendroglial processes in their straight course and uniform diameter. Reduced from ×5,000. (Courtesy of Luse, S. A.: J. Histochem. 8:398-411, November, 1960.)

The structures known to have neurosecretory activity have in common one ultrastructural characteristic: cytoplasmic microvesicles, which may be large or small, translucent or opaque. Such vesicular structures in the hypothalamus, posterior pituitary and synaptic endings, whether filled or empty, provide a possible anatomic location of presecretory material.

Scars in the brain after injury, vascular insults, tumors or edema may result in localized or occasionally diffuse alteration of the hematoencephalic barrier. Electron microscopy shows the capillaries in gliotic scars and in brain tumors to be surrounded by a space containing collagen and occasional connective tissue cells.

Electron microscopy also shows that neoplastic oligodendroglial cells, like normal oligoglia (Fig. 2), have abundant pale cytoplasm. Although their nuclei may be bizarre, the most striking abnormality is in the mitochondria. In neoplastic cells, mitochondria may be so greatly increased in number that they are crowded together.

► [One can scarcely exaggerate the importance of this work by Luse (and that by others) in demonstrating through electron microscopy: (1) that extracellular space practically does not exist in the nervous system; (2) that edema of the brain is edema of the oligodendroglia; and (3) that probably the oligodendroglia constitute the vessel for water (and other?) transport in the nerve tissues. The glia are to be considered, therefore, as of vast importance in neurologic metabolism. In this connection, Cammermeyer perhaps assumes more in the following article than is yet demonstrated.—Ed.]

Is the Perivascular Oligodendrocyte Another Element Controlling the Blood Supply to Neurons? Jan Cammermeyer[3] (Nat'l Inst. of Health) observed a pattern in the perivascular arrangement of oligodendrocytes which suggests a function not previously ascribed to these cells.

A knowledge of the cellular organization of the nervous system is needed to hypothesize about the functional significance of the oligodendrocytes, *O* (Fig. 3). The tissue is free of perivascular and perineuronal spaces, and one is concerned about only one system of channels in which fluid circulates. After repeated division, the vessels continue into a capillary network which forms multichanneled connections between the larger vascular trunks. Bundles of connective tissue fibers, *C*, form an additional anchorage for the vessels.

(3) Angiology 11:508-517, December, 1960.

In the vascular network, the neuron, *N*, is in contact with the nutrient vessel (this had been previously noted in the cat spinal cord and later in the entire nervous system of all species examined by the author). However, both the number of vessels which embrace a neuron and the length of contact between a neuron and its vessel are regionally variable. The contact between neuron and vessel seems to be intimate. Polysaccharides are known to accumulate on the surface of neurons, particularly over the largest neurons throughout the central nervous system, and these are apparently con-

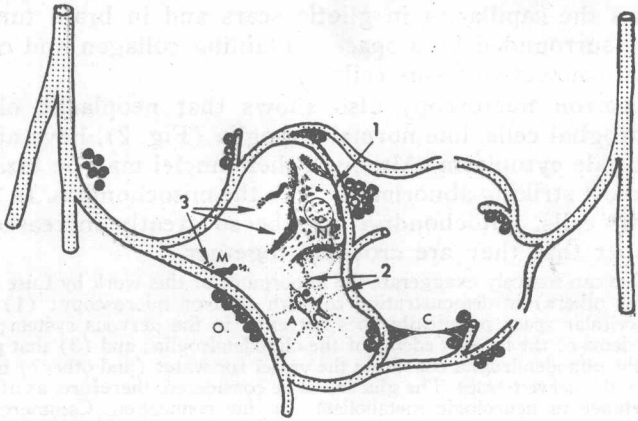

Fig. 3.—Model of gray matter organization. (Courtesy of Cammermeyer, J.: Angiology 11:508-517, December, 1960.)

fined to the pre-and intrasynaptic regions. A heavy precipitate of silver formed on the layer of polysaccharides by means of special technics may erroneously be interpreted as an extraneuronal plexus of fibers, the so-called outer Golgi net. No deposition of polysaccharides is demonstrated on the neuronal surface where it adheres to a vessel. This part of the vessel would seem to be useful for the rapid exchange of substances because of its close contact with the neuron (route *1*, Fig. 3).

Polysaccharide-like material is dispersed throughout the gray matter and is believed to be distributed within the cell bodies of astrocytes (*A*). The latter, because of their many processes and contacts with vessels and neurons, offer an excellent path for the transport of substances. They could