NEUROLOGY

By

ROY R. GRINKER, M.D.

Chairman, The Department of Neuropsychiatry
of the Michael Reese Hospital, Chicago

THIRD EDITION

Revised and Largely Rewritten
Fourth Printing

With the Assistance
of
NORMAN A. LEVY, M.D.
Associate Neuropsychiatrist
Michael Reese Hospital, Chicago

With a Chapter on BRAIN TUMORS
by
PAUL C. BUCY, M.D.
Professor of Neurology and Neurological Surgery
University of Illinois, College of Medicine, Chicago

CHARLES C THOMAS · *Springfield* · *Illinois* · *U.S.A.*

Published by CHARLES C THOMAS
at BANNERSTONE HOUSE
301-327 EAST LAWRENCE AVENUE, SPRINGFIELD, ILLINOIS

Published simultaneously in Canada by
THE RYERSON PRESS, TORONTO

First Edition, January, 1934
Second Edition, September, 1937
Third Edition, Second Printing, April, 1944
Third Edition, Third Printing, February, 1945
Third Edition, Fourth Printing, February, 1946

Printed in the United States of America

NEUROLOGY

To the Memory of

MY FIRST TEACHER OF NEUROLOGY

My Father

JULIUS GRINKER, M.D.

Preface to the Third Edition

PROGRESS in the field of neurology since the last edition of this book has been sufficiently great to warrant rewriting many sections, adding and deleting others and thoroughly revising much of the substance. My genial publisher, Mr. Charles C Thomas, has aided this task by generously reprinting the book with an entirely new format. The constructive criticisms of medical teachers and specialists of various phases of neurology, for which I am grateful, have been incorporated wherever possible. However, the goal of a scientific presentation of an integrated neurology has not been abandoned for the sake of false simplicity. Those who truly wish to understand the nervous system are confronted with a difficult task but with satisfying recompenses. The author sincerely hopes that this volume will facilitate the strivings of the earnest student.

ACKNOWLEDGMENTS

My colleague, Dr. Norman A. Levy, has assisted me greatly in the task of bringing the third edition up-to-date. Without his steadfast help it could not have been so thoroughly rewritten and so completely revised. It is my great pleasure to have Dr. Paul C. Bucy as a colleague in authorship with the responsibility for the chapter on brain tumors. I am indebted to Mrs. Anna M. Fishbein for editing several difficult chapters, to Miss Ella Salmonsen, medical librarian of the John Crerar library, for facilitating access to the literature, for editorial assistance and for efficient and rapid preparation of the manuscript. My secretary, Miss Gerthrude Kuehn, ably assisted me in numerous details and valiantly protected me against onslaughts on my time. Mrs. Frederick Green expertly made the index. Not least is the credit due to my family who suffered without complaint through this arduous period of revision just prior to my leaving for active service with the medical corps of the Army Air Force.

ROY R. GRINKER

THIRTY NORTH MICHIGAN AVENUE
Chicago, January, 1943

Preface to the First Edition

THIS book is an attempt at a correlation of certain biological data which are considered of importance to the study of the human nervous system in health and in disease. It is my belief that in this manner an adequate instruction of neurology to students of medicine can be presented, and that such a correlation is essential for a comprehension of clinical neurology by those who contemplate this field as a specialty. The physician rarely has an adequate grasp of the whole subject because his instruction in neurology is usually separated into distinct departments of embryology, anatomy, and physiology. In each of these, one special viewpoint is but weakly linked to another. Neurology as a special field in the biological sciences should include, in close association, the academically separated aspects of the nervous system.

The student of medicine is primarily interested in the human nervous system hence; the material presented here has been selected because of its application to man. The student of biology may, also, find discussed some problems in human functions which may help him with his studies on other animals. In the absence of correlated courses of neurological instruction in the universities, I hope that the student may utilize this book in all departments where some phases of neurology are presented, gathering more and more of the relationship between structure and function, as he progresses. Finally, in his clinical studies the student will visualize human nervous functions and their disorders better, if explanations of the effects of diseases are based, as herein, on disordered morphology and physiology.

In the limited space of one volume it has been necessary to exercise considerable selection in regard to the material included. I realize that much of importance may have been omitted from the text, but reference to the bibliography may compensate for these omissions. The neuroses as a group have been omitted for I believe that they require special consideration in psychiatric texts.

I am deeply indebted to my surgical colleagues in the Division of Neurology and Neurosurgery, Drs. Percival Bailey and Paul C. Bucy for their greatly needed assistance in preparing the chapters concerned with neoplasms of the nervous system, for their wise counsel at many points during the progress of this work and for the many years of delightful and stimulating association in clinic and laboratory. Drs. Douglas N. Buchanan, Norbert U. Zielinski, and A. Earl Walker, Douglas Smith Fellow in neurology, furnished numerous drawings and sketches. Miss Dorothy Apolsky and Miss Josephine Newson assisted me greatly with their expert and unstinted stenographic work. Dr. Walker also furnished valuable assistance in reading the proofs.

Acknowledgment is expressed to D. Appleton & Company for permission to reproduce several cuts and portions of my chapter in Volume 2 of their "Practitioners' Library" and to the Press of the American Medical Association for permission to use material and illustrations from my previously published articles.

The clinical material pictured in this book was studied in my neurological outpatient department in the Max Epstein Clinic and neurological service of the Albert Merritt Billings Hospital, both of the University of Chicago. Evelyn Stevens Hunt has performed technical wonders in my laboratory of neuropathology, evidenced by the microscopical sections illustrated in this book.

ROY R. GRINKER

THE UNIVERSITY OF CHICAGO
August 1, 1933

Contents

NEUROLOGY

CHAPTER I

General Embryological Considerations

EMBRYOLOGICAL DEVELOPMENT is a complex dynamic process of well-integrated progressive steps. The adult nervous system is the most complex organization in the human body and its detailed and intricate interconnections and functions are difficult to understand. Yet the complicated finished structure has been built up by a series of simpler embryological steps (*26*), the knowledge of which not only elucidates many obscure phenomena of the normal adult organism but also affords greater understanding of malformations. Studies of comparative anatomy (*8*) supplemented by comprehension of embryological processes, which briefly recapitulate phylogeny, permit a broader perspective of the relation of structure to function.

The Neural Tube.—In the mid-dorsal portion of the germinal area, the differentiated ectoderm thickens and forms a multilayered area called the neural or *medullary plate*. The lateral margins of this plate roll upward and form neural folds which fuse in the midline, thus closing a cavity known as the *neural tube*. The non-neural ectoderm or future body integument, rolls externally to the neural ectoderm. Cut off between the ectoderm and the neural tube on each side, are groups of cells called the *dorsal* or *neural crests*.

The neural tube is quickly filled with fluid secreted by activity of the lining cells which constitute the primitive ependyma. The hydrostatic pressure produced keeps the walls of the tube distended. Two openings through the ectoderm and tube, the anterior and posterior *neuropores,* permit circulation into the tube of amniotic fluid which provides nutritive materials before vascular functions become effective. These openings close when circulation of blood begins.

At first, the walls of the neural tube are composed of simple columnar epithelium with definite cell boundaries which develop into spongioblasts or precursors of neuroglia. The layer closest to the tube is most active in mitosis (germinal layer). Cells migrate from it to the middle and external or mantle layers (Fig. 1). As each cell arises it develops its own processes which continue to remain part of the cell. Syncytial structures do not form. Mitotic densities vary within areas of the germinal layer and have orienting influences on the configuration of the tube.

Round vesicular cells, actively dividing by mitosis, may be observed among the undifferentiated columnar epithelial cells of the germinal layer. These *germinal cells* are destined to become neuroblasts. Certain other indifferent cells are probably bipotential, capable of spongioblastic or neuroblastic

growth, since they frequently form malignant tumors in which the two lines of differentiation may be seen. Although they are termed medulloblasts (*1*) such germinal cells have not been observed in normal histogenesis.

The inner cellular walls of the medullary epithelium form an *internal limiting membrane.* Cells multiply and migrate into the mantle layer becoming elongated and fusiform but maintain a protoplasmic attachment to the internal limiting membrane. This prolongation of the cell gradually thins as a process appears at the opposite pole of the cell to become attached to the *external limiting membrane,* which is formed by the mesoderm around the outside of the neural tube, the primitive leptomeninx. This cell is the primitive spongioblast which in early embryonic life is the only supporting structure of the neural tube.

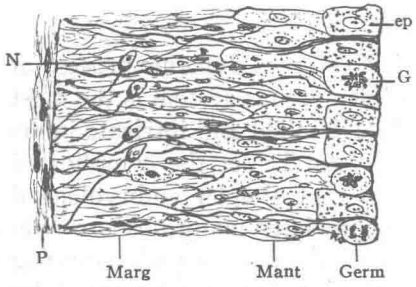

FIG. 1.—Drawing of a section of primitive neural tube showing the germinal layer (Germ), the mantle layer (Mant) and the marginal layer (Marg) against the primitive pia mater (P). In the germinal layer columnar epithelial cells (ep) and germinal cells are undergoing mitoses (G). The developing neuroblasts (N) have reached the marginal layer. The spongioblasts and their processes are composed of single cells; there is no syncytium.

Many spongioblasts gradually migrate outward, lose their connections with the internal limiting membrane and become *astroblasts* (*15*). Many later also lose their connections with the external limiting membrane. Those special astrocytes which maintain their processes against the pia mater, form the *external pia-glial membrane.* Only a few ependymal cells of the adult midbrain have processes which reach the surface at the ventromedian sulcus. In the meantime, the nervous system has become invaded by blood vessels so that the migratory spongioblasts attach one process to the blood vessel wall as a characteristic *"sucker foot"* which is maintained in adult life, whereas their attachment to the internal limiting membrane is lost. *Gliafibrillae* appear in certain astroblasts about the fourth month of intra-uterine life, forming the *fibrous astrocytes.* Those astrocytes which do not form gliafibrillae are called *protoplasmic astrocytes.* Simultaneously, the shape of the *astrocyte* becomes more angular and the cells tend to migrate nearer the vessel walls. More processes develop from the surfaces of the cells. Less differentiated spongioblasts, the ependymal cells, remain columnar in form and stay close to the internal limiting membrane. They lose their cilia but preserve their *blepharoplasten,* which are cytoplasmic structures concerned, in some manner, with the formation of cilia (Fig. 2).

From the indifferent cells or primitive medullary epithelium another type of glia, the *oligodendroglia,* develop. These cells are the small round interfasicular, satellitic glia which are poor in cytoplasm; they have chromatin-rich nuclei and fine delicate processes. Oligodendrogliae arise directly from migratory spongioblasts, but do not become attached to blood vessels or to the limiting membranes. They increase rapidly about the time of birth and then develop large gliosomes. It is believed that they function in the elaboration of myelin for central nerve fibers.

Eventually, these cells entwine their processes about the central axons and become homologous to the Schwann cells of the peripheral nerve sheaths. However, they also develop from the dorsal crests and accompany the peripheral cranial and spinal nerves a short distance.

The *microglia* are regarded as of mesodermal origin and have not been

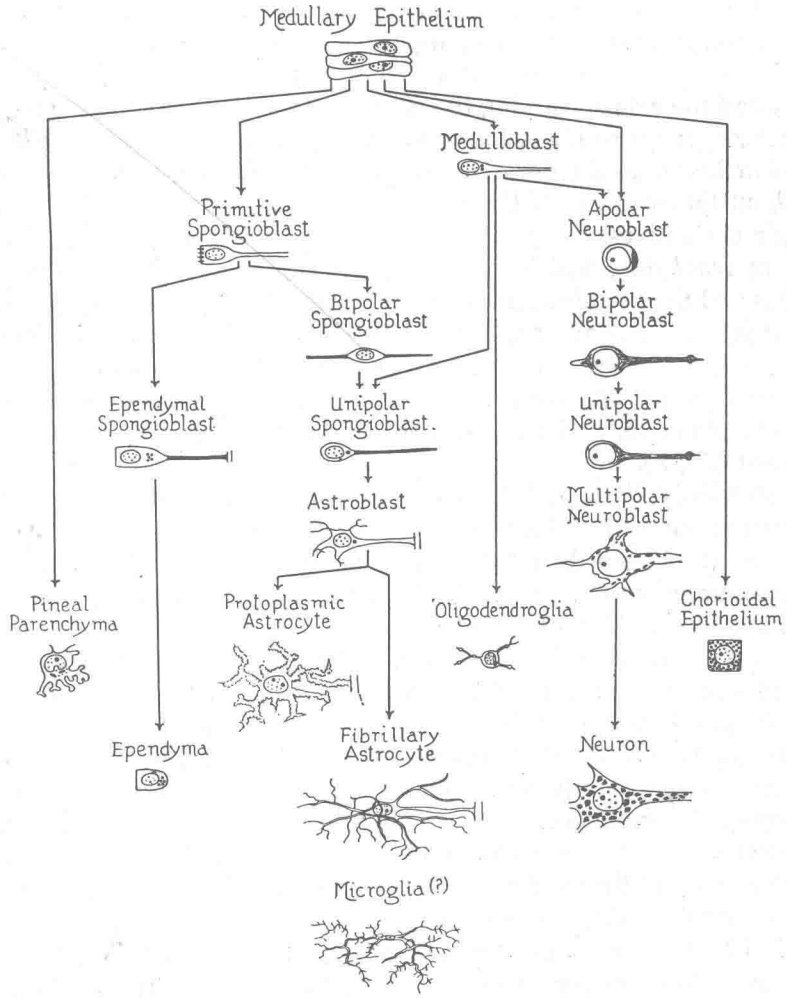

FIG. 2.—Scheme of the histogenesis of the neural tube (after Bailey).

known to originate from the medullary epithelium. These cells are morphologically similar to polyblasts of other organs and apparently function like them. They enter the nervous system during the third month of embryonic life, migrating along the blood vessels and from the pia mater. Beneath the superior and inferior tela choroidea are two "fountains" from which the invading hordes of microglia originate. At first, these cells are deeply argentophilic and have small, round nuclei with short processes. On maturity, they

develop elongated nuclei with little cytoplasm and long, spiny, dichotomously branching processes.

As the neural tube closes, the dorsal borders of the two lips differentiate into special cell groups which multiply at the dorsolateral angles of the closed tube. These are the neural or *dorsal crests*. From them, the cells of the sensory ganglia and their capsule cells develop. They are the source of cells which arrange themselves in columns ventrally along the neuraxis and later condense and form the orthosympathetic paravertebral chain. They also produce cells which follow the spinal nerves and differentiate into the sheath cells around the axons, forming the neurilemma or *sheath of Schwann*. They first enclose groups of fibers but later invade the bundles and enclose single fibers. Furthermore, the dorsal crests probably produce non-nervous structures about the head-end of the organism, such as parts of the gill structures and their derivatives.

The *mesenchyme,* which condenses about the neural tube, forms the meninges and the vertebrae and is the source of the blood vessels. Weed has shown that pia mater and arachnoid split into two separate membranes from the mesenchyme, only at the time when cerebrospinal fluid is produced by the choroid plexus. In experimental transplants, unaccompanied by choroid plexus, the pia mater and arachnoid do not separate and they continue as one membrane (*25, 7*).

The *germinal cells,* in active mitoses, assume globular form with cytoplasm condensed at one pole and acquire an affinity for silver. At first, the cells are apolar and pear-shaped, but soon develop elongations at both poles. The true axon supplants one process and the other disappears, so that the cells are then unipolar. They tend to form clusters and send out processes in strands. Later, the nucleoli are visible, dendrites appear, Nissl substance is produced and finally the mature *neurocyte* emerges. In tissue cultures, the neuroblasts appear as isolated cells with knob-like processes that are elongated and motile. Neuroblasts tend to rupture through the external limiting membrane rather rapidly and follow solid surfaces in their development. This tropism is significant in determining the direction of growth.

Derivatives of the neural tube.—In the earlier embryos, the cephalic and caudad ends of the neural tube project above the surface of the ectoderm. Even before the tube closes, the cephalic end is divided by constrictions into three divisions representing the forebrain, midbrain and hindbrain (*16*). The cephalic portion soon flexes anteriorly at a point which denotes the future midbrain. The various flexures and modifications of form are probably based on a differential rate of growth in portions of the tube, explicable in phylogeny (*23*).

Within the first month, the *spinal cord* differentiates into the germinal, mantle and marginal zones. The roof and floor regions remain extremely thin. As histogenesis progresses the neural tube is encroached upon, until it remains only as a central canal lined with ependyma. Eventually, its patency is lost, it assumes microscopic dimensions and is filled with debris and cilia. Early, a sulcus appears in the medial wall of the entire tube, which demarcates the neuraxis into a dorsal sensory alar plate and a ventral

motor basal plate. These divisions have functional significance throughout the entire adult central nervous system (*10*). In the cord, the medial walls of the alar plate press together and form the dorsomedian septum. The spinal roof plate thus disappears; the central canal is projected ventrally and lies close to the ventral surface. The floor plate persists as the shallow anteromedian septum formed by the extensive growth of the basal plate, which projects on either side of the floor plate.

The neurons of the basal plate send processes from the neural tube into the surrounding mesenchymal tissue; these become the *ventral root* fibers. Later, the ventral cells separate from a lateral group of cells. The cells of the alar lamina send out processes which remain within the neural structure and usually radiate ventrally. These processes tend to curve ventrally around the wall of the neural tube and cross the floor to reach the opposite side within the same segment in which they arose; however, some fibers deviate in a caudal-cranial direction. When the crossing fibers reach the opposite basal lamina, they adopt a similar longitudinal path. These fibers form the secondary spinothalamic neurons, most of which bear sensations of pain and temperature. Other alar cells send fibers which pass ventrally to the ipsilateral marginal zone of the basal plate and from there proceed longitudinally. The processes of the cells of the alar plate remain as intra- or intersegmental fibers.

In the meantime, the cells in the *dorsal ganglia* send out peripheral processes which form the sensory portion of the spinal nerves. The central processes of these nerves form the posterior root, and grow into the alar lamina of the neural tube. On entering the cord, the fibers split dichotomously, one toward the cranium, the other caudally in the marginal zone but continue dorsal to the entrance zone of the dorsal root. Most of these fibers eventually grow into the dorsal grey columns. Underneath the marginal zone of the alar lamina, cells from the mantle zone which come into contact with incoming root fibers, send their processes medially. Numerous cells become synaptically interposed between incoming root fibers and other intrinsic cell groups.

The nearest approach to ancient *metamerism* appears in the spinal region as an adaptation to the somites. In the branchial region, segmentation indicates active cell proliferation and denotes foci within the brain stem of the cranial nerve nuclei. Further forward, true segmentation does not appear and rigid geometrical division of the cerebral cavities into three primary vesicles does not occur. Streeter (*22*) contends that such terminology is only a convenience.

The division of the cerebral laminae into three portions persists after the neural tube has closed, so that three communicating vesicles are formed (Fig. 3). Three paired grooves appear, destined to be optic, trigeminal and acoustico-facial evaginations. The optic evagination forms a vesicle connected with a stalk to a part of the prosencephalon which marks its division into *telencephalon* (forebrain) and *diencephalon* ('tweenbrain).

A *pontine flexure* appears first as a slight thickening of the floor of the hindbrain, with a corresponding thinning of the roof (*24*). It does not form a complete bend. The result is a division of the *rhombencephalon* into

metencephalon (cerebellum), and *myelencephalon* (medulla). At the junction of the brain and the spinal cord, a posterior *cervical flexure* is visible opposite in direction to the cephalic flexure. The *mesencephalon* is separated from the *metencephalon* by an indentation called the *isthmus,* the roof of which is the origin of the anterior medullary velum. The posterior medullary velum develops from the roof of the myelencephalon. Both these structures overlie those parts of the fourth ventricle not covered by the cerebellum.

The *myelencephalon* or medulla has a thin roof. Over its flattened dorsal surface are the cerebellar vermis and hemispheres, and the anterior and posterior medullary velum. Histogenesis here is similar to that in the spinal cord, except that with the greater flattening in the anteroposterior direction

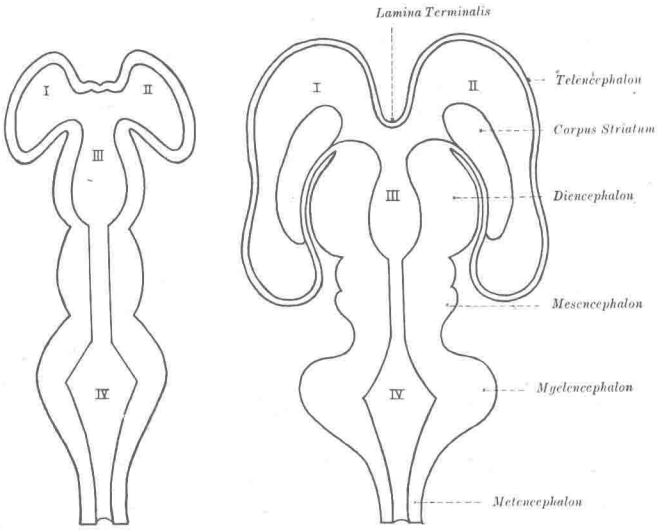

FIG. 3.—Schematic representation of the primary derivatives of the neural tube. The numbers refer to the ventricular subdivisions.

and the outward displacement of the alar plate, the motor and sensory nuclei are shifted. The somatic sensory cells are pushed dorsolaterally, and the somatic motor cells become ventromedial. The invagination by the tela choroidea of the thin roof plate or posterior medullary velum forms the choroid plexus of the fourth ventricle and its lateral recesses. From the alar plate are derived the nuclei of gracilis and cuneatus, the inferior olivary bodies and the nuclei of the sensory cranial nerves. The basal plate is the source of the nuclei of the motor cranial nerves and of the reticular formation.

The *cerebellum* evolves from the alar plates of the metencephalon. Arising from the acoustic area these alar plates grow dorsally and medially, and meet to fuse in the median line. The cerebellar plates form a central vermis and later extend laterally and develop neocerebellar hemispheres and their nuclei. The posterior or rhombic lip of the cerebellar plate resolves into the nodulus and the flocculus. Thus, the metencephalic roof plate forms the cephalic part of the posterior medullary velum and of the cerebellar vermis. The floor plate becomes the median raphe. The alar plate is the origin of the

pontile nuclei, the nuclei of the sensory cranial nerves arising from the pons, and the lobes of the cerebellum. The basal plate forms the reticular structure and the nuclei of the motor cranial nerves.

The *mesencephalon* or midbrain includes the corpora quadrigemina, median geniculate body and red nuclei from its alar plate, and the nuclei of the third and fourth cranial nerves as well as the tegmentum from the basal plate. The cerebral peduncles pass through its base. The neural tube here forms the narrow aqueduct of Sylvius.

From the base of the *diencephalon,* two shallow pockets develop ventrally; one is the primordium of the infundibulum, the other the mammillary recess. The optic vesicle, which grows away from the brain, is invaginated into a cup and mesoderm penetrates its lateral surface. However, it is still connected to the brain by the optic stalk which later becomes the optic tract. In the lateral wall of the diencephalon, a sulcus hypothalamicus appears which divides the alar from the basal plates. The roof plate and dorsal part of the alar plates constitute the epithalamus which includes the habenula and pineal body. The craniolateral part of the alar plates forms the thalamus and the caudolateral produces the metathalamus or lateral geniculate bodies. The basal plates and floor plates develop into hypothalamus. A transverse groove called the velum transversum appears in the roof plate. Caudally to it the roof plate forms the tela choroidea superior and gives rise to the choroid plexus of the third and lateral ventricles. As the brain stem develops and elongates the velum becomes invaginated into a fissure-like structure, the choroidal fissure. The hypothalamic infundibular outpouching meets a dorsocaudad evagination of stomodeal epithelium (Rathke's pouch) to make the *hypophysis*. The lamina terminalis or original anterior end of the neuraxis is the source of the anterior commissure and corpus callosum.

The *telencephalon* itself develops into the pallium of the hemispheres from the alar plates which extend backward, eventually covering the entire brain stem (*17*). The *striatum* arises from paired median thickenings in the floor of the telencephalon which grow caudad to encircle the thalamus, separated from it only by the tenia semicircularis. The striatum begins in the alar plate and later differentiates into pallidum and neostriatum. The basal plate forms the anterior part of the tuber cinereum and the anterior part of the pars optica hypothalami. The lamina terminalis projects backward, giving rise to a septum pellucidum on either side; these separate the lateral ventricles from each other medially.

EMBRYOLOGICAL PHYSIOLOGY

Embryological physiology is a new field of science concerned more with the dynamic mechanisms in development than with static descriptions of the process (*3, 12, 21*). The recent book of Paul Weiss (*26*) and the Annual Review of Physiology should be consulted for fundamental principles.

In the earliest stages of development all the embryonic tissues are plastic or equipotential in their capacity to produce certain structures. At this time the future growth of a group of cells depends on its location. Later, cells