Medical Neurosciences

An Approach to Anatomy, Pathology, and Physiology by Systems and Levels

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To the students of the Mayo Medical School and the residents in the Department of Neurology who have provided the stimulus for this venture by teaching us as we have taught them, who have helped us to refine our objectives and methods of presentation, and who through their enthusiasm have encouraged us to write this book.

Preface

Know this: that this school at its inception was dedicated to the purposes of revolution, a revolution in the academic spirit uniting faculty and students alike into a professional elite. Together, they cherished an imperative for the humane in an age made rich by technology and science.

And this was the covenant of their ordination: that with the eyes of compassion they assessed the brilliance of their technologies, and with the yardstick of the humane they measured the benefactions of their science.

With those words, spoken by Dean Raymond D. Pruitt at its convocation, Mayo Medical School began on September 7, 1972.

This book has evolved from the neuroscience course that was presented to first-year students that year and is truly a joint effort of faculty and students. Years before the students arrived in Rochester, preparations for this unique medical school were under way. Under the challenging leadership of Jerry G. Chutkow, M.D., the first chairman of the Neuroscience Curriculum Committee, Drs. Jasper R. Daube, Thomas J. Reagan, and Burton A. Sandok met in an effort to design a program of study. It was decided, prior to determining the course content, that the objectives developed would be based on the following basic tenets:

1. The primary responsibility for curricular design for medical practitioners must rest with physicians and therefore, although the advice, support, and talents of available basic science personnel should be utilized, the final curricular content and design should be determined by clinicians.
2. The goals of a basic neuroscience course must be consistent with the primary goal of the medical school—the training of capable clinicians.
3. If the medical student learns the skills of self-education, then certain facets of the traditional curriculum can be omitted, since the student will be able to seek and acquire them when necessary.
4. Since the amount of "factual" basic scientific knowledge required by a group of clinical neurologists to practice their specialty is limited when examined critically, then the amount of such knowledge required to allow the nonneurologic physician to deal intel-

ligently with common neurologic problems must be no greater and likely is less.

5. The major tool of the practicing neurologist is the skill of clinical problem solving. This skill must be defined, developed, and integrated as a major component of the neuroscience course.
6. The patient represents the best "laboratory model" available for the study of neurologic behavior and should, therefore, be used whenever possible.

From these initial discussions, the objectives, content, and organization of the curriculum were developed and an initial syllabus was prepared by the committee. With passing years, the committee, the course, and the syllabus have undergone revision, but the basic organization has consistently proved to be a useful and an effective means of presenting material not only to medical students but also to residents in neurology. Although seemingly of diverse interests, the two groups did not differ in the type of material needed to understand neurologic problems but differed only in their individual educational objectives. While the students, whose objectives are limited to the principles of neurologic diagnosis, use this text as a resource in their study and understanding of clinical problems, the residents in neurology have found this text an organized framework of background material on which to build their knowledge.

Although the current text is the product of the authors, there are many others who have contributed significantly to its development and content and whose help we wish to acknowledge.

Present and former faculty members of the Neuroscience Curriculum Committee:

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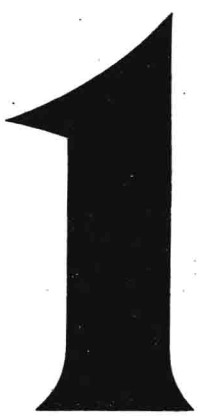
Finally, we acknowledge the invaluable contributions made by Ms. Patricia Hanson and Ms. Lillian Werner, our secretaries, express appreciation to our many colleagues in the Department of Neurology who willingly provided advice and criticism, and especially thank Donald W. Mulder, M.D. (former Chairman of the Department of Neurology), who had the foresight to organize the initial curriculum committee and the confidence to allow us to develop freely a program that we felt to be exciting and instructive.

J. R. D.
B. A. S.

Contents

Medical Neurosciences

Integrated Neuroscience for the Clinician



Neurologic disorders are common, and clinicians must be capable of dealing confidently with them. Many steps are required in accomplishing this task. Patients seldom present to their physician with a well-defined diagnosis for which appropriate therapy can be readily dispensed. Instead they arrive with a vast array of complaints that constitute a clinical problem which the physician must attempt to resolve. The solution of a clinical problem in neurology, as in any area of medicine, requires a knowledge of anatomy, physiology, and pathophysiology. This book is an attempt to organize the body of information contained in the basic neurologic sciences into the format used by clinicians in dealing with diseases of the nervous system.

The process used by a clinician who examines a patient with a neurologic disorder (that is, one involving the brain, spinal cord, nerves, or muscles) is that of inductive reasoning. It is a familiar process in which a number of distinct pieces of information are put together to reach a general conclusion. For example, if a woman has a 1-year history of slowly progressive numbness and weakness of the left side of her face, left arm, and left leg, the physician concludes that the patient may have a neoplastic lesion at the supratentorial level on the right side. The physician utilizes the data obtained by interviewing and examining the patient to produce a history which is a chronologic account of the patient's symptoms and their evolution with time (the temporal profile). The specific symptoms in the history can be categorized into broad groups and related to particular anatomic structures and certain disease categories. In a patient with neurologic disease, these symptoms often are identified with changes in sensation, activity, movement, thinking, or consciousness. And often the physical examination of a patient with neurologic disease allows an even more precise definition of abnormal function, which, based on the clinician's knowledge of anatomic structure and function, can be related to specific areas of the nervous system.

Throughout the interview and the examination, the clinician is constantly organizing and reorganizing the collected data in order to ar-

rive at hypotheses about the nature of the disorder. In the previous example, the hypothesis of a right cerebral tumor was reached because the temporal profile of slow progression is common with neoplastic disorders, and weakness and numbness on the left side of the body often are due to disease of structures that are controlled at the supratentorial level on the right.

The physician must answer three questions. Is there disease involving the nervous system? If so, where is the disease located? And what kind of disease is it (that is, what is the pathologic nature of the disease)? The first question is often one of the most difficult to answer, since an answer depends not only on the knowledge to be presented in this book but also on experience with disease involving all other body systems. This book will focus primarily on answering the two simpler questions: "Where is the lesion located?" and "What is its pathologic nature?"

Objectives

Neurologic diseases include all the major pathologic types seen in other organ systems and can involve one or several areas within the complex human nervous system. However, adequate management of neurologic problems can be based on a simple expansion of the questions: "Where is the problem?" and "What is the problem?" The elaboration and analysis of these specific questions form the major objectives in the study of the neurosciences. The answers to these questions are based on a knowledge of the gross anatomic structures of the nervous system (Fig. 1-1), the usual patterns of disease, and the forms of treatment available. This simplified approach to neurologic disease is the one customarily used by many neurologists, and it includes four questions:

1. Is the responsible lesion located at
   a. The supratentorial level
   b. The posterior fossa level
   c. The spinal level
   d. The peripheral level
   e. More than one level

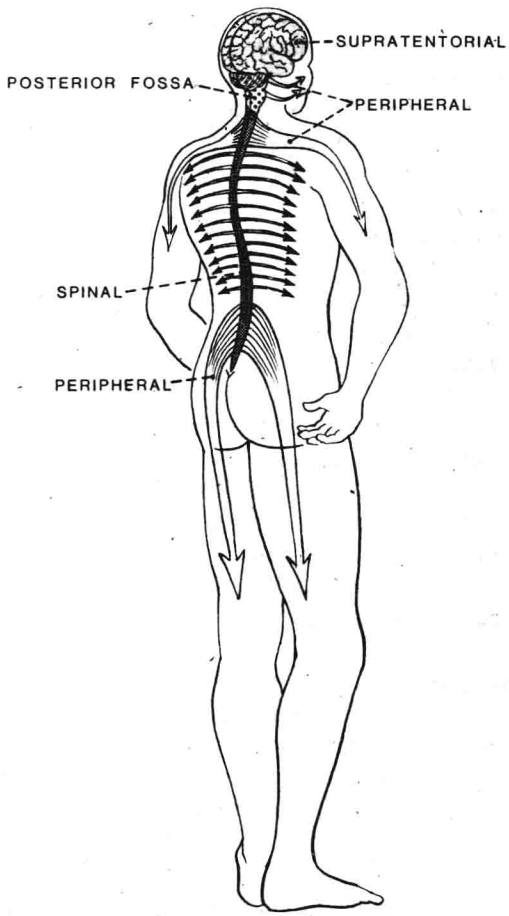


Figure 1-1. Levels of the neuraxis. Supratentorial level includes cerebral hemispheres and portions of cranial nerves I and II within the skull. Posterior fossa level includes brain stem, cerebellum, and portions of cranial nerves III through XII within the skull. Spinal level includes spinal cord and portions of nerve roots contained within the vertebral column. Peripheral level includes portions of both cranial and peripheral nerves that lie outside the skull and spinal column, and structures innervated by these nerves.

2. Is the responsible lesion
   a. Focal, and located on the right side of the nervous system
   b. Focal, and located on the left side of the nervous system
   c. Focal, but involving midline and contiguous structures on both sides of the nervous system
   d. Diffuse, and involving homologous, sym-

metric, noncontiguous areas on both sides of the nervous system
3. Is the responsible lesion
   a. Some form of mass lesion
   b. Some form of non-mass lesion
4. Is the lesion most likely
   a. Vascular
   b. Degenerative
   c. Inflammatory
   d. Neoplastic
   e. Toxic-metabolic
   f. Traumatic

The major objective of this text therefore is to provide the information necessary to answer these questions for any clinical problem involving the nervous system and to provide a description of the mechanism by which the patient's symptoms and findings are produced by the underlying disorder.

Organization

The solution of a neurologic problem requires three levels of knowledge, and this text is therefore organized into three sections. Section I provides general information necessary to understand how neurologic disorders are diagnosed. The remainder of the text is organized to enable a precise topographic and etiologic diagnosis. Topographic localization initially requires relating the patient's functional impairment to one of six major longitudinal systems (Section II) and then localizing the lesion at a well-defined level of the nervous system (Section III).

Survey of the Neurosciences

The clinician must first have an understanding of the methods utilized in diagnosing a neurologic disorder. How is a lesion localized, and what do the general anatomic terms used to describe localization refer to? How is a pathologic or etiologic diagnosis determined, and what do the terms used to describe them mean? These questions require a general knowledge of the diagnostic principles of neurologic disorders as these principles relate to the anatomy, physiology, and pathology of the nervous system. Chapters 2 through 5 provide a common basic vocabulary and the background knowledge necessary to begin solving clinical problems. These chapters cover the following subjects:

Chapter 2: Organization of the Nervous System: Neuroembryology
Chapter 3: Diagnosis of Neurologic Disorders: Anatomic Localization
Chapter 4: Diagnosis of Neurologic Disorders: Neurocytology and the Pathologic Reactions of the Nervous System
Chapter 5: Diagnosis of Neurologic Disorders: Transient Disorders and Neurophysiology

Longitudinal Systems

Increasingly detailed knowledge of the anatomy and physiology of the nervous system is required for a precise diagnosis of a neurologic disorder. The clinician usually first identifies the patient's symptoms and signs as indicative of disease involving one or more of six major longitudinal subdivisions of the nervous system. These longitudinally organized groups of structures are called *systems* within the nervous system, each subserving a specific function. In this section the anatomy, physiology, and clinical expression of disease as it affects the following six major longitudinal systems are described:

Chapter 6: The Cerebrospinal Fluid System
Chapter 7: The Sensory System
Chapter 8: The Consciousness System
Chapter 9: The Motor System
Chapter 10: The Visceral System
Chapter 11: The Vascular System

The name of each system characterizes its function. Correlation of the symptoms and signs with the appropriate system permits localization of the disease process in one dimension.

Levels of the Neuraxis

The final step in localizing a lesion requires identification of an additional dimension—de-

termining its location along the length of the systems involved. Although a precise localization can be made in many cases, most clinicians classify the disorder according to one of four major regions defined by the bony structures surrounding much of the nervous system. The final part of the text explores the ways in which functions in each major system are integrated and modified at each of the following levels:

Chapter 12: The Peripheral Level
Chapter 13: The Spinal Level
Chapter 14: The Posterior Fossa Level
Chapter 15: The Supratentorial Level

In all these sections, there is repetition of material, with each subsequent section building on the basic information presented earlier to provide amplification and reemphasis. This approach to clinical neurologic problems can be used with any of the problems that may be encountered and is particularly useful in problems that are new, unfamiliar, or unusual to the clinician. While the identification of diseases by recognition of a particular syndrome sometimes can be very efficient, the method of inductive reasoning presented herein is consistently more accurate and more reliable.

Survey of the Neurosciences

Organization of the Nervous System: Neuroembryology

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The study of neurosciences begins with a survey of neuroembryology because it provides a framework and background for understanding the anatomy of the nervous system in the adult. The eventual location of the structures in the brain is not a random occurrence, but is a reflection of the orderly development of the primitive nervous system. Neuroembryology also serves as an aid in understanding the pathogenesis of developmental neurologic abnormalities that are encountered not only in the newborn and pediatric periods but also in later life.

Overview

By the eighteenth day of embryonic development, the early stage of gastrulation has been completed. The embryo consists of two layers and a thickened area, the primitive streak. A long, narrow group of cells, the notochord, extends forward from the primitive streak between the ectoderm and the endoderm. The ectoderm overlying the notochord folds in to form the neural tube from which the entire central nervous system develops.

The neural tube undergoes longitudinal differentiation into six regions: telencephalon (cerebral hemispheres), diencephalon (thalamus and hypothalamus), mesencephalon (midbrain), metencephalon (pons and cerebellum), myelencephalon (medulla), and the spinal cord. At the same time, two columns of cells (the neural crests) separate from the neural tube and will form most of the peripheral nervous system. These subdivisions of the neural tube are the precursors of the four major anatomic levels in the adult: supratentorial (telencephalon and diencephalon), posterior fossa (mesencephalon, metencephalon, and myelencephalon), spinal (spinal cord), and peripheral.

The neural tube also undergoes transverse differentiation with the formation of a dorsal region, the alar plate, which will subserve sensory functions, and a ventral region, the basal plate, which will subserve motor functions. At each level, the cavities of the tube are modified to form the fluid-filled spaces, the ventricular system. Mesodermal tissues grow into the neural tube and form blood

vessels. These transverse subdivisions are the basis of the major functional systems: sensory, consciousness, motor, visceral, cerebrospinal fluid, and vascular.

Throughout the length of the neural tube, cells differentiate into neurons and supportive cells (ependyma, astrocytes, and oligodendroglia). The neurons formed initially in the ependymal layer migrate outward to the mantle layer where they send out axons to form the peripheral, marginal layer. The cells of the neural crest differentiate into the dorsal root ganglia, the autonomic ganglia, and Schwann cells.

Disorders of development of the nervous system may occur in any of these steps. These disorders can be classified as failures of fusion of the neural tube (for example, spina bifida and myelomeningocele) or failure of proliferation and migration (for example, lissencephaly and polymicrogyria).

Formation of the Neural Tube

The nervous system is commonly divided into central and peripheral components. The central nervous system is that part located within the spinal column and skull. It is formed from the neural tube between the eighteenth and the twenty-fifth day of gestation. The peripheral nervous system is derived from the neural crest. Before these structures are formed, at the end of the second week of gestation, gastrulation has been completed. The longitudinal axis of the two-layered embryonic disk is established by the formation of an area of rapidly proliferating cells, the *primitive streak*. The midline of the embryo is defined by the growth of the *notochord,* a group of mesodermal cells that grow forward from one end of the primitive streak (Hensen's node) in a plane between the ectoderm and the endoderm. The mesoderm of the remainder of the embryonic disk is formed by the outgrowth of mesodermal cells from the lateral margins of the primitive streak. As the notochord and mesodermal tissues grow forward, the primitive streak becomes incorporated into the tailbud, and a three-layered embryo with a clearly delineated longitudinal axis is formed. These early changes set the stage for the subsequent events that establish the neural tube, the morphologic substrate of the adult nervous system.

The neural tube is formed in approximately 1 week, beginning on the eighteenth day. The initial step in its formation is a thickening of the ectoderm in the dorsal midline overlying the notochord to form the *neural plate* (Fig. 2-1 *A, B*). The lateral edges of the neural plate thicken more rapidly than the center and begin to roll toward the midline, creating the *neural groove,* which has lateral margins, the *neural folds*. With continued growth, the neural folds

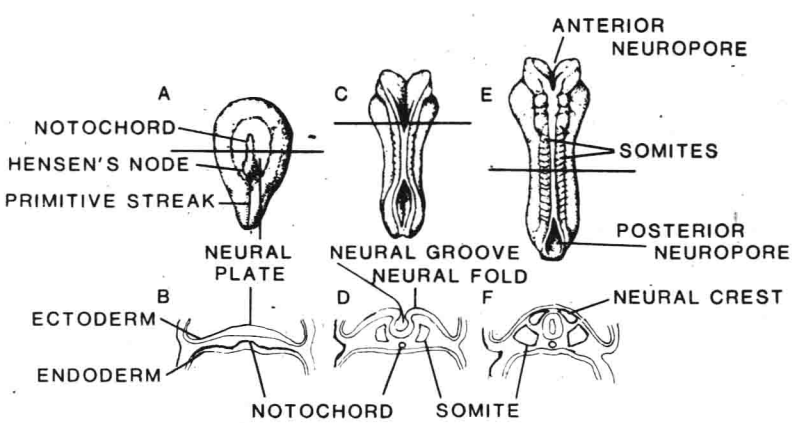

Figure 2-1. Formation of neural tube (eighteenth to twenty-fifth day). A. *Dorsal view of neural plate forming over notochord, which has grown forward from Hensen's node between ectoderm and endoderm.* B. *Cross section through neural plate shown in* A. C. *Dorsal view of early closure of neural tube.* D. *Cross section through neural tube shown in* C. E. *Dorsal view of almost complete closure of neural tube, and formation of well-defined somites.* F. *Cross section through* E.