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SECOND EDITION

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Neuroscience

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DEDICATION

To my mentor, Dr. Patricia Butler who, as the Associate Dean of Educational Programs at the University of Texas Medical School at Houston, inspires us all to excellence in the dissemination of knowledge. She has made a tremendous impact on countless medical students and faculty.

—ECT

My work on this book is dedicated to the memory of my father, Harry Snyder, and in honor of my mother, Martha Snyder, who inspired me to strive for excellence in helping others. I also dedicate this to my sons, Ciaran and Madden, whom I hope, in turn, to inspire in the same way. And I dedicate this to my wife, Angela, who helps me to be the best person I can.

—EYS

To my greatest mentors—my parents Joseph and Farideh. Your guidance and support have allowed me to always follow my passion and dreams. For this, I am eternally grateful.

—JN

To my grandfather, Mani Ram Jandial, for creating a family foundation of both loyalty and audacity, principles from which I continue to benefit and hope to pass on to my own beloved sons, Ronak, Kai, and Zain.

—RJ

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We appreciate all the kind remarks and suggestions from the many medical students over the past 5 years. Your positive reception has been an incredible encouragement, especially in light of the short life of the *Case Files*[®] series. In this second edition of *Case Files*[®]: *Neuroscience*, the basic format of the book has been retained. Improvements were made in updating many of the chapters including a new case correlation section, in which related cases are referenced to allow the student to review other neurobiological concepts or disease concepts. A new case of subarachnoid hemorrhage has been added. Expanded neuroscience pearls with clinical points highlighting common material covered in the USMLE step 1 have been included. The multiple-choice questions have been carefully reviewed and rewritten to ensure that they comply with the National Board and USMLE format. Through this second edition, we hope that the reader will continue to enjoy learning diagnosis and management through the simulated clinical cases. It certainly is a privilege to be teachers for so many enthusiastic and receptive students, and it is with humility that we present this second edition.

The Authors

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Eugene C. Toy, MD

Mastering the extensive and diverse areas of knowledge within a field as broad as neuroscience is a formidable task. It is even more difficult to draw on that knowledge, relate it to a clinical setting, and apply it to the context of the individual patient. To gain these skills, the student learns best with good models, appropriate guidance by experienced teachers, and inspiration toward self-directed, diligent reading. Clearly, there is no replacement for education at the bench. Even with accurate knowledge of the basic science, the application of that knowledge is not always easy. Thus, this collection of patient cases is designed to simulate the clinical approach and stress the clinical relevance to the neurosciences. However, it should also be remembered that, although we often talk about basic research as going “from bench to bedside”, it is actually the inquisitiveness and insight and hypotheses of the clinician that drives basic researchers to ponder certain questions at the bench. Hence the pathway of “bedside-to-bench” is equally as powerful. It is that pathway that we hope this book might also stimulate among its readers.

Most importantly, the explanations for the cases emphasize the mechanisms and structure–function principles rather than merely rote questions and answers. This book is organized for versatility to allow the student “in a rush” to go quickly through the scenarios and check the corresponding answers or to consider the thought-provoking explanations. The answers are arranged from simple to complex: the bare answers, a clinical correlation of the case, an approach to the pertinent topic including objectives and definitions, a comprehension test at the end, neuroscience pearls for emphasis, and a list of references for further reading. A listing of cases is included in Section III to aid the student who desires to test his/her knowledge of a certain area or to review a topic including basic definitions. We intentionally used open-ended questions in the case scenarios to encourage the student to think through relations and mechanisms.

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SECTION I

Approach to Learning Neurosciences

Part 1. The Big Picture

Part 2. Know the Tracts

Part 3. Understand the Terminology

The Big Picture

Neuroscience is unique in that it incorporates an understanding of science on multiple levels, from a molecular understanding of events such as with receptors, at the synaptic level, to a global understanding of the sensory/motor tracts and their spatial interactions. It is by understanding all these concepts that a student can better grasp the clinical presentations of neurological disorders and the theory behind treatment options. The student should thus approach each neuroscience topic from both aspects if applicable. For example, when studying **multiple sclerosis (MS)**, the student should understand that on the molecular level this disease involves destruction of **oligodendrocytes**, which are responsible for creating and maintaining **myelin sheaths** around axons of the central nervous system. The student should then review the **nodes of Ranvier** and concepts pertaining to **saltatory conduction**. Next, the student should take a step back and look at the condition from a neuroanatomic perspective. For example, if the patient with MS presents with left impaired adduction on right gaze, but has normal convergence, and normal left abduction on left gaze, not only should the student be able to diagnose the patient with a left **intranuclear ophthalmoplegia (INO)**, but should also understand that the lesion is in the left **medial longitudinal fasciculus (MLF)** and then proceed to review the anatomy of the MLF tract (ie, that the left MLF yokes the left cranial nucleus VI to the right cranial nucleus III). The student should strive for an understanding such that symptoms should make sense rather than rely on blind memorization!

Know the Tracts

There is no way to avoid it; the student has to memorize the various neural tracts (ie, spinothalamic tract, corticospinal tract, etc.) **forward and backward**. It is easier to first take each tract separately and memorize the exact pathway the neurons in that tract travel throughout the body, noting any decussations or synapses so that the student can determine whether lesions would have ipsilateral (same side as the lesion) or contralateral (opposite side of the lesion) symptoms, or which nuclei are involved. The **second step** would be to **synthesize this information** by taking various cross-sections of the nervous system (from the spinal cord to the brain) and being able to identify where each tract is, reviewing at the same time where that tract is coming from upstream and going to downstream. It is important to note that the terms *upstream* and *downstream* may be different spatially, depending on the tract referred to. For example, *upstream* means a cross-section *above* the one being studied when referring to the corticospinal tract since the tract travels caudally. However, *upstream* means a cross-section *below* the one being studied when referring to the spinothalamic tract since this tract travels cranially (from the peripheral inputs to the cortex). The third step involves knowing the cross-sections so thoroughly that the student can draw any cross-section, incorporating all the tracts and nuclei involved in that cross-section. Throughout the studying process, the students should be asking themselves, *if there is a lesion in this structure or at this level, what symptoms will be manifested?*

Understand the Terminology

Although it takes less effort to memorize medical terminology without understanding the origin of the term, it is much more effective in the long term to understand the reason behind the name of a structure or pathological condition. Going back to our example of MS, the *scleroses* refers to the plaques or lesions in the white matter, while the term *multiple* refers to variety in location and time. In other words, in order to diagnose MS, a patient must have at least two anatomically separate lesions occurring at two distinct time periods. Similarly, the student should not just simply memorize structures like the previously mentioned *spinothalamic tract* and *corticospinal tracts*. Rather, the student should understand that the *spinothalamic* tract receives input at the *spinal* cord level that travels to and synapses in *thalamic* nuclei. Likewise, the *corticospinal* tract sends information originating from cells in motor *cortex* to the *spinal cord*, which eventually coordinates muscular movement via the lower motor neurons.

NEUROSCIENCE PEARLS

- ▶ The student should seek to understand the neuroscience on a molecular level, synaptic level, and a higher level such as sensory/motor tract level.
- ▶ An understanding of the neural tracts should allow synthesis and drawing the cross-sections from brain to spinal cord.
- ▶ The student should strive to understand medical terminology rather than blindly memorizing.

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SECTION II

Clinical Cases

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CASE 1

A 53-year-old man presents to the emergency department following a new-onset generalized seizure. After recovery from the seizure period, he is alert and oriented to person, place, and time, although he has no specific memory of the seizure. There are no neurological deficits noted on the physical examination, but magnetic resonance imaging (MRI) and positron emission tomography (PET) scans indicate the presence of a sizable lesion. The patient undergoes surgery for resection of the malignancy and is diagnosed with a malignant primary brain tumor, which is identified as a glioblastoma multiforme (GBM). The neurosurgeon's plan is to place the patient on long-term seizure prophylaxis and steroids in combination with stereotactic radiotherapy.

- ▶ What other types of tumors are most closely related to this patient's malignancy?
- ▶ What are the imaging findings most characteristic of these types of tumors?
- ▶ What are the hallmark pathological findings of these types of tumors?

ANSWERS TO CASE 1:

Cell Types of the Nervous System

Summary: A 53-year-old man with new-onset seizure and a left parietal lobe mass undergoes surgery to resect a primary brain tumor, diagnosed as a GBM. He also receives adjuvant radiation treatment.

- **Related tumors:** Low-grade astrocytomas and anaplastic astrocytomas.
- **Imaging characteristics:** A ring-enhancing lesion in the left parietal lobe with surrounding edema and mass effect.
- **Neuropathological findings:** GBMs exhibit marked hypercellularity, nuclear pleomorphism, microvascular proliferation, and pseudopalisading of tumor cells around areas of necrosis.

CLINICAL CORRELATION

The clinical presentation of this patient is very typical for GBM, the most severe and malignant form of primary intracranial tumor.

Astrocytomas are a group of primary brain tumors derived from astrocytes, the star-shaped glial cells forming the latticework structure that supports neuron function (see Discussion). The World Health Organization (WHO) classifies astrocytomas on a continuum from grades I to IV, based on pathological findings. Grades I and II consist of low-grade astrocytomas, grade III consists of anaplastic astrocytomas, and grade IV includes GBMs, which represent 15%-20% of all primary brain cancers. Tumor types on the WHO continuum exhibit progressively more hypercellularity and nuclear pleomorphism (a nonhomogeneous group of cells with nuclei of various sizes and shapes). Proliferation of tumor cells around vascular structures along white matter tracts occurs in both anaplastic astrocytomas and GBMs. Necrosis with pseudopalisading of tumor cells is only found in GBMs.

A wide array of symptoms ranging from drowsiness and fatigue to motor and communication difficulties has been reported. Treatment consists of surgery, radiotherapy, and chemotherapy, either individually or in combination. Despite continued advances in therapeutic approach, the prognosis of GBM remains unfavorable, and median survival for patients has remained consistently low (Table 1-1). Due to the highly aggressive nature of GBMs and the frequency of tumor recurrence, regular

Table 1-1 • SURVIVAL ESTIMATES FOR ASTROCYTOMAS

Astrocytoma Type (WHO Grade)	Median Survival
Low-grade astrocytomas (I)	8-10 years
Low-grade astrocytomas (II)	7-8 years
Anaplastic astrocytomas (III)	~2 years
Glioblastoma multiforme (IV)	<1 year

tumor surveillance through imaging and clinical evaluation remains vital for disease management.

Oligodendroglioma is another type of primary brain tumor that arises from the oligodendrocyte. This is the glial cell that provides the myelin sheaths around the axons of neurons in the central nervous system. Oligodendrogliomas generally affect adults in their fifth decade of life, developing in the frontal lobes and presenting with seizures. They have a characteristic appearance on radiographs and on microscopic examination, due to the calcifications pattern in the tumor. Similar to the management of astrocytomas, treatment is multimodal and consists of an appropriate surgical procedure followed by radiation and chemotherapy. The presence or absence of specific chromosomal deletions on the long arm of chromosome 1 or the short arm of chromosome 19 has been shown to affect the sensitivity of these tumors to chemotherapy. Oligodendrogliomas tend to have a better prognosis than astrocytomas, with a 10-year survival of 10%-30% reported in the literature.

Other tumors arising from cells of the nervous system include mixed tumors with oligodendral and astrocytic components, **schwannomas** arising from **Schwann cells** of the peripheral nervous system, and **gangliogliomas** arising from both glial cells and neurons. This list is not exhaustive but is representative of the variety of pathologies found in primary brain tumors.

APPROACH TO:

Cell Types of the Nervous System

OBJECTIVES

1. Differentiate between the central and peripheral nervous systems.
2. Know the names of each cell type in the nervous system.
3. Describe the role of each cell type within the nervous system.
4. Identify the components that make up the blood-brain barrier (BBB).

DEFINITIONS

MENINGES: A series of three membranes which encapsulates the central nervous system (CNS).

SUBARACHNOID SPACE: The space between the arachnoid and pia maters that contains delicate connective tissue, blood vessels, and cerebrospinal fluid (CSF).

GLIAL CELLS: Cells that support neurons and form the structural framework for the nervous system. These include astrocytes, oligodendrocytes, and microglia.

MYELIN: A phospholipid bilayer which insulates the axon and allows for faster propagation of an action potential, commonly referred to as saltatory conduction.

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