HOSPITAL PHYSICIAN®

NEUROLOGY BOARD REVIEW MANUAL

STATEMENT OF EDITORIAL PURPOSE

The *Hospital Physician Neurology Board Review Manual* is a peer-reviewed study guide for residents and practicing physicians preparing for board examinations in neurology. Each manual reviews a topic essential to the current practice of neurology.

NOTE FROM THE PUBLISHER:
This publication has been developed without involvement of or review by the American Board of Psychiatry and Neurology.

Ischemic Stroke: Pathophysiology and Principles of Localization

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INTRODUCTION

Stroke is a sudden loss of neurologic function resulting from focal disturbance of cerebral blood flow due to ischemia or hemorrhage. Depending on the duration of the cerebrovascular disturbance, stroke can cause permanent neurologic damage, disability, or death. A transient ischemic attack (TIA; stroke symptoms lasting < 1 hr) may not cause neurologic damage but is strongly associated with a risk for subsequent stroke within the next 90 days. Stroke is the third leading cause of death in the United States, with only heart disease and cancer accounting for more mortality.[1] Ischemic stroke accounts for 87% of all strokes.[1] Among persons aged 45 to 64 years, 8% to 12% of ischemic strokes result in death within 30 days.[1]

Although a life-threatening emergency, ischemic stroke is a treatable condition; the degree of disability is linked with response to treatment. The adept clinician must efficiently synthesize a broad array of clinical data to make rapid decisions when managing this critically ill population. Despite an ever-growing arsenal of sophisticated neuroimaging techniques and laboratory studies for managing suspected stroke, the clinical approach to these patients remains firmly grounded in its dependence on the core principles neurology: diagnosis of the disease process and lesion localization based on history and neurologic examination.

This manual, the first part of a 2-part review of ischemic stroke, provides an overview of stroke pathophysiology and principles of stroke localization. The next manual will discuss the approach to evaluation of a patient with suspected ischemic stroke, acute and later-stage treatment of ischemic stroke, and strategies for prevention.

PATHOPHYSIOLOGY OF ISCHEMIC STROKE

MECHANISMS OF ISCHEMIA

Although there are many etiologic mechanisms, the common pathway of ischemic stroke is lack of sufficient blood flow to perfuse cerebral tissue. Interruption of forward blood flow at any point can lead to irreversible neuronal damage. The mechanisms of ischemia can generally be divided into 5 main categories: thrombosis, embolism, systemic hypoperfusion, arterial luminal obliteration, and venous congestion. Cerebral venous thrombosis can lead to vascular congestion, impairment of forward flow, and eventually infarction. The evaluation and management of venous thrombosis requires many unique considerations in contrast to arterial etiologies and is beyond the scope of this review. Ischemic stroke mechanisms in the other 4 main categories are summarized in **Table 1** and discussed in more detail below.

Many classification schemes exist for assigning an etiologic mechanism for ischemic stroke, the most widely used of which is TOAST (a set of criteria originally developed for the Trial of Org 10172 in Acute Stroke Treatment).[2] The refined and updated TOAST criteria, known as SSS-TOAST, use a combination of historical, laboratory, cardiovascular, and neuroimaging data to assign a mechanism using a degree of certainty derived from the annual or one-time primary stroke risk threshold for each evaluated factor based on best evidence from the literature. Causative mechanisms are grouped into 1 of 5 categories: large artery atherosclerosis, cardioaortic embolism, small artery occlusion, other causes (an identified cause recognized as an etiology for stroke, such as arterial dissection), or undetermined based on descriptive criteria.[3]

Thrombosis

In situ thrombosis is the formation of a clot in an artery that persists long enough to cause ischemic insult to the cerebral tissue supplied by the affected vessel. Thrombosis is often triggered by pathology in the local endothelium. Atherosclerotic plaques are inherently prothrombotic, overexpressing plasminogen activator inhibitor-1 (the main inhibitor of tissue plasminogen activator) and tissue factor. *Chlamydia pneumoniae* is associated with atherosclerotic plaques, and further inflammatory activity is attributable to activated macrophages and T cells that congregate in high-shear regions. In