CHAPTER 5

TREATMENT ALGORITHMS FOR NEUROLOGICAL DISORDERS

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Abstract

Neurological treatment algorithms are highly time-sensitive and etiology-specific, aimed at preventing neuronal death, controlling abnormal signaling, or slowing progressive degeneration. The algorithm for acute ischemic stroke is one of emergency reperfusion, stratified by time from onset, using intravenous thrombolysis (alteplase) within 4.5 hours or mechanical thrombectomy up to 24 hours for large vessel occlusions. The epilepsy algorithm is stratified by seizure type (focal vs. generalized), with the goal of achieving seizure freedom via first-line monotherapy (e.g., levetiracetam, valproate); failure leads to a stepwise trial of alternative or adjunctive agents. The status epilepticus algorithm is a rapid, timed protocol beginning with benzodiazepines. Multiple sclerosis management is bifurcated: acute relapses are treated with high-dose corticosteroids, while the long-term algorithm involves early initiation of disease-modifying therapies (DMTs), selected based on an "escalation" vs. "induction" strategy. Parkinson's disease follows a symptomatic algorithm, initiating therapy with MAO-B inhibitors or dopamine agonists in younger patients, and progressing to levodopa/carbidopa as the gold standard for motor control, with adjunctive therapies to manage motor fluctuations. Alzheimer's disease management is currently symptomatic, using cholinesterase inhibitors (e.g., donepezil) for mild-to-moderate stages and memantine for moderate-to-severe disease to modestly improve cognition and function.

Keywords: *Neurological Algorithms, Stroke, Epilepsy, Multiple Sclerosis, Parkinson's Disease, Alzheimer's Disease*

Learning Objectives

After completion of the chapter, the learners should be able to:

- Identify the critical time window for alteplase (tPA) administration in the treatment algorithm for acute ischemic stroke.
- Explain the rationale for selecting a first-line anti-epileptic drug based on seizure type (e.g., focal vs. generalized vs. absence).
- Select an appropriate therapeutic algorithm (e.g., abortive vs. prophylactic) for a patient with chronic migraines.
- Differentiate the treatment algorithms for acute multiple sclerosis relapses versus long-term disease-modifying therapy.
- Justify the sequencing of pharmacological agents (e.g., levodopa vs. dopamine agonists) in the management of Parkinson's disease based on patient age and symptoms

STROKE

A stroke is a medical emergency characterized by a sudden interruption of the blood supply to the brain, causing neurologic deficits. The treatment algorithm is one of the most time-sensitive in medicine, as "time is brain."

Pathophysiology

Stroke is a clinical syndrome of acute focal neurologic deficit caused by a vascular event. The pathophysiology is dichotomous, defining the two major types of stroke.

Ischemic Stroke (80-85%)

The core pathophysiology is the abrupt cessation of blood flow to a region of the brain, leading to infarction. This occlusion is typically thrombotic (an atherosclerotic plaque ruptures within a cerebral artery) or embolic (a clot, often from the heart in atrial fibrillation, travels to and lodges in a cerebral artery). The brain tissue at the center of the occlusion, the "ischemic core," dies within minutes. Surrounding this core is the "penumbra," a region of dysfunctional but viable tissue maintained by collateral circulation. The entire acute treatment algorithm is based on salvaging this penumbra before it, too, infarcts.

Hemorrhagic Stroke (15-20%)

The pathophysiology is not ischemia, but direct tissue damage from an expanding hematoma and the toxic effects of blood components. **Intracerebral Hemorrhage (ICH)** is most often caused by chronic hypertension leading to rupture of small, deep-penetrating arteries (e.g., lenticulostriate). **Subarachnoid Hemorrhage (SAH)** is typically due to the rupture of a saccular "berry" aneurysm at an arterial bifurcation in the Circle of Willis. In both, the expanding blood collection causes a toxic injury and increases intracranial pressure (ICP), which can lead to herniation and death.

Diagnosis and Classification

The diagnostic algorithm begins with rapid clinical recognition of symptoms (e.g., F.A.S.T. - Face, Arms, Speech, Time). Upon emergency department arrival, the algorithm mandates an immediate non-contrast head CT scan. This imaging is the critical first branch point, differentiating:

- **Ischemic Stroke (85%):** Caused by a thrombus or embolus. The CT scan is typically normal in the first few hours.
- **Hemorrhagic Stroke (15%):** Caused by bleeding into the brain (intracerebral) or surrounding space (subarachnoid). The CT scan immediately shows hyperdense (white) blood. A Transient Ischemic Attack (TIA) is a transient stroke syndrome without acute infarction; its algorithm is one of urgent secondary prevention.

Differential Diagnosis

Stroke "mimics" are common. The differential diagnosis includes seizure with post-ictal paralysis (Todd's paralysis), complex migraine (hemiplegic migraine), hypoglycemia, systemic infection with sepsis-associated encephalopathy, and Bell's palsy (for isolated facial droop). A non-contrast head CT and a point-of-care glucose test are the fastest tools to navigate this differential.

Treatment Algorithm

Acute Ischemic Stroke Algorithm

This algorithm is strictly time-dependent.

- **Intravenous Thrombolysis:** Patients presenting within a 4.5-hour window from "last known normal" who have no contraindications (e.g., active bleeding, recent major surgery, uncontrolled hypertension) are candidates for intravenous alteplase (tPA). The "door-to-needle" time goal is < 60 minutes.
- **Mechanical Thrombectomy:** Patients with a large vessel occlusion (LVO) in the proximal anterior circulation are candidates for endovascular thrombectomy. The algorithm allows for this intervention up to 24 hours from last known normal, based on advanced imaging (CT perfusion) that identifies a salvageable penumbra.
- **General Measures:** All patients require blood pressure management (permissive hypertension, e.g., < 185/110 mmHg for tPA, < 220/120 mmHg if no tPA) and supportive care.

Secondary Prevention Algorithm

After the acute phase, the algorithm shifts to preventing recurrence. This includes:

- **Antiplatelet Therapy:** Aspirin is given acutely. For minor strokes or TIA, dual antiplatelet therapy (DAPT) with aspirin and clopidogrel is given for 21-90 days, followed by antiplatelet monotherapy.
- **Anticoagulation:** If the stroke is determined to be cardioembolic (e.g., from atrial fibrillation), antiplatelet therapy is transitioned to long-term anticoagulation.
- **Statin Therapy:** All patients with ischemic stroke, regardless of baseline LDL, are started on high-intensity statin therapy (e.g., atorvastatin 80 mg).
- **Risk Factor Control:** Aggressive management of hypertension, diabetes, and lifestyle factors is initiated.

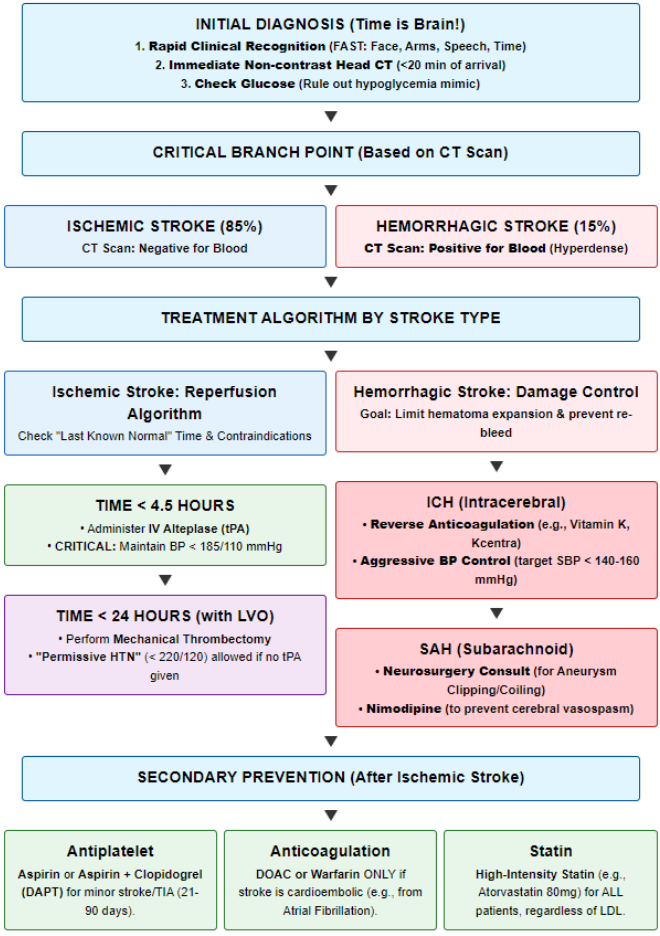

Figure 5.1: Stroke

Monitoring and Follow-Up

Ischemic Stroke

Post-reperfusion monitoring is critical.

- Post-tPA: The patient must be monitored in an ICU or stroke unit. Neurologic checks (using the NIHSS) and vital signs are required every 15 minutes for 2 hours, then every 30 minutes for 6 hours, then hourly for 16

hours. The primary focus is monitoring for hemorrhagic conversion (worsening NIHSS, severe headache, N/V), which requires an emergent head CT. Blood pressure must be meticulously kept below 180/105 mmHg.

- Post-Thrombectomy: Monitoring involves frequent neuro checks and vital signs, as well as puncture site (e.g., femoral) checks for bleeding or hematoma.

Table 5.1: Acute Stroke Management Algorithms

Stroke Type	Diagnostic Test	Immediate Treatment Algorithm
Ischemic (Acute)	Non-contrast Head CT (to exclude bleed)	**If < 4.5 hrs:** IV Alteplase (tPA). **If Large Vessel Occlusion (LVO):** Mechanical Thrombectomy (up to 24 hrs).
Hemorrhagic (ICH)	Non-contrast Head CT	**Reverse** anticoagulation. **Aggressive BP control** (e.g., target SBP < 140-160 mmHg). Surgical consultation.
TIA / Stroke (Secondary Prevention)	MRI, CTA/MRA, Echo	Antiplatelet (Aspirin + Clopidogrel x 21d then monotherapy), High-intensity Statin, BP control.

Hemorrhagic Stroke

Monitoring is focused on ICP and hematoma expansion. Patients are managed in a neuro-ICU with continuous ICP monitoring (if an external ventricular drain is placed), frequent neurologic exams (GCS), and serial head CT scans to ensure the hematoma is not expanding. Blood pressure must be aggressively controlled. For SAH, monitoring also involves screening for cerebral vasospasm (usually 4-14 days post-bleed) using transcranial dopplers.

Long-Term Management / Secondary Prevention

Secondary prevention is the cornerstone of long-term stroke care and is tailored to the stroke's etiology.

Ischemic Stroke

- Cardioembolic (e.g., Atrial Fibrillation): Long-term management is therapeutic anticoagulation (e.g., with a DOAC like apixaban or rivaroxaban).
- Large Artery Atherosclerosis (e.g., Carotid Stenosis): Management includes high-intensity statin therapy, antiplatelet therapy (e.g., aspirin + clopidogrel), and potential carotid endarterectomy or stenting for significant stenosis.
- Small Vessel (Lacunar): Management is strict blood pressure control and an antiplatelet agent.
- Universal: All ischemic stroke survivors require aggressive management of risk factors: hypertension (BP goal < 130/80), hyperlipidemia (high-intensity statin), diabetes, and smoking cessation.

Hemorrhagic Stroke

Management is focused on preventing re-bleeding. For SAH, this involves definitive neurosurgical (clipping) or endovascular (coiling) treatment of the ruptured aneurysm. For ICH, the focus is on aggressive, long-term blood pressure control (e.g., target < 130/80 mmHg).

Patient Counseling Points

1. "**Time is Brain":** This is the most critical counseling point for the patient and their family. They must be taught to recognize the F.A.S.T. (Face drooping, Arm weakness, Speech difficulty, Time to call emergency services) signs and to call emergency services *immediately*. Counsel them *not* to "wait and see" or "drive to the hospital."
2. **Risk Factor Modification:** "A stroke is a 'brain attack,' and it is a warning." Emphasize that the risk of a *second* stroke is extremely high and that controlling blood pressure, cholesterol, and blood sugar (and stopping

smoking) is not optional, but essential for survival.

3. **Anticoagulation vs. Antiplatelet:** For patients with AFib, explain the difference. "An aspirin is not enough. Your stroke came from a clot from your heart, which requires a 'blood thinner' (anticoagulant) to prevent. An antiplatelet is for clots from plaque in the arteries."
4. **Rehabilitation:** Frame rehabilitation (PT, OT, speech therapy) as the active, primary treatment for recovery. Emphasize that neurologic recovery is a long process that requires intensive work and participation.

Common Pitfalls in Management

The most critical pitfall is a delay in diagnosis or treatment, resulting in a missed tPA or thrombectomy window. Another is violating tPA contraindications, leading to hemorrhagic transformation. In secondary prevention, a common error is failing to screen for atrial fibrillation (e.g., with prolonged cardiac monitoring), thereby missing an indication for anticoagulation. Misdiagnosing a stroke mimic *as* a stroke can lead to unnecessary and harmful tPA administration.

Case Study

A 68-year-old female (Ms. Johnson) is at home when she suddenly develops slurred speech and a complete right-sided facial droop and arm weakness. Her husband calls emergency services immediately. She arrives at the ED **60 minutes after symptom onset**. Her BP is 175/98 mmHg.

Discussion

This is a classic acute stroke presentation, well within the "golden hour." The algorithm is "Time is Brain." The immediate priority is to get a non-contrast head CT to differentiate ischemic from hemorrhagic stroke, as this is the main branch point of the entire algorithm.

Treatment Algorithm

1. **Triage:** A "Stroke Alert" is called. The patient is taken directly to the CT scanner.
2. **Algorithm Step 1 (Imaging):** A **Non-Contrast Head**

CT is completed. It is **NEGATIVE for any bleeding**.

3. **Diagnosis:** This confirms an **Acute Ischemic Stroke**.
4. **Algorithm Step 2 (Reperfusion):**
    - **Time:** Her "last known normal" is 60 minutes ago, placing her well within the **4.5-hour window for thrombolysis**.
    - **Contraindications:** She has no contraindications. Her BP is <185/110 mmHg.
    - **Therapy:** The algorithm dictates immediate IV **Alteplase (tPA)**.
5. **Monitoring:** She is admitted to the Stroke Unit for close neurologic and blood pressure monitoring.

Outcome

Ms. Johnson receives IV tPA at 75 minutes after symptom onset. Over the next 24 hours, her arm strength and speech begin to improve significantly

EPILEPSY

Epilepsy is a chronic neurological disorder characterized by an enduring predisposition to generate epileptic seizures. A diagnosis of epilepsy requires at least two unprovoked seizures occurring > 24 hours apart.

Pathophysiology

A seizure is a transient occurrence of signs/symptoms due to abnormal, excessive, or synchronous neuronal activity in the brain. The core pathophysiology is a state of **neuronal hyperexcitability**. This is caused by an imbalance between excitatory (glutamatergic) and inhibitory (GABAergic) neurotransmission. This imbalance can arise from many causes: genetic mutations in ion channels (channelopathies), structural brain lesions (e.g., tumors, scars from a prior stroke or trauma), or metabolic/autoimmune processes. A "seizure focus" is a region of the brain where this hyperexcitability begins. A focal seizure remains localized to one hemisphere, while a generalized seizure involves and spreads to both hemispheres

from the onset.

Diagnosis and Classification

The diagnostic algorithm begins with a detailed clinical history of the seizure event (semiology) and a neurologic exam. An electroencephalogram (EEG) is used to look for interictal epileptiform discharges, and brain imaging (MRI) is used to search for a structural etiology. The algorithm then classifies the epilepsy type, which is the most critical step for treatment selection:

Focal Onset

Seizures originating in one hemisphere (e.g., focal aware, focal impaired awareness).

Generalized Onset

Seizures originating in and rapidly engaging bilateral networks (e.g., absence, tonic-clonic, myoclonic).

Unknown Onset

Insufficient evidence to classify.

Differential Diagnosis

The primary differential is syncope (cardiovascular vs. vasovagal), which is characterized by a brief loss of consciousness with a rapid recovery, unlike the typical post-ictal confusion of a seizure. Other main differentials include complex migraines, TIAs, and psychogenic non-epileptic seizures (PNES), a psychiatric condition that requires video-EEG monitoring to diagnose.

Treatment Algorithm

Chronic Epilepsy Algorithm

The goal is seizure freedom with minimal side effects.

- **Step 1: First-Line Monotherapy:** An anti-seizure medication (ASM) is chosen based on the epilepsy type.
    - **Focal Epilepsy:** First-line agents include levetiracetam, lamotrigine, or carbamazepine.
    - **Generalized Epilepsy:** Broad-spectrum agents are required. Valproic acid is highly