Ischaemic Stroke: Pathophysiology, Signs and Treatment

Acute ischemic stroke is a sudden neurological deficit caused by an interruption of blood flow to a part of the brain due to thrombotic or embolic occlusion of cerebral arteries. It accounts for approximately 85–90% of all strokes, making it significantly more common than hemorrhagic stroke (which accounts for 10–15%).

A **stroke** refers to a spectrum of diseases characterized by the abrupt onset of neurological dysfunction due to brain injury caused by:

- **Ischemia** : Inadequate blood supply to the brain tissue (ischemic stroke).
- **Hemorrhage** : Bleeding into the brain parenchyma or surrounding spaces (hemorrhagic stroke).

A transient ischemic attack (TIA) is a transient episode of neurological dysfunction caused by focal brain ischemia without acute infarction, lasting less than 24 hours.

Etiology and Causes of Ischemic Stroke

- **Thrombotic stroke** : Caused by in situ thrombosis over atherosclerotic plaques that narrow cerebral arteries, commonly at carotid bifurcation or large intracranial vessels.
- **Embolic stroke** : Arises from emboli traveling from cardiac sources (e.g., mural thrombi after myocardial infarction, infective endocarditis vegetations, atrial fibrillation).
- **Paradoxical emboli** : Venous emboli bypass pulmonary circulation via right-to-left shunts (e.g., patent foramen ovale).
- **Other causes** : Vasculitis, arterial dissection, hypercoagulable states.

Risk Factors for Stroke

Non-modifiable:

- Age >55 years (stroke risk doubles every decade after 55)
- Male sex (30% higher risk than females)
- Genetic predisposition influencing atherosclerosis and cardiac disease

Modifiable:

- Hypertension (most important risk factor)
- Diabetes mellitus
- Hyperlipidemia
- Cigarette smoking
- Obesity and sedentary lifestyle
- Cardiac diseases (atrial fibrillation, coronary artery disease)
- Substance abuse (e.g., cocaine, amphetamines)

Pathophysiology

Ischemic stroke results from vascular occlusion leading to ischemia and hypoxia in brain tissue. The loss of oxygen supply causes:

- Failure of ATP-dependent ion pumps (Na+/K+ ATPase)
- Cellular depolarization and calcium influx
- Cytotoxic edema due to intracellular water accumulation
- Release of excitatory neurotransmitters (glutamate) causing excitotoxicity
- Generation of free radicals and activation of apoptotic pathways
- Irreversible neuronal injury can occur within minutes (~5 min) in vulnerable brain areas (e.g., hippocampus, neocortex)

The infarct core undergoes necrosis, surrounded by the ischemic penumbra, a region of potentially salvageable tissue targeted by reperfusion therapies.

Clinical Features

The clinical presentation depends on the brain area affected but generally includes:

- **Sudden focal neurological deficits** :
  - Hemiparesis or monoparesis
  - Hemisensory loss
  - Aphasia (dominant hemisphere involvement)
  - Dysarthria
  - Visual field deficits (homonymous hemianopia)
  - Facial droop
  - Ataxia and vertigo (brainstem or cerebellar involvement)
  - Diplopia, nystagmus
- Sudden decrease in consciousness may occur in large strokes.

Diagnostic Evaluation

History and Physical Examination:

- Onset and progression of neurological symptoms
- Stroke risk factors and comorbidities

Neuroimaging:

- **Noncontrast CT scan** : First-line to exclude hemorrhage; may be normal early in ischemic stroke.
- **MRI with diffusion-weighted imaging (DWI)** : Most sensitive for early ischemia detection.
- **CT or MR angiography** : To identify vascular occlusions.
- **Cerebral angiography** : Reserved for intervention planning.

Laboratory Studies:

- Complete blood count (CBC): Detect polycythemia or infection.

- Basic metabolic panel: Rule out metabolic mimics (hypoglycemia, hyponatremia).
- Coagulation profile: Identify coagulopathies.
- Cardiac biomarkers: Evaluate for concurrent myocardial ischemia.
- ECG and echocardiography: Assess cardiac sources of emboli.

Additional tests:

- Lumbar puncture: If suspicion for subarachnoid hemorrhage with negative CT or meningitis.

Management of Ischemic Stroke

Initial stabilization:

- ABCs (Airway, Breathing, Circulation)
- Supportive care including oxygen, fluids, and blood pressure management

Reperfusion therapy:

- **Intravenous thrombolysis (IV tPA)** within 3-4.5 hours of symptom onset (Alteplase 0.9 mg/kg; max 90 mg)
- **Mechanical thrombectomy** for large vessel occlusion within 6-24 hours in selected patients

Antiplatelet therapy:

- Aspirin initiated 24–48 hours post thrombolysis to reduce recurrent stroke risk
- Alternatives: Clopidogrel or dipyridamole if aspirin contraindicated

Secondary prevention:

- Control hypertension, diabetes, and hyperlipidemia
- Smoking cessation and lifestyle modification
- Statins for atherosclerotic disease
- Anticoagulation for cardioembolic sources (e.g., atrial fibrillation)

Neuroprotection (investigational):

- Targeting glutamate excitotoxicity, free radicals, calcium influx, and apoptotic pathways to preserve the ischemic penumbra (currently experimental)

High-Yield Notes for NCLEX/USMLE

- Ischemic stroke accounts for ~85% of strokes; hemorrhagic for ~15%.
- Stroke risk doubles every decade after 55 years of age.
- Sudden onset focal neurological deficit lasting >24 hours is stroke; <24 hours is TIA.
- **Most common cause:** thrombotic occlusion over atherosclerotic plaques.
- Reperfusion with IV tPA must be initiated within 3-4.5 hours.
- Mechanical thrombectomy is for large vessel occlusions and can extend treatment window.
- Early aspirin reduces recurrent ischemic stroke risk but is delayed until 24 hours after

thrombolysis.
- Neuroimaging is essential to rule out hemorrhage before thrombolysis.
- Penumbra: ischemic brain tissue at risk but potentially salvageable with timely treatment.
- Control modifiable risk factors aggressively to prevent primary and secondary stroke.