



**FIGURE 446-2** Major steps in the cascade of cerebral ischemia. See text for details. iNOS, inducible nitric oxide synthase; PARP, poly-A ribose polymerase.

hyperglycemia as much as possible. The value of induced mild hypothermia to improve stroke outcomes is the subject of continuing clinical research.

## TREATMENT ACUTE ISCHEMIC STROKE

After the clinical diagnosis of stroke is made, an orderly process of evaluation and treatment should follow (Fig. 446-1). The first goal is to prevent or reverse brain injury. Attend to the patient's airway, breathing, and circulation (ABCs), and treat hypoglycemia or hyperglycemia if identified. Perform an emergency noncontrast head CT scan to differentiate between ischemic stroke and hemorrhagic stroke; there are no reliable clinical findings that conclusively separate ischemia from hemorrhage, although a more depressed level of consciousness, higher initial blood pressure, or worsening of symptoms after onset favor hemorrhage, and a deficit that is maximal at onset, or remits, suggests ischemia. Treatments designed to reverse or lessen the amount of tissue infarction and improve clinical outcome fall within six categories: (1) medical support, (2) IV thrombolysis, (3) endovascular revascularization, (4) antithrombotic treatment, (5) neuroprotection, and (6) stroke centers and rehabilitation.

### MEDICAL SUPPORT

When ischemic stroke occurs, the immediate goal is to optimize cerebral perfusion in the surrounding ischemic penumbra. Attention is also directed toward preventing the common complications of bedridden patients—infections (pneumonia, urinary, and skin) and deep venous thrombosis (DVT) with pulmonary embolism. Subcutaneous heparin (unfractionated and low-molecular-weight) is safe and can be used concomitantly. Use of pneumatic compression stockings is of proven benefit in reducing risk of DVT and is a safe alternative to heparin.

Because collateral blood flow within the ischemic brain may be blood pressure dependent, there is controversy about whether blood pressure should be lowered acutely. Blood pressure should be lowered if there is malignant hypertension (Chap. 298) or concomitant myocardial ischemia, or if blood pressure is >185/110 mmHg and thrombolytic therapy is anticipated. When faced with the competing demands of myocardium and brain, lowering the heart rate with a  $\beta_1$ -adrenergic blocker (such as esmolol) can be a first step to decrease

cardiac work and maintain blood pressure. Routine lowering of blood pressure has been found to worsen outcomes. Fever is detrimental and should be treated with antipyretics and surface cooling. Serum glucose should be monitored and kept at <10.0 mmol/L (180 mg/dL) using an insulin infusion if necessary.

Between 5 and 10% of patients develop enough cerebral edema to cause obtundation or brain herniation. Edema peaks on the second or third day but can cause mass effect for ~10 days. The larger the infarct, the greater the likelihood that clinically significant edema will develop. Water restriction and IV mannitol may be used to raise the serum osmolarity, but hypovolemia should be avoided because this may contribute to hypotension and worsening infarction. Combined analysis of three randomized European trials of hemicraniectomy (craniotomy and temporary removal of part of the skull) shows that hemicraniectomy markedly reduces mortality, and the clinical outcomes of survivors are acceptable. The size of the diffusion-weighted imaging volume of brain infarction during the acute stroke is a predictor of deterioration requiring hemicraniectomy.

Special vigilance is warranted for patients with cerebellar infarction. These strokes may mimic labyrinthitis because of prominent vertigo and vomiting; the presence of head or neck pain should alert the physician to consider cerebellar stroke from vertebral artery dissection. Even small amounts of cerebellar edema can acutely increase intracranial pressure (ICP) by obstructing cerebrospinal fluid (CSF) flow leading to hydrocephalus or by directly compressing the brainstem. The resulting brainstem compression can manifest as coma and respiratory arrest and require emergency surgical decompression. Prophylactic suboccipital decompression of large cerebellar infarcts before brainstem compression, although not tested rigorously in a clinical trial, is practiced at most stroke centers.

### INTRAVENOUS THROMBOLYSIS

The National Institute of Neurological Disorders and Stroke (NINDS) rtPA Stroke Study showed a clear benefit for IV rtPA in selected patients with acute stroke. The NINDS study used IV rtPA (0.9 mg/kg to a 90-mg maximum; 10% as a bolus, then the remainder over 60 min) versus placebo in ischemic stroke within 3 h of onset. One-half of the patients were treated within 90 min. Symptomatic intracranial hemorrhage occurred in 6.4% of patients on rtPA and 0.6%