Observational studies provide evidence that certain behaviors prevent stroke. Smoking cessation leads to a reduction by 5 years in stroke risk to levels similar to non-smokers. Consumption of alcohol in moderation, up to 2 drinks daily for men and one daily for women is associated with a lower level of stroke risk than in those who do not drink. Physical activity, weight loss when appropriate, and management of diabetes are recommended.

Acute Treatment of Ischemic Stroke

For patients with ischemic stroke evaluated within 3 hours of symptom onset with no evidence of hemorrhage on a brain CT or MRI, recombinant tissue plasminogen activator (rt-PA), a thrombolytic agent, improves functional outcomes at 3 months compared to placebo. Among the 624 ischemic stroke patients treated within 3 hours in the original landmark study, the proportion of patients achieving normal or near-normal neurological and functional status by 3 months was significantly higher among those receiving rt-PA, though there was no definite benefit at 24 hours. The proportion of patients who achieved independence in their performance of activities of daily living was increased from 38% to 50%, an absolute benefit of 12%. The absence of an immediate (24-hour) benefit, coupled with the finding of a benefit at 3 months, is consistent with the hypothesis that thrombolytic treatment works to reduce the size of the infarct penumbra by reperfusing tissue before permanent infarction of the entire territory occurs, despite some irreversible injury to a core component.

Patients treated with rt-PA had a tenfold increase in incidence of hemorrhagic conversion of the infarction (from 0.6% in placebo-treated patients to 6.0% in rt-PA–treated patients). Overall, the rates of neurological deterioration and mortality within the first day after stroke were similar between the groups. Rt-PA was approved for patient use by the FDA in 1996, and it is now considered standard of care for ischemic stroke patients presenting within 3 hours (Level A). Specific guidelines for eligibility and exclusion must be met when using rt-PA to reduce the risk of complications (Table 116-6).

Because of the potential to reduce cerebral perfusion below the limits permitted by autoregulation in the setting of acute brain injury, current guidelines recommend that blood pressure not be reduced acutely after ischemic stroke, and systolic blood pressure levels as high as 220 mm Hg are allowed. Before and following thrombolytic treatment, however, systolic blood pressure should be kept below 180 mm Hg to reduce the risk of hemorrhagic conversion. In addition, antiplatelet and anticoagulant medications must be withheld for 24 hours after rt-PA.

Subsequent meta-analyses and individual trials have demonstrated that the benefit of thrombolytic therapy decreases as the time interval between symptom onset (the presumed beginning of ischemia) and treatment increases, but that the therapeutic time window may persist as long as 4.5 hours after stroke. Advanced imaging techniques, such as diffusion-weighted (DWI) and perfusion-weighted images (PWI), that can distinguish irreversibly injured versus underperfused or "at risk" tissue have been investigated as a means to identify ischemically viable tissue that may respond to revascularization. Recent trial results, however, have not confirmed their value, at least using the imaging parameters under study.

TABLE 116-6 ELIGIBILITY AND EXCLUSION CRITERIA FOR TREATMENT OF ACUTE ISCHEMIC STROKE WITH INTRAVENOUS RT-PA

ELIGIBILITY
Age ≥18 years
Diagnosis of ischemic stroke causing measurable neurological deficit
Well-documented onset of symptoms <4.5 hours before beginning treatment
MAJOR EXCLUSION CRITERIA
Stroke or head trauma within the preceding 3 months
Major surgery within the preceding 2 weeks
History of intracerebral hemorrhage
Systolic blood pressure >185 mm Hg
Diastolic blood pressure >110 mm Hg
Rapidly improving or minor neurological symptoms and signs
Symptoms suggestive of subarachnoid hemorrhage
Gastrointestinal or urinary tract bleeding within 3 weeks
Arterial puncture at a noncompressible site within 1 week
Platelet count <100,000/mm^3
INR >1.7
RELATIVE EXCLUSION CRITERIA (MUST WEIGH RISKS AND BENEFITS)
Seizure at stroke onset
Myocardial infarction within 6 weeks
Infective endocarditis
Hemorrhagic eye disorder
Blood glucose <30 mg/dL (2.7 mmol/L)
Blood glucose >400 mg/dL (21.6 mmol/L)
Patients requiring very aggressive therapy for blood pressure reduction

Interventional techniques to revascularize occluded vessels has promise in the management of patients with ischemic stroke. For patients with MCA occlusions presenting up to 6 hours after symptom onset, there is evidence that intra-arterial thrombolytic agents delivered via catheter into the face of the occluding thrombus can improve functional outcomes, despite an increase in risk of hemorrhage similar to that seen with intravenous rt-PA (Level B). More recently, the FDA has approved the use of mechanical devices specifically engineered to facilitate clot extraction and dissolution in the setting of ischemic stroke. These devices are promising in that they are associated with higher recanalization rates of occluded vessels than occurs spontaneously, but they have not yet been demonstrated to lead to better clinical outcomes than standard treatment with intravenous rt-PA in randomized trials. There is evidence, however, that earlier treatment (within 2 hours) may lead to better outcomes, and further studies are ongoing to test whether other devices used quickly enough will improve clinical outcomes.

Treatment with heparin and various heparinoids for acute stroke are not of benefit and are not recommended in acute stroke. In some patients with massive hemispheric strokes, surgical decompression (hemicraniectomy) can be lifesaving with acceptable functional outcomes, particularly for younger patients (Level A).

Since stroke is characterized by a cascade of events that can cause further neuronal injury for hours or days after stroke, experimental animal stroke studies have tested strategies that might limit this injury (i.e., neuroprotection), including drugs targeting N-Methyl-D-Aspartate (NMDA)-receptors, glycine receptors, calcium channels, adhesion molecules, free radicals, albumin, inflammation, and membrane constituents. However, none of these have been of benefit in human clinical trials.