This is a summary of the American College of Emergency Physicians (ACEP) clinical policy (guideline) regarding use of intravenous (IV) tissue plasminogen activator (tPA) for the management of acute ischemic stroke in the emergency department (ED). The American Academy of Neurology (AAN) fully endorsed this clinical policy, which was the result of a collaborative project of the AAN and ACEP. The clinical policy was developed following a process which the two organizations mutually agreed upon and which is substantially similar to the AAN's 2004 guideline development process.

Please refer to the full clinical policy at www.acep.org/clinicalpolicies for more information, including definitions of the classifications of evidence and recommendations.

IS IV TPA SAFE AND EFFECTIVE FOR PATIENTS WITH ACUTE ISCHEMIC STROKE IF GIVEN WITHIN 3 HOURS OF SYMPTOM ONSET?

| High Degree of Clinical Certainty | In order to improve functional outcomes, IV tPA should be offered to patients with acute ischemic stroke who meet National Institute of Neurological Disorders and Stroke (NINDS) inclusion/exclusion criteria and can be treated within 3 hours after symptom onset (Level A).* |

IS IV TPA SAFE AND EFFECTIVE FOR PATIENTS WITH ACUTE ISCHEMIC STROKE TREATED BETWEEN 3 TO 4.5 HOURS AFTER SYMPTOM ONSET?

| Moderate Degree of Clinical Certainty | In order to improve functional outcomes, IV tPA should be considered in patients with acute ischemic stroke who meet European Cooperative Acute Stroke Study (ECASS) III inclusion/exclusion criteria and can be treated between 3 to 4.5 hours after symptom onset (Level B).* |

*The effectiveness of tPA has been less well established in institutions without the systems in place to safely administer the medication.

Note: Within any time window, once the decision is made to administer IV tPA, the patient should be treated as rapidly as possible. As of this writing, tPA for acute ischemic stroke in the 3 to 4.5 hour window is not US Food and Drug Administration (FDA) approved.

Putting the Evidence Into a Clinical Context**

Safe and effective administration of tPA relies on a hospital's having a system in place for treating patients with stroke. Patients must undergo rapid and accurate diagnosis of acute ischemic stroke, including rapid access to laboratory test results, brain imaging, and accurate image interpretation. Protocols must be in place for drug administration, close clinical monitoring, active blood pressure management, and treatment of hemorrhagic complications (systemic or intracerebral) if they occur. If a given hospital is unable to provide this infrastructure, protocols should be in place for transferring patients to a facility that can. Whatever a hospital's approach is, an ongoing quality assurance program ought to be in place. Physician expertise and written protocols are therefore hypothesized to be important for use of tPA but may be in short supply in smaller centers without an abundance of stroke specialists. Adequate physician acute stroke care expertise has not been rigorously defined in the literature, on the basis of either credential or degree of experience, or studied in clinical trials. The definition should not be restricted to neurologists and should include emergency physicians or other physicians with expertise and experience in stroke care.

For centers without on-site acute stroke specialists, telestroke technology offers a means to obtain remote consultation about the administration of IV tPA. In a study by Fisher, the formation of “telestroke” networks allowed inexperienced centers to obtain expert medical and radiologic consultation by remote video linkage. Accumulating data show that this model of stroke care produces results similar to those obtained by on-site consultation with stroke experts. The American Heart Association published recommendations on the use of telemedicine for acute stroke care.

There has been clinical concern about treatment of patient groups who would meet NINDS criteria but have a poor prognosis for good outcome, irrespective of tPA use, including those with advanced age, severe clinical deficits, and CT hypodensity in a large portion of the middle cerebral artery territory or hemisphere.

Addendum

After this document was completed, the International Stroke Trial 3 (IST-3) was electronically published in Lancet. IST-3 was designed to evaluate the effects of tPA on patients with ischemic stroke up to 6 hours from symptom onset in whom benefit was deemed to be uncertain (the vast majority of whom had contraindications to tPA defined by NINDS criteria in the 0- to 3-hour window or ECASS-3 criteria in the 3- to 4.5-hour window). IST-3 looked at a different cohort of patients than those upon which this policy focuses. The published trial data were carefully reviewed by the writing panel, and it was determined that the study’s methodology was such that the findings did not impact the recommendations made in this practice guideline.

**The “Putting the Evidence into a Clinical Context” section is presented here in summary form.