Intravenous tPA for acute stroke

To the editor:

We are encouraged that the *CJEM* Journal Club chose to address the use of tissue plasminogen activator (tPA) for the treatment of acute stroke in nonspecialist centres.[1] Dr. Rhine's review of the Cleveland area experience[2] is timely and relevant. The question is, can communtiy hospitals administer tPA and achieve outcomes comparable to those reported by the NINDS trial?[3] If not, should access to tPA be limited to specialist centres?

The best evidence comes from well-designed randomized controlled trials. These trials have been summarized in a recent Cochrane Collaboration systematic review,[4] which includes information on intravenous tPA use derived from over 2,500 patients in 7 randomized trials, including NINDS. The systematic review shows early hazard related to symptomatic intracranial hemorrhage, but an overall longer-term benefit in selected groups of patients treated within 3 hours of symptom onset. Unfortunately, none of these trials included patients randomized in nonspecialist, community hospital settings.

As Dr. Rhine indicated,[1] the evidence about tPA use in nonspecialist centres comes from nonrandomized comparisons. The Cleveland investigators[2] evaluated 3 treatment groups (patients treated with tPA, matched patients not treated with tPA, and all ischemic stroke patients) in 29 teaching and nonteaching hospitals. However, because of nonrandom allocation, these comparisons are subject to a number of biases, which may have caused the results to deviate significantly from the truth. In addition, only 70 (1.8%) of the Cleveland patients received tPA. This 1.8% treatment rate reflects other published figures, but the number of patients and adverse outcomes is small, therefore vulnerable to the play of chance. As interesting as the results are, they may not be accurate, and it is probably not reasonable to use them to suggest that tPA should be limited to tertiary care centres.

There is a need for further randomized comparisons. The Third International Stroke Trial (IST-3), now ongoing in the UK and Europe, is a large, well designed multicentre trial evaluating the use of tPA in patients with acute ischemic stroke. IST-3 is recruiting patients who present within a 6-hour time window from a wide variety of hospital settings, and will provide more valid data regarding the use of tPA in nonspecialist centres.

Tissue plasminogen activator is one small part of a "systems approach" to stroke treatment. More patients will benefit from stroke units and ASA because the vast majority of stroke victims are eligible for these, while only a small number currently receive tPA. Having said this, tPA has been the impetus for tremendous changes in stroke care, and it is anticipated that trials like IST-3 will help make tPA available to a larger number of people.

Finally, we disagree that subcutaneous heparin offers "similar benefits with less risk and lower cost." A recently published systematic review[5] suggests that the use of anticoagulants (including heparin) for the treatment of acute stroke results in no net improvement in long-term outcome, and increases the chance of fatal and nonfatal intracranial hemorrhage. In general, anticoagulants should be avoided in the management of the acute stroke patient.

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References

1. Rhine D. Intravenous tPA for acute stroke: Any and all hospitals? Any and all docs? CJEM 2000;2(3):189-91.
2. Katzan IL, Furlan AJ, Lloyd LE, Frank JI, Harper DL, Hinchley JA, et al. Use of tissue-type plasminogen activator for acute stroke: the Cleveland area experience. JAMA 2000;283(9):1151-8.
3. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. N Engl J Med 1995; 333(24):1581-7.
4. Wardlaw JM, del Zoppo G, Yamaguchi T. Thrombolytic therapy in acute ischaemic stroke. Part 1: Thrombolysis versus control. Oxford: Update Software. The Cochrane Library 2000: issue 2.
5. Gubitz G, Sandercock P, Counsell C, Signorini D. Anticoagulants for acute ischaemic stroke. Oxford: Update Software. The Cochrane Library 2000: issue 2.

For reasons of space, letters may be edited for brevity and clarity.

[Dr. Rhine responds:]

I agree with Drs. Gubitz and Phillips[1] that tPA is one small part of a "systems approach" to stroke treatment. I also agree that more patients will benefit from stroke units and ASA because the vast majority of stroke victims are eligible for these, while only a small number currently receive tPA. The importance of the Cleveland paper[2] is to emphasize that the risks of tPA may be higher in community hospitals than in research settings. I also intended to infer that, in community hospitals, stroke patients may benefit more from stroke teams, stroke units and other potentially less injurious interventions, such as ASA.

The CAEP Position Statement on "Thrombolytic Therapy for Acute Ischemic Stroke," published in this issue[3] of *CJEM*, agrees with my interpretation of the evidence and suggests that stroke thrombolysis should be limited to centres with rapid 24-hour access to specialized neurological expertise and neuro-imaging resources. Requirements suggested in the document, along with the currently recog-

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nized 3-hour time barrier from symptom onset, effectively limit stroke thrombolysis to tertiary care centres (which provide a minority of emergency medical care in Canada). Practitioners in non-tertiary centres must be aware of the risks and limitations of stroke thrombolysis so that they can provide their patients with the best local standard of care and "do no harm."

Gubitz and Phillips correctly point out that low molecular weight heparins (LMWH) are unlikely to benefit patients with acute stroke. Although one study[4] showed impressive results in this setting, these results have not been replicated elsewhere, and a recent Cochrane Review (published after the *CJEM* Journal Club article went to press) concluded that, although LMWH appears to decrease the occurrence of deep vein thrombosis, there are too few data to provide reliable information on their effect on other important outcomes, including death and intracranial hemorrhage.[5]

The Cleveland study demonstrates that outcomes achieved in research settings may not be reproducible in all settings. Until such time as community-based effectiveness studies demonstrate safety, emergency physicians should remain skeptical. In the wrong hands, tPA may cause more harm than good for acute stroke victims.

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References

1. Gubitz G, Phillips S. Intravenous tPA for acute stroke [letter]. CJEM 2001;3(1):5.
2. Rhine D. Intravenous tPA for acute stroke: Any and all hospitals? Any and all strokes? CJEM 2000;2(3):189-91.
3. Canadian Association of Emergency Physicians Committee on Thrombolytic Therapy for Actue Ischemic Stroke. Thrombolytic therapy for acute ischemic stroke [position statement]. CJEM 2001; 3(1):8-12.
4. Kay R, Wong KS, Yu YL, Chan YW, Tsoi TH, Ahuja AT, et al. Low-molecular-weight heparin for the treatment of acute ischemic stroke. N Engl J Med 1995;333:1588-93.
5. Counsell C, Sandercock P. Low-molecular-weight heparins or heparinoids versus standard unfractionated heparin for acute ischaemic stroke. Cochrane Database of Systematic Reviews 2000;2:CD000119.

Prehospital DNR orders: an ethical dilemma

To the editor:

Thanks to Sherbino and colleagues[1] for addressing the important topic of prehospital do-not-resuscitate (DNR) orders. They make a number of excellent suggestions, including the need to develop clear policies, adopt standard DNR forms, improve public education and improve the emergency medical technician's (EMT's) access to on-line control.

A significant problem is the lack of published data on Canadian emergency medical services policies. In British Columbia a standard DNR form has been developed, and EMTs are authorized to honour it in the field.[2] Nova Scotia is now developing policies to allow paramedics to honour DNR forms. At present, they have access to on-line control and may honour a DNR form with base physician approval. Other provinces may have similar policies but few are published, leaving each region to reinvent the wheel. Ontario has unique problems related to specific legislation. With a forum like *CJEM*, emergency medical services (EMS) directors and policy-makers could share their experience with others and address these problems at a national level.

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References

1. Sherbino J, Guru V, Verbeek PR, Morrison LJ. Prehospital emergency medical services' ethical dilemma with do-not-resuscitate orders. CJEM 2000;2(4):246-51.
2. Innes G, Wanger K. Dignified death or legislated resuscitation? [editorial]. CMAJ 1999;161(10):1264-5.

Fee-for-service remuneration

To the editor:

Your editorial[1] in the October issue of *CJEM* appropriately highlighted some of the problems associated with fee-for-service (FFS) payment plans. One of the biggest problems with FFS in any branch of medicine is that it encourages financially motivated physicians to produce "doctor dependent patients," encouraging, for example, visits for self-limiting viral illness and unnecessary re-checks. This flies in the face of the current philosophy of making patients (or, should we say, people in general) more responsible for their own health care and status.

One aspect of your editorial might, however, suggest to FFS emergency physicians that their lives will become significantly easier with alternate funding arrangements (AFA). Like you, we work under an AFA in a high volume, high acuity setting. We are (relatively) happy with our earnings, and our coverage is (reasonably) adequate. We do not, however, have "more time to spend with patients in the trauma room," we still work long shifts without eating, drinking (or, for that matter fulfilling the other end of the oral intake arrangement). We still have 17 decisions hanging over our heads, are constantly bickering with admitting services and disgruntled patients, and the "short snapper" patients are still the most desired because their beds can be freed more quickly. It is the rare shift that we are reminded how much we enjoy our job by an interesting and challenging patient presentation, or even an enjoyable procedure — more often, we are obliged to refer the patient, for whom our skills were developed, so that we can continue to wade through the hordes of undifferentiated

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