Addressing Healthy People 2010 Objectives for Stroke

To the Editor:

Healthy People 2010 objectives were set for the United States to improve patient knowledge of early warning symptoms for stroke (objective 12-8) and myocardial infarction (MI; objective 12-2). Objectives were also established to emphasize the importance of calling 911 for emergency care for MI (objective 12-2) and to increase the proportion of eligible MI patients who receive thrombolytic therapy within 1 hour of symptom onset (objective 12-3).1 However, corresponding objectives for stroke (ie, calling 911 and increasing the proportion of ischemic stroke patients who receive thrombolytic therapy) were not included. We are writing to recommend that although these corresponding objectives for stroke were not established, they are very important and should also be evaluated.

In the United States, stroke is the third leading cause of mortality.2 The American Heart Association recommends thrombolytic therapy treatment for ischemic stroke within 3 hours of the onset of symptoms.3 A potential benefit of this therapy is to reduce functional limitations resulting from the stroke,4 which may be considerable, as stroke is also the leading cause of neurological disability.5 However, most stroke patients arrive at the hospital too late to even be considered for thrombolytic treatment. A review of 48 published studies on prehospital stroke delay indicates that for most studies, the median time from symptom onset to arrival in the emergency department is 3 to 6 hours.6 For stroke patients, the use of emergency medical services (EMS) is associated with earlier department management of stroke in Houston, Texas.7–9 It occurs most often in hypo-
thermia but is also seen in normothermia, electrolyte disorders, brain injury, or subarachnoidal hemorrhage. In this letter we wish to demonstrate a clear J wave in association with severe hypothermia.

A hiker found a 70-year-old male comatose at his fishing pool on a cold winter day. The summoned paramedic intubated the patient and ventilated him mechanically. In the emergency room, his first ECG demonstrated a prominent J wave (Figure). His body temperature was 25.2°C. The blood gas analysis revealed a pH of 7.13 (normal 7.35 to 7.45), with a base excess of $216.4$ mmol/L (normal $22$ to $13$ mmol/L). Potassium was slightly diminished (3.1 mmol/L; normal 3.5 to 5.0 mmol/L). A cranial CT scan revealed severe intracerebral hemorrhage as the underlying cause of coma.

The patient was gradually (1°C/10 minutes) warmed up by use of extracorporal circulation. An ECG performed 2 days later was normal. Unfortunately, the cerebral disease progressed, and 1 day later brain death occurred.

The J wave was first described by Tomaszewski in 1938 and may occur in hypothermia, electrolyte disorders, myocardial ischemia, inborn Brugada syndrome, and also in brain injury and subarachnoidal hemorrhage.

Pathophysiologically, the presence of a prominent action potential notch in the epicardium but not in the endocardium is supposed, which provides a voltage gradient that manifests itself as a J wave or elevated J point in the ECG. The heterogeneous distribution of a transient outward current–mediated spike-and-dome morphology of the action potential across the ventricular wall is thought to underlie its manifestation.

To conclude, stroke caregivers should be familiar with the ECG J wave for 2 reasons. First, in the clinical setting of severe unintentional hypothermia with impairment of consciousness, the J wave indicates a risk of life-threatening dysrhythmias. Second, with increasing use of therapeutic hypothermia in stroke and neurocritical care, the occurrence of the J wave should be regarded as a sign that the patient has been overcooled.

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Re: Stroke and Pregnancy

To the Editor:

Jaigobin and Silver performed a retrospective analysis of stroke during pregnancy or the puerperium among women who delivered at a single tertiary referral hospital in Canada over a 17-year period. The frequency of all strokes was 26 per 100,000, when corrected to represent the catchment area (ie, by excluding referred patients). This value is similar to that reported in several large studies using administrative data from the United States, as well as other population-based epidemiological studies in which clinical records were reviewed. The study by Jaigobin and Silver provides interesting clinical information about such patients, but several issues warrant clarification or elaboration. First, the authors identified potential cases as those with both stroke and pregnancy diagnostic codes, as well as by review of pregnant patients with procedure codes for CT, MRI, or cerebral angiography. The “stroke codes” reportedly used for screening potential cases were 430 to 439, using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). However, there is no ICD-9-CM 439 code for stroke in the US version of this classification system. Furthermore, codes for cerebrovascular disease (ie, ICD-9-CM 430 to 438) in the US version specifically exclude “any condition classifiable to 430 to 434, 436, 437 occurring during pregnancy, childbirth, or the puerperium, or specified as puerperal (674.0).” These cases should properly be coded to ICD-9-CM 674.0, while cerebral venous thrombosis or thrombosis of intracranial venous sinuses is a complication of pregnancy or the puerperium should be coded to 671.5. In studies using US administrative hospital data from the National Hospital Discharge Survey or the Healthcare Cost and Utilization Project, some patients with pregnancy codes also had non-pregnancy-related stroke codes (ie, 430 to 434, 436 to 437), generally in addition to codes 674.0 or 671.5, but most cases of stroke during pregnancy or puerperium were coded only with codes 674.0 or 671.5 (Lanska and Kryscio, unpublished observations, 1997 to 1999). Did Jaigobin and Silver review these codes as well? If so, what was the relationship between codes 430 to 438 and codes 674.0 and 671.5 in these cases?

Second, the authors identified 51 potential cases by ICD-9-CM codes, only 34 of which were felt to have had a stroke after review of the medical records. What were the other diagnoses in the patients who did not have a stroke? What were the ICD-9-CM codes used in these cases? How many were identified by some stroke diagnosis code, and how many were identified by a diagnostic test procedure code?

Third, the study spanned a long period, from 1980 to 1997. Was ICD-9-CM in use in Canada during this entire period? Were there changes in the frequency of pregnancy-related stroke over this period?

Fourth, did any of the cases receive bromocriptine for lactation suppression? Postpartum lactation suppression was removed as an indication for the use of bromocriptine in 1994 in the United States. Was bromocriptine used for this indication during the entire study period in Canada? If not, was there any change in the frequency of stroke before and after removal of postpartum lactation suppression as an indication for the use of bromocriptine? Did any of the cases receive other ergot derivatives, phenylpropanolamine, or other drugs purported to be associated with stroke?

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us to identify pregnant or puerperal patients with stroke codes as a primary or secondary diagnosis. We agree that code 439 codes for the late effects of stroke. However, because of previous reports of the inaccuracy of hospital discharge coding for stroke, we included all stroke-related codes in our study design to avoid excluding any possible patients with stroke-associated with pregnancy.

Second, although 51 potential cases were identified, only 34 had a diagnosis of stroke after review of the medical records. The nonstroke diagnoses consisted of the following: epilepsy, prior neurological deficit, embolization for epistaxis, subglottic stenosis, Bell’s palsy, cerebral abscess, delirium, ovarian cyst, neurogenic bladder, neoplasm, and multiple sclerosis. An additional 2 patients had nonspecific neurological symptoms with no clinical or radiographic evidence of stroke. All patients with nonstroke diagnoses were identified by a diagnostic test procedure code.

Third, between 1980 to 1985, discharge diagnoses were translated into ICD-9 codes. After 1985, ICD-9-CM classification was used. We regret this error.

Finally, to the best of our knowledge, none of the patients with stroke during the postpartum period received bromocriptine for lactation suppression or any other medications purported to be associated with stroke. However, this information was collected by chart abstraction and should be interpreted with some caution.

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Heterogeneity of Apparent Diffusion Coefficients Within Infarcts

To the Editor:

Back et al. recently reported apparent diffusion coefficient (ADC) measurements in acute stroke, finding no ADC fluctuations in peri-infarct regions over a 15-minute period. The reported data are convincing with regard to the temporal stability of infarct area within the 15-minute time window studied. We wish to address the issue of ADC spatial heterogeneity in stroke, specifically the authors’ contention that “there was a gradient of ADC reduction from the infarct periphery toward the infarct core.” They conclude that “this observation supports the view that the ischemia-induced early change in ADC is a blood flow-dependent event which reflects the severity (and duration) of the perfusion deficit.” As the authors have noted, this core-versus-periphery distinction in diffusion imaging has been previously advanced and is commonly accepted by the community of stroke researchers.

However, it is possible that much of the ADC heterogeneity illustrated in Figures 2 through 4 of the article by Back et al. may reflect differences in ADC reduction between gray matter and white matter. Within the infarct, white matter structures appear to display lower ADC values than gray matter, a finding that is consistent with results from our investigation of acute and early subcortical middle cerebral arterial stroke using diffusion tensor MR imaging. Indeed, the “peel-like structure” of the region of greatest ADC reduction (Figure 4) noted by Back et al. closely resembles the morphology of white matter tracts. Our results from diffusion tensor imaging demonstrate that these areas of greatest ADC reduction within the infarct correspond also to the regions of highest diffusion anisotropy, a signature of white matter.

This difference in ADC reduction between gray and white matter is not likely to result from differences in severity of ischemia, as oxygen extraction fraction measured with positron emission tomography has not shown differences between ischemic gray and white matter. It is possible that, superimposed on these gray-white matter ADC differences, there may also be infarct ADC heterogeneity caused by varying degrees of ischemia, as suggested by Back et al. We feel that it is important to account for the variation in ADC due to these differences in gray matter–white matter anatomy before invoking heterogeneity of the ischemic process. Correlation of the ADC data with diffusion anisotropy can be helpful in this respect.

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Response

We thank Mukherjee and colleagues for their comments on our recent paper. Indeed, we agree on the intrathecal heterogeneity and differential behavior of the ADC in gray and white matter, as observed by Mukherjee and others. Exactly as is described in their paper, in Figure 4 of our article a lower ADC in white matter than in gray matter is shown, and the description of a peel-like internal structure of ADC ranges when applying various ADC thresholds for analysis may appear misleading. Yet in regard to the main point of our paper, the stability of ADC values and the lack of any very short-term ADC change suggestive of peri-infarct depolarizations, white matter and gray matter ADCs were not different and in neither was any change of the ADC observed.

In regard to the differential behavior of gray and white matter ADC, one should consider the dynamic characteristics of the ADC over time as demonstrated in human and animal stroke. In a serial clinical study, we observed the earliest ADC reductions as early as 2 hours after symptom onset in gray matter (neuronal tissue may be more vulnerable to ischemia than white matter), followed by cortical swelling within 24 hours accompanied by a slow increase in the ADCs toward “pseudonormal” values. ADC reductions in the white matter occurred with a delay, but did not pseudonormalize as observed in gray matter. In this phase, as reported by Mukherjee et al (16 hours after symptom onset) and as shown in our Figure 4, gray matter ADCs were reduced but higher than white matter ADCs. Yet exactly the opposite may be observed in the earliest phase of visible ADC changes in ischemic tissue, thus the time point after stroke is
Restricted Dissociated Sensory Loss in Lateral Medullary Infarction

To the Editor:

In a recent article published in Stroke, Cerrato et al.1 described a patient with right lateral medullary infarction (LMI) who presented with abnormal spinothalamic sensation in the left arm and impaired dorsal column sensation in the right hand. Although this is an interesting observation, I have several concerns about this report.

First, the authors wrote that “dissociated sensory pattern involving upper limbs has not yet been reported.” However, I previously described 3 patients who had ipsilateral dorsal column sensory impairment who had otherwise typical symptoms/signs of LMI.2 Actually, one of them (case 3) showed exactly identical sensory pattern as described by Cerrato et al; dissociated sensory impairment limited to upper extremities. I suggested that involvement of the fibers at the nucleus gracilis/cuneatus or the crossing fibers toward the medial lemniscus may explain this sensory variant, a hypothesis again nearly identical with that proposed by the authors. Therefore, their observation and hypothesis are not new.

Second, their Figure 3 was drawn as if the fibers from the nucleus cuneatus run ventrally and those from the nucleus gracilis dorsally into the contralateral medial lemniscus. Actually, it has been shown that in the medullar lemniscus at the medulla level, sensory topography is arranged in such a way that the leg representation area is located ventrally and the arm representation area dorsally.3 Thus, the dorsal column sensory fibers are likely to decussate in a more complex manner than shown in Figure 3. Therefore, I think the lesion may have involved the nucleus cuneatus itself or the proximal portion of the decussating fibers.

Finally, it has been shown that a vertebral artery dissection may cause ipsilateral radiculopathy in the arm by way of the compression of the nerve roots due to enlarged vessels or induction of ischemia in the spinal roots.4,5 Although this is unlikely in the presence of normal MR angiogram findings, one must exclude this possibility with the help of electromyogram when ipsilateral sensory symptoms are encountered in a patient with LMI.

Response

Kim’s letter raises 3 points about our article, “Restricted Dissociated Sensory Loss in a Patient With a Lateral Medullary Syndrome: A Clinical-MRI Study.”1

The first comment is that our report is not so original because he had described 3 patients with similar sensory impairment in 1995.2 Actually, in those patients the sensory pattern did not involve only the upper limbs, as in our case, but also the face and the trunk and was, therefore, not so “restricted.” Moreover, sensory disturbances were not isolated, but there were also other neurological features (Horner’s sign and ipsilateral weakness of the limbs, ipsilateral limbs ataxia, ipsilateral facial paresis). Finally, the lower medulla ischemic areas in the patients of Dr. Kim were much greater than the small area in our case (involving also the cerebellum in 2 of them). Therefore, we think that the actual peculiarity of our report consists in the occurrence of a “truly restricted” dissociated sensory loss as the unique neurological consequence of lateral medullary infarction.

The second comment by Kim regards the anatomy of sensory systems in medulla oblongata. Certainly, the anatomy of lemniscal decussation is more complex than in our scheme.1 Anyway, the “strategic” location of the ischemic lesion in our patient and the subsequent clinical-anatomical correlation is evident. The simultaneous involvement of the inner spinothalamic fibers and the proximal portion of the lateral archiform fibers (both containing afferents from the upper limbs) clearly explains such a “restricted” and “dissociated” sensory pattern.

In his last comment, Kim raises the hypothesis that a vertebral artery dissection may have caused a compressive or ischemic radiculopathy and may explain the ipsilateral sensory symptoms. In our case, the vertebral artery dissection was ruled out by neuroimaging and ultrasonographic data (MR angiography and extracranial vessel duplex ultrasonography of cervical vessels were normal). Moreover, clinical findings of radiculopathy, such as neck pain and radicular sensory and/or motor deficit and asymmetry of deep tendon reflexes, were absent.

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Letters to the Editor

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Re: Stroke Severity Determines Body Temperature in Acute Stroke

To the Editor:

Boysen and Christensen, in a recent *Stroke* article,¹ have introduced another dimension to the relationship of body temperature following a stroke and its influence on outcome. Only 5% of their patients had an elevated temperature on admission, which grew later to 12% in patients with major strokes. More significantly, the patients with major stroke had lower temperatures on admission, and this phenomenon was associated with higher mortality. One explanation for the rise in temperature in major strokes after admission is the aspiration pneumonia due to impaired swallowing, and the explanation for their higher mortality is also likely to be dysphagia,² although, regrettably, this relationship has not been reported in their paper. The authors very justifiably recommend a randomized trial of hypothermic therapy in acute strokes, although antipyretic use has been advocated³ despite the lack of evidence of its beneficial effect.

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Response

We thank Dr Sharma for his comment on our article. He suggests that the rise in temperature in the acute stroke patients was due to aspiration. We cannot rule out this possibility entirely. The rise in temperature, however, occurred within 6 to 8 hours after stroke onset in patients who were on intravenous fluids and was due to aspiration. We cannot rule this possibility entirely. We thank Dr Sharma for his comment on our article. He suggests that the rise in temperature in the acute stroke patients was due to aspiration. We cannot rule out this possibility entirely. The rise in temperature, however, occurred within 6 to 8 hours after stroke onset in patients who were on intravenous fluids and was due to aspiration. We cannot rule out this possibility entirely.


Hypertension in Acute Stroke: What to Do?

To the Editor:

Hypertension is common during the acute phase of stroke, and its management remains controversial. To explore this issue further, we held an ad hoc workshop at the World Stroke Conference, Melbourne, November 2000, and report here its discussion and conclusions.

Hypertension is common (>50%) in both ischemic and hemorrhagic stroke, although its incidence depends on definitions and when and how blood pressure (BP) measurements are made. Hypertension is associated with a poor outcome,⁴ a relationship which is probably independent of stroke severity or clinical subtype. The cause of the negative relationship between BP and outcome is unclear but may relate to the development of reinfarction, cerebral edema, or hemorrhagic transformation.

Our workshop agreed that trials are needed to test whether BP should be lowered in subjects with acute primary intracerebral hemorrhage. In contrast, significant differences of opinion existed on whether BP should be elevated or reduced in acute ischemic stroke. Existing data do not provide an answer: trials of beta receptor antagonists (β-RA) and some calcium channel blockers (CCB)—in which BP lowering occurred—and aspirin cross-linked hemoglobin (which increases BP) were all complicated by worsened outcome in the treatment groups.²–⁷ It is unlikely that a single mechanism explains these findings, but CCB can reduce cerebral perfusion.⁸,⁹ We did not feel that the BP management strategy utilized in the NINDS and ECASS II thrombolysis trials¹⁰,¹¹ helped in deciding how to manage BP in general, because patients not treated with thrombolotics are a different population with a different natural history.

A question that we could not answer was that of what agent should be used to alter BP, although the group agreed that differences between drug classes might be important and that extrapolating the findings of one class (e.g., CCB) to other classes was inappropriate. Excluding β-RA and CCB (in which the existing data are not encouraging), small studies of angiotensin converting enzyme inhibitors, angiotensin receptor antagonists, and nitric oxide donors have been completed or are underway.¹²–¹⁶ These agents are multimodal in their action, thereby increasing the likelihood that efficacy trials might be possible: eg, angiotensin receptor antagonists will counteract the effects of activation of the renin-angiotensin system, nitrates will replace low vascular nitric oxide levels,¹⁷ and both are neuroprotective in experimental stroke. A phase II clinical trial of elevating BP (with dobutamine) is also underway in ischemic stroke.¹⁸ The group felt that any efficacy trial aiming to change BP would need to be of sufficient size to assess effects in subgroups, including subjects with or without prior hypertension and patients with different subtypes of stroke (e.g., lacunar or cortical infarction).

The method of delivery for any intervention was also discussed. We felt that intravenous formulations were not necessarily ideal because they would increase monitoring requirements, would be more susceptible to causing sudden or extreme changes in BP, and might delay or limit early mobilization and rehabilitation. Attractive routes of delivery included oral "melt" and transdermal preparations, both of which avoid problems with dysphagia, a common complication of acute stroke.

Although we discussed when treatment should commence after stroke, current information does not give any guidance; trials of changing BP should factor this question into their design and analyses. We felt that treatment should continue for a week or so, a time period over which hypertension will settle in most patients and after which most clinicians are comfortable about initiating routine treatment.

Although the ultimate question is to determine the effect of changing BP on functional outcome, studies are also required to assess the effect of vasoactive drugs on cerebral perfusion. Very few studies have been performed,¹⁸ and further (semi-quantitative) assessment is urgently required, eg, with positron emission tomography, single-photon emission CT, transcranial Doppler, MR perfusion and diffusion (with assessment of mismatch), quantitative CT perfusion, or xenon CT scanning. A further critical question is whether prior antihypertensive medi-
cation should be continued or stopped, since current practice varies.19 Once again, no randomized trial data exist, and it is vital that this question is examined, either as part of a BP modulation trial or separately.

Workshop attendees are involved with ongoing trials,16 and we plan to meet again.

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Addressing Healthy People 2010 Objectives for Stroke
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