Recommended Readings
By Michael Schneck, MD, FAAN, Communications Work Group Leader, and Alejandro Rabinstein, MD, Stroke Section Member

As you all know, we have introduced a column of 10 articles (though with the editorial privilege of sometimes combining two articles, we have 12 in this edition of the newsletter) for the six to 12 months prior to each edition of the newsletter. I want to thank my coauthor, Dr. Alejandro Rabinstein, for his contributions to the column. The choice of articles is always idiosyncratic, and while we try to include something on a variety of stroke topics, we apologize if we left off something of interest to the individual reader. Dr. Rabinstein and I encourage members of the section to email us if they see a clinically important or perhaps intriguing paper to include in the next (spring) newsletter. You can send your suggestions to Dr. Michael Schneck at mschneck@lumc.edu.

This report from the October issue of Neurology showed a dramatic improvement in outcome for patients treated within six to 24 hours (mean 13) with oral minocycline. The authors presumed that improvement “is not due to the drug’s basic antibiotic effect, but rather its anti-inflammatory effect and ability to protect brain cells from destruction. Minocycline has already been shown in other studies to have a neuroprotective effect in animal models of multiple sclerosis, Parkinson’s disease, Huntington’s disease, and Lou Gehrig’s disease, or ALS.”

If confirmed in a larger and double-blind randomized study, this is potentially a revolutionary breakthrough as to date no experimental neuroprotectant has been shown to have benefit whereas this “old” antibiotic may yet prove to be the ‘Holy Grail” from Israel of stroke neuroprotection.


The abstract conclusion is eloquent: “Most patients who experience spontaneous intracerebral hemorrhage (SICH) have severe baseline infarcts and already are destined for poor outcomes. For every 100 patients treated with tPA, approximately 1 will experience a severely disabled or fatal final outcome as a result of tPA-related SICH.”

I note that, by comparison, the need to treat benefit analysis for tPA is 10 times greater! The benefit to risk ratio is equal to that of carotid endarterectomy for symptomatic stroke.


This observational study represents the largest collected experience (study population close to 6,500 patients) confirming the safety and effectiveness of intravenous thrombolysis for the treatment of acute ischemic stroke within three hours of symptom onset. We know this. We can only hope that reports like this will help dissipate unfounded fears and therapeutic nihilism among those colleagues who remain reluctant to use this very useful and well-validated treatment.

Bridging therapy using intravenous thrombolysis (two-thirds of the usual rt-PA dose begun within three hours of symptom onset) followed by intra-arterial therapy in patients who fail to recanalize continues to appear promising. In this latest version of the IMS trial that randomized 81 patients with severe strokes (median NIHSS 19 at baseline), the rate of symptomatic intracranial hemorrhage was very acceptable (9.9 percent) and better three-month functional outcomes than rt-PA treated patients in the NINDS trial. Stay tuned (and keep your fingers crossed) for the results of the IMS III trial.


The design of this study was unorthodox (pooled analysis of three small trials with different designs), but the main result is clinically relevant and deserves attention. It indicates that early hemicraniectomy can save life and function in patients younger than 60 years with massive ischemic infarctions. However, it is important to underline the message emphasized by the investigators: the final decision on whether to offer and pursue hemicraniectomy needs to be considered on an individual basis in each patient.


The Oxford Vascular Study (OVS) has been an important resource for data on the changing patterns for stroke. In a previous report, it was noted that the rates of overall stroke were projected to surpass the rate of myocardial infarction. Here OVS notes that hemorrhage rates (ICH) have remained unchanged as the ICH rate in <75 year old persons has declined, but the ICH rate has increased in >75 year old persons (in this age group there was an increase in lobar ICH as well). The ICH rate related to hypertension has decreased, but the rate related to antithrombotic use and possibly amyloid angiopathy has increased.


This paper notes that recurrent hemorrhagic stroke rates are as frequent as ischemic stroke rates following an incident ICH. Whether we should then start patients with a history of ICH on any antithrombotic therapy is a challenging question, though not starting any antiplatelet therapy puts these patients at increased risk for cardiovascular events (including ischemic stroke and myocardial infarction).


These two papers highlight the issue of risk/benefits of antiepileptics in hemorrhagic stroke. The Rosengart and colleagues paper would suggest that the risks of drugs outweigh the benefits. However, the Claasen and colleagues paper supports the argument that while seizures may be rare, there is a significantly worse outcome for patients with SAH with generalized convulsive epilepsy. Thus, the issue remains exceedingly complex, and there are two many confounding variables (i.e., size of bleed, presence of hydrocephalus, clinical status, medications used) to make any clear recommendations. In addition, reports are now
suggesting that nonconvulsive seizures are underdiagnosed in hemorrhagic stroke. A randomized study is needed, but the design of the study will be challenging because of all of the confounders.


In 2004, Tufts New England Medical Center purportedly had a very high rate for the stroke DRG. A review of the charts revealed, however, very high patient co-morbidities. The authors note that mortality statistics related to DRG are a meaningless scorecard for academic hospitals accepting critically ill patients.

Recently at Loyola University (Dr. Schneck’s institution), Thomas Origitano, the Chair of Neurosurgery, presented an abstract at a neurosurgical meeting showing similar findings; transfer and emergency patients have a six-times-greater mortality rate than elective cases. Outside hospitals that had transferred patients to the university reported fewer mortalities and received higher ratings on various ranking scores.


In the first top ten issue we remarked on an association between birthday and ischemic stroke. Calendar issues and stroke are apparently seen in other cultures. It is interesting that certain days are associated with increased hemorrhage in Japan. The article notes, “On Japanese national holidays the relative risk of intracerebral hemorrhage is significantly higher than on other days, certainly due to much more alcohol consumption on holidays. During RokuYo, the relative risk of intracerebral hemorrhage is extremely low on the traditionally unlucky days of BatsuMetsu and TomoBiki, as many Japanese people restrain their activities on these days.” An interesting research question would be to investigate the effect of Friday the 13th on stroke incidence in Western cultures.