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INSIDE

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Special Feature

What You Need To Know About West Nile Virus

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This article originally appeared in the January 2007 issue of Critical Care Alert. It was edited by David J. Pierson, MD, and peer reviewed by William Thompson, MD. Dr. Pierson is Professor, Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington, and Dr. Thompson is Staff Pulmonologist, VA Medical Center; Associate Professor of Medicine, University of Washington. Dr. Pierson and Dr. Thompson report no financial relationships relevant to this field of study.

West nile virus (WNV) infection is a growing epidemic that impacts more persons and more aspects of our health care system yearly. A significant percentage of affected patients require admission to, and care in, an intensive care unit (ICU). Those with the most severe manifestations — meningoencephalitis and/or acute flaccid paralysis — may have prolonged ICU stays with considerable long-term morbidity and mortality. Thus, it is essential that all health care personnel in the critical care community become familiar with WNV.

Epidemiology

WNV is a single-stranded RNA virus of the family *Flaviviridae*, which includes the arboviruses Japanese encephalitis and St. Louis encephalitis viruses. It was first discovered about 70 years ago in Uganda. It was not until the 1990s that it began to spread across the world and ultimately appeared in the United States in 1999.[1-2] (The strain found in the United States is genetically almost identical to a strain from the Middle East and has not changed significantly since 1999.) Most human WNV infections occur at the times of peak mosquito activity which in the United States is July through October. However, cases have been reported from April to December. Persons of all ages may be affected.[2]

Between January 1 and November 28, 2006, 4028 cases of human WNV infection from across the continental United States were reported to the Centers for Disease Control and Prevention (CDC). This number represents a 27-fold increase in cases since 2001. The largest numbers

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of cases were detected in Idaho (889). Neuroinvasive disease (meningitis, encephalitis, or myelitis) occurred in 34.4% or 1386 of these cases. Overall mortality was 3.4% (135 persons). This year, the median age of affected patients was 51 years and 55% of patients were male. [3]

Transmission

Mosquitoes (of the *Culex* species) serve as the primary transmitters of WNV. They acquire infection by feeding on infected birds and subsequently transmit the virus by biting humans or other birds and animals. (Birds of more than 100 species may be affected by WNV but the most common hosts are crows, jays and ravens in the Corvidae family.) Although fecal-oral transmission may occur among birds, its significance remains unclear. Humans and other animals do not develop high enough levels of viremia to be carriers of disease that uninfected mosquitoes can acquire: that is, there is no human-to-human transmission by mosquitoes and no animal-to-human transmission. There is, however, WNV transmission via human tissue and body fluids. This includes blood products (packed red cells, platelets and plasma), solid organs (either via organ transplantation or exposure of health care workers during autopsy), and breast milk. Transplacental transmission with devastating fetal outcomes has also been reported although this appears to be rare.[4,5]

Clinical Features and Outcomes[2,4,6-7]

The incubation period for human WNV infection is 2-14 days. It is estimated that 80% of infected persons are asymptomatic. The most common clinical presentation is that of a mild flu-like illness or what is termed West Nile fever: general malaise, fever, headache, myalgias and anorexia lasting 3-6 days, but more protracted courses have been described. Lymphadenopathy or a transient erythematous fine maculopapular rash of the face and trunk may be seen. Symptoms resolve fully with supportive care.

Neuroinvasive disease is the next most common manifestation: meningitis, encephalitis and/or myelitis with acute flaccid paralysis are well-described. These are estimated to represent less than 1% of WNV infections.[8] Advanced age (> 50 years) is a clear risk factor for development of neuroinvasive disease. There is suggestion that diabetes and alcohol abuse may be factors as well. [9]

WNV meningitis resembles other viral meningitides and presents with fever, headache, nausea, vomiting, nuchal rigidity and photophobia. WNV encephalitis may present with all of these plus altered mental status, focal neurological changes and, less commonly, seizures. In WNV encephalitis, tremor is common and other movement disorders have also been reported. WNV acute flaccid paralysis may be symmetric or asymmetric and clinically and pathologically resembles poliomyelitis. There is hypo- or a-reflexia and often bowel and bladder dysfunction. Sensation, however, is intact. Pathology generally reveals destruction of anterior horn cells. Rarely, demyelinating syndromes have been reported. Guillain-Barré syndrome is in the differential and must be ruled out with history, serological testing and, if needed, electromyographic and nerve conduction studies. Finally, WNV has also been reported to cause chorioretinitis and vitritis.[8]

On routine blood work, patients may have a mild leukocytosis or leukopenia and mild hyponatremia. With neuroinvasive disease, spinal fluid reveals mild to moderate pleocytosis (typically < 500 cells/mm^3 although > 2000 have been reported), usually lymphocytic, with elevated protein and normal glucose. Head CT is generally unremarkable. Brain and spine MRI are normal in the majority of patients but in about one-third may reveal leptomeningeal or periventricular enhancement or increased signal on T2-weighted images of the thalamus, basal ganglia, brainstem, or spinal cord.

Rarely, WNV has been reported to cause acute pancreatitis, hepatitis, nephritis, myocarditis, or a septic shock-like syndrome with multisystem organ failure.

Overall, about one-third of patients with WNV infection are hospitalized. In one series from the Colorado experience in 2003, 34-38% of patients with encephalitis or limb weakness required intubation and mechani-

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Questions & Comments

Please call Leslie Hamlin, Managing Editor, at (404) 262-5416 or e-mail at leslie.hamlin@ahcmedia.com between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

Table 1

Laboratory criteria for diagnosis

Laboratory criteria for diagnosis

- Fourfold or greater change in virus-specific serum antibody titer, or
- Isolation of virus from or demonstration of specific viral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid, or
- Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF by antibody-capture enzyme immunoassay (EIA), or
- Virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific serum immunoglobulin G (IgG) antibodies in the same or a later specimen by another serologic assay (e.g., neutralization or hemagglutination inhibition).

Case classification

Probable: an encephalitis or meningitis case occurring during a period when arboviral transmission is likely, and with the following supportive serology: 1) a single or stable (less than or equal to twofold change) but elevated titer of virus-specific serum antibodies; or 2) serum IgM antibodies detected by antibody-capture EIA but with no available results of a confirmatory test for virus-specific serum IgG antibodies in the same or a later specimen.

Confirmed: an encephalitis or meningitis case that is laboratory confirmed.

cal ventilation[9]; in another recent review of WNV-associated acute flaccid paralysis, 54% of patients required ventilatory support.[10] ICU lengths of stay for these patients may be quite long (up to 118 days in one study).[11] Mortality of those with neuroinvasive disease is up to 7-18% and even higher in patients with acute flaccid paralysis with quadriparesis or those requiring mechanical ventilatory support.[7,10,12] Significant neuropsychological impairments remain at 8-12 months of follow-up of patients with WNV neuroinvasive disease, with complaints including general fatigue and weakness, memory loss, cognitive dysfunction, tremor, gait abnormalities, and depression. Those with acute flaccid paralysis in particular appear to have only limited recovery at best. [12-13]

Diagnostic Studies[4,6]

Presence of WNV virus in any body fluid or tissue (usually detected by PCR) confirms the diagnosis of WNV infection. However, the likelihood of isolating the virus is quite low; by the time symptoms of illness develop, only very low levels of viremia are present. For instance, sensitivity of WNV PCR of CSF for patients with neuroinvasive disease is ≤ 50%.

Thus, diagnosis is generally made by detection of serum or CSF antibodies to WNV in the appropriate clinical setting. Measurement of WNV IgM and IgG by antibody capture enzyme linked immunoabsorbent assay (MAC-ELISA) is the recommended method for confirming diagnosis. WNV IgM antibodies become positive by the 8th day of illness in ≥ 90% of patients; it is important to note that they may persist for ≥ 6-12 months. Presence of WNV IgM in the CSF confirms neuroinvasive disease. WNV IgG antibodies begin to appear at one week and are positive by 3 weeks in most infected patients; thus, an increase in titer over this time period is strongly suggestive of acute infection. (*The CDC case epidemiological case definitions for WNV infection are listed in the Table 1.*)

The duration of viremia, and time to development of antibodies, may be delayed in immunocompromised patients.

There is cross-reactivity between antibodies against WNV and antibodies against other viruses of the *Flaviviridae* family. Thus, it is important to obtain appropriate clinical history to evaluate for these and to confirm any positive WNV antibody result by MAC-ELISA with further, more specific testing (plaque reduction neutralization assay).

Treatment[14-16]

Supportive care is the mainstay of therapy for WNV infection. There have been in vitro or animal studies and anecdotal human reports of therapy with WNV-specific-IV-immunoglobulin, ribavirin, interferon-alpha and corticosteroids. Results have been mixed. At this time there is insufficient evidence to recommend any of these therapies. PREVENTION[2,4,7]

An equine WNV vaccine was licensed in 2003 and is currently in use. No human vaccine is yet available although studies of candidate vaccines are ongoing.

Avoiding exposure to infected mosquitoes is the primary route of prevention of WNV infection. This is particularly important for persons who are elderly, pregnant, or immunocompromised. Recommended methods include using insect repellent (containing DEET, permethrin, picaridin or oil of lemon eucalyptus), wearing long-sleeved and long-legged clothing, limiting outdoor activity during dusk to dawn (the peak mosquito hours), and using door and window screens on homes and draining standing water to avoid creating mosquito breeding areas. Local mosquito control programs including spraying of large areas with larvicides or insecticides may be necessary in some locations.

The FDA recommends routine screening of blood products for WNV between June 1 and November 30. Furthermore, donors with symptoms of flu-like illness in the week prior to presentation to blood banks are asked to defer donation for one month. Cases of persons who are found to develop WNV infection after donation or persons with WNV illness who received transfusion in the month preceding onset of illness are also investigated in order to identify and remove infected blood products from the supply.

Summary

WNV infection is an increasing problem in the United States. Our knowledge of its epidemiology and clinical

impact is still developing. Until targeted therapies and a specific preventive vaccine are identified, supportive care remains the mainstay of treatment. It is clear that for now we will continue to encounter WNV infection cases resulting in severe illness, substantial morbidity including need for prolonged critical care services and support for long term neurological deficits, and significant mortality. ■

References

1. Nash D, et al. 1999 West Nile Outbreak Response Working Group. The outbreak of West Nile virus infection in the New York City area in 1999. *N Engl J Med.* 2001;344:1807-1814.
2. Hayes EB, Gubler DJ. West Nile virus: epidemiology and clinical features of an emerging epidemic in the United States. *Annu Rev Med*. 2006;57:181-194.
3. http://www.cdc.gov/ncidod/dvbid/westnile/index.htm.
4. Sampathkumar P. West Nile virus: Epidemiology, clinical presentation, diagnosis and prevention. *Mayo Clin Proc.* 2003;78:1137-1144.
5. O'Leary DR, et al. Birth outcomes following West Nile Virus infection of pregnant women in the United States: 2003-2004. *Pediatrics.* 2006;117:e537-545.
6. Petersen L, et al. West Nile virus. *JAMA.* 2003;290:524-528.
7. Tyler KL. West Nile virus infection in the United States. *Arch Neurol.* 2004;61:1190-1195.
8. Sejvar JJ, Marfin AA. Manifestations of West Nile neuroinvasive disease. *Rev Med Virol.* 2006;16:209-224.
9. Bode AV, et al. West Nile virus disease: a descriptive study of 228 patients hospitalized in a 4-county region of Colorado in 2003. *Clin Infect Dis.* 2006;42:1234-1240.
10. Saad M, et al. Acute flaccid paralysis: the spectrum of a newly recognized complication of West Nile virus infection. *J Infect*. 2005;51:120-127.
11. Fan E, et al. West Nile virus infection in the intensive care unit: a case series and literature review. *Can Respir J.* 2004;11:354-358.
12. Sejvar JJ, et al. West Nile Virus-associated flaccid paralysis outcome. *Emerg Infect Dis.* 2006;12:514-516.
13. Sejvar JJ, et al. Neurologic manifestations and outcome of West Nile virus infection. *JAMA.* 2003;290:511-515.
14. Gea-Banacloche J, et al. West Nile virus: pathogenesis and therapeutic options. *Ann Intern Med*. 2004;140:545-553.
15. Kalil AC, et al. Use of interferon-alpha in patients with West Nile encephalitis: report of 2 cases. *Clin Infect Dis.* 2005;40:764-766.
16. Anderson JF, Rahal JJ. Efficacy of interferon alpha-2b and ribavirin against West Nile virus in vitro. *Emerg Infect Dis.* 2002;8:107-108.

Listeria Meningitis

ABSTRACT & COMMENTARY

By Stan Deresinski, MD, FACP

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This article originally appeared in the January 2007 issue of Infectious Disease Alert. It was edited by Dr. Deresinski, and peer reviewed by Connie Price, MD. Dr. Price is Assistant Professor, University of Colorado School of Medicine. Dr. Price reports no financial relationship relevant to this field of study.

Source: Brouwer MC, et al. Community-acquired *Listeria monocytogenes* meningitis in adults. C*lin Infect Dis.* 2006; 43:1233-1238.

Of 696 episodes of community-acquired meningitis in adults identified by the nationwide Dutch Meningitis Cohort Study from 1998 to 2002, 30 (4%) were due to *Listeria monocytogenes*. The mean age was 65 ± 18 years; all 10 of the previously immunocompetent patients were > 50 years of age.

Symptoms were present for > 4 days prior to presentation in 8 (27%) patients. While the entire meningitis triad of nuchal rigidity, fever, and altered mental status was present in only 43% of patients, 97% had at least 2 of 4 symptoms and/or signs if headache is added to the triad. Ten percent were comatose (Glasgow coma score < 8) and an additional 70% had altered mental status (Glasgow score < 14). Eighteen of 23 had a normal brain CT on admission, but left unstated is whether IV contrast was administered. Abnormalities noted on CT included cerebral edema in 2 patients and a recent cerebral infarction in one. A single MRI was performed and it was normal.

All patients underwent lumbar puncture. The CSF pressure was > 250 mm of water in 5 of 8 for whom manometry was performed. CSF WBC ranged from 24 to 16,003 WBC/mL, with a median value of 620 WBC/mL; 13% had < 100 WBC/mL. There was no relationship between CSF leukocyte count and the presence or absence of immunocompromise. The median CSF protein concentration was 2.52 g/L (range 1.1-19.3 g/L) and the median CSF: blood ratio of glucose was 0.30 (range 0.03-0.86), but 23% of patients "had no individual CSF findings indicative of bacterial meningitis."

A Gram stain was performed on the CSF of 25 patients and was negative in 60%, demonstrated Gram positive bacilli in 28%, and Gram negative bacilli in 2 patients (4%). CSF culture yielded *L. monocytogenes* in

all patients (this was a criterion for inclusion the cohort) and 12 (46%) of 26 had positive blood cultures. Three-fourths of patients were hyponatremic.

Initial antibiotic therapy was inadequate (not active against *L. monocytogenes)* in 30%, but this did not appear to affect mortality, which occurred in 5 (17%) patients. All 5 deaths occurred in the first 3 days of hospitalization.

COMMENTARY

Adults at increased risk of Listeria infection include pregnant women (especially during the 3rd trimester), those with lymphoma and other malignancies, and those receiving immunosuppressive therapy for organ transplantation and other indications. Cases have been reported in recipients of anti-TNF therapy with both infliximab and etanercept. In addition, however, approximately one-third with infection have none of these underlying problems, but almost all are greater than 50 years of age.

While, as in this study, there is a broad range of acuity and severity with which meningitis due to *L. monocytogenes* presents in adults, in many cases the presentation is subacute. Thus, Brouwer and colleagues report that just over one-fourth of patients were ill for 4 or more days prior to presentation. In some cases, the illness may be more accurately termed meningoencephalitis, rather than meningitis, because of clinical evidence of parenchymal involvement of the brain. Patients may present with seizures, cranial neuropathies, hemiplegia, and other evidence of focal disease, as well as with global cerebral dysfunction manifested as coma. *L. monocytogenes*, in fact, has an unusual propensity to invade brain parenchyma, causing cerebritis, which may progress to frank abscess formation. The presence of a brain stem abscess should especially alert the clinician to the Listeria as the possible etiology of the infection.

A subacute presentation, together with, in some cases, CSF lymphocytosis, makes it necessary to differentiate meningitis due to *L. monocytogenes* from that due to *Mycobacterium tuberculosis* and other causes of granulomatous meningitis. Since only a minority of patients with *Listeria meningitis* have a positive CSF Gram stain, the diagnosis generally remains in doubt until CSF and/or blood cultures yield the organism. Even in cases in which organisms are microscopically visualized, their appearance may be misleading, such as in this study in which the occasional Gram-variability of the organism led to the identification of Gram negative, rather than Gram positive bacilli in 2 cases. Furthermore, even when the organism stains Gram positive, it may be mistaken for diphtheroids and inappropriately discounted. Listeria can be distinguished from diphtheroids in the microbiology laboratory by their beta-hemolysis and tumbling motility. ■

Sex Differences in Acute Coronary Symptoms

ABSTRACT & COMMENTARY

By Michael H. Crawford, MD

Professor of Medicine, Chief of Clinical Cardiology, University of California, San Francisco

Dr. Crawford is on the speaker's bureau for Pfizer.

This article originally appeared in the January 2007 issue of Clinical Cardiology Alert. *It was edited by Dr. Crawford, and peer reviewed by Rakesh Mishra, MD, FACC. Dr. Mishra is Assistant Professor of Medicine, Weill Medical College, Cornell University; Assistant Attending Physician, NewYork-Presbyterian Hospital.*

Synopsis: *The same appearances in presentation of men and women with ACS can largely be explained by factors other than sex.*

Source: Arslanian-Engoren C, et al. Symptoms of Men and Women Presenting with Acute Coronary Syndromes. *Am J Cardiol*. 2006;98:1177-1181.

It is well known that women with acute coronary syndromes (ACS) arrive later, get fewer evidence-based therapies, and have worse outcomes. Chest pain is the critical symptom that starts the ACS management cascade. It has been suggested that women with ACS present with different symptoms than men; thus, explaining their delayed and often inadequate therapy. Arslanian-Engoren and colleagues analyzed 1941 patients in the Acute Coronary Syndrome Registry at the University of Michigan to see if any differences in the presenting symptoms of men and women were sex related or could be explained by other factors. Women represent 35% of the patients, 72% of whom had myocardial infarction and 28% unstable angina. Women were older than the men (67 vs 61 years, $P < 0.01$). As compared to men, women > 65 years were more likely to be obese; women < 65 were more often lean; women had systemic hypertension more often and were less likely to have had coronary revascularization in the past. Women delayed more than men before coming to the hospital (14.5 vs 12 hours, $P < 0.01$). Men were more likely to present with chest pain, but the difference was small (89% vs 82%, $P < 0.01$). Left arm radiation (30% vs 25%, $P < 0.05$) and diaphoresis (38% vs 29%, $P < .01$) were more common in men and nausea was more common in women (29% vs 25%, $P < 0.05$). Dyspnea was not different. Logistic regression analysis showed that only diaphoresis and nausea were predicted by sex, but the strongest predictor of nausea was inferior ST-segment elevation. Arslanian-Engoren et al concluded that sex should be considered in

the evaluation of ACS, but factors other than sex explained most of the small differences found between men and women.

COMMENTARY

This study confirms my clinical impression that there is no major difference in the presenting symptoms of men and women with ACS. Most present with chest pain; > 80% in both sexes. The small differences in other symptoms largely disappear when other clinical factors are considered. For example, diabetes is more common in women < 65 years of age as compared to young men (34% vs 27%, $P < 0.01$). Only diaphoresis seemed to be explained mainly by sex, being more common in men, but this difference was driven by younger men (incidence 42%); older men had similar rates as women (33 vs 29%). Thus, most of the differences in the presentation of ACS in men and women can be explained by differences in age, comorbidities, and location of ischemia.

The major message of this paper is that in order to recognize ACS quickly, so that timely interventions can be undertaken to reduce the risk of arrhythmias, heart failure, cardiac arrest or a large infarction, presentations other than chest pain need to be considered indications for performing a STAT ECG. This may be more important in women who can present atypically because of other clinical factors, but it is imperative in both sexes to pay attention to more subtle presentations such as diaphoresis, nausea and dyspnea. More important than sex is the fact that older aged individuals of both sexes are less likely to present with chest pain. Finally, the sobering reminder in this study that patients delay 12 to 15 hours before seeking medical attention for their symptoms needs to be addressed. Clearly more public education is in order, especially for women who delay the longest.

Preventing Nosocomial Infection in Cardiac Surgery

ABSTRACT & COMMENTARY

By David J. Pierson, MD

This article originally appeared in the January 2007 issue of Critical Care Alert.

Source: Segers P, et al. Prevention of nosocomial infection in cardiac surgery by decontamination of the nasopharynx and oropharynx with chlorhexidine gluconate: A randomized, controlled trial. *JAMA* 2006;296:2460-2466.

SEGERS AND COLLEAGUES OF THE UNIVERSITY OF Amsterdam conducted this randomized, double-blind clinical trial at a 480-bed community hospital that performs 1200 cardiac surgical procedures annually. They sought to determine whether the routine application of the disinfectant chlorhexidine to the nasopharynx and oropharynx of patients undergoing cardiac surgery would decrease the incidence of nosocomial infection, nasal carriage of *Staphylococcus aureus*, and the duration of hospital stay.

All patients over 18 years of age who underwent sternotomy for electively-scheduled cardiac procedures and gave consent during the 25-month study period were included. They were randomized to receive 0.12% chlorhexidine gluconate both as a nasal gel and as a 10-mL mouth rinse or an apparently identical placebo. Application of the experimental solutions began on hospital admission and continued 4 times daily until the nasogastric tube was removed postoperatively, usually the day after surgery. Nosocomial infections were diagnosed using accepted criteria from the CDC, and nasal surveillance cultures for S. aureus were performed at fixed intervals. All patients underwent perioperative skin cleansing and administration of intravenous cefuroxime according to institutional protocols.

In this study, 991 patients were randomly administered chlorhexidine decontamination or placebo. The overall incidence of nosocomial infection was 19.8% in the chlorhexidine group as compared to 26.2% in the placebo group (absolute risk reduction [ARR], 6.4%; 95% confidence interval [CI], 1.1%-11.7%; $P = 0.002$). The most severe infections — lower respiratory tract infections and deep surgical site infections — were significantly less common in the active treatment group: ARR, 6.5% and 3.2%, respectively, $P = 0.002$ for each. The number needed to treat in order to prevent one nosocomial infection was 16. In addition, *S. aureus* nasal carriage was reduced by 57.5% in the patients who received chlorhexidine, as compared with 18.1% in the placebo group ($P < 0.001$). Total hospital stay for patients treated with chlorhexidine gluconate was 9.5 days, compared with 10.3 days in the placebo group (ARR, 0.8 days; 95% CI, 0.24-1.88; $P = 0.04$). One patient in the active treatment group experienced temporary discoloration of the teeth; there were no other reported adverse effects.

COMMENTARY

Nosocomial infections occur in as many as 20% of patients who undergo cardiac surgery and are an important cause of mortality, morbidity, prolongation of hospitalization, increased antibiotic utilization, and excess costs. The source of these infections is often the patient's own organisms, the suppression of which by means of topical decontamination would seem a logical and practical strategy for reducing their incidence.

This was a study in patients undergoing elective cardiac surgery, whose ICU stays were generally short. Whether beneficial effects of routine naso- and oropharyngeal decontamination with chlorhexidine similar to those obtained in this study would be observed in medical ICU patients or in a general surgical ICU population is not known at this point.

The treatment as used in this study was both safe and inexpensive. The reported daily cost for the decontamination regimen employed was $7.20. With an average duration of decontamination of 2 days, the cost to prevent one nosocomial infection was estimated to be $230. Costs would undoubtedly be higher using the prepackaged commercial kits for oral hygiene and decontamination that are currently being marketed in the United States; an estimation of the cost to prevent one infection, assuming clinical effectiveness similar to the efficacy demonstrated by Segers et al and using actual current costs in your hospital, would be a worthwhile exercise prior to widespread adoption of this treatment. ■

TIA Management: Emphasis on Urgent Evaluation and Treatment

ABSTRACT & COMMENTARY

By Dana Leifer, MD

Associate Professor, Neurology, Weill Medical College, Cornell University.

Dr. Leifer reports no financial relationship relevant to this field of study. This article originally appeared in the December 29, 2006 issue of Internal Medicine Alert. It was edited by Stephen Brunton, MD, and peer reviewed by Gerald Roberts, MD. Dr. Brunton is Clinical Professor, University of California, Irvine, and Dr. Roberts is Clinical Professor of Medicine, Albert Einstein College of Medicine. Dr. Brunton is a consultant for Sanofi-Aventis, Ortho-McNeil, McNeil, Abbott, Novo Nordisk, Eli Lilly, Endo, EXACT Sciences, and AstraZeneca, and serves on the speaker's bureau for McNeil, Sanofi-Aventis, and Ortho-McNeil. Dr. Roberts reports no financial relationship relevant to this field of study.

Synopsis: *Patients with transient ischemic attacks should usually be admitted to the hospital and receive rapid evaluation and treatment.*

Source: Johnston, SC, et al. National Stroke Association Guidelines for the Management of Transient Ischemic Attacks. *Ann Neurol.* 2006:60:301-313.

A GROWING BODY OF EVIDENCE INDICATES THAT there is a significant risk of stroke in the days immediately after a transient ischemic attack. Johnston and colleagues found that 5% of TIA patients had a stroke within 48 hours and another 5% had a stroke within 90 days. Several other groups have obtained similar results. In addition, Rothwell et al showed that approximately 20% of stroke patients have a TIA before their stroke and that of these, 26% occurred on the day of the stroke or the day before the stroke, and an additional 19% occurred between 2 and 7 days before the stroke.[1] Taken together, these data indicate a need to take TIAs seriously, to initiate appropriate preventive treatment quickly, and to facilitate rapid intervention if a stroke develops.

In this background, the National Stroke Association (NSA) established an expert panel to develop guidelines for TIA management. The panel was chosen objectively on the basis of publications related to TIA and stroke. After a literature search, the quality of evidence was rated, and recommendations were derived from the rated evidence. Multiple rounds of comments from the panel were used to derive a consensus, and panel members were excluded from contributing to topics for which they had a possible conflict of interest. This approach was designed to avoid bias in selection of experts, to prevent overweighting of dominant personalities in the consensus process, and to permit efficient updating of the recommendations.

The guidelines emphasize the need for timely treatment of TIAs. The chief points are: 1) Hospitalization should be considered for all patients presenting within 48 hours of their first TIA to facilitate thrombolytic therapy if a stroke develops and to begin secondary prevention rapidly. An important corollary that the guidelines do not address, however, is that if patients are admitted, they need to be monitored closely to minimize the delay in recognizing in-hospital strokes. 2) Timely referral to a hospital is also advisable for all patients within one week of a TIA and hospital admission is generally recommended for patients with crescendo TIAs, TIAs lasting more than one hour, > 50% carotid stenosis if symptomatic, known cardioembolic sources, known hypercoagulability, and combinations of other factors placing patients at high risk based on recently developed scales for rating stroke risk after TIA (*Stroke.* 2006;37:320-322).

The guidelines also make recommendations about the infrastructure that should be available for evaluation of TIA patients: 1) Local protocols should be established to identify patients who will be admitted and those who will be referred for outpatient evaluation. Specialty clinics for outpatient evaluation within 24 to 48 hours should be available for patients who are not admitted. Patients who are not admitted should be instructed to return at once if they have recurrent symptoms. 2) Patients not

admitted should have access within 12 hours to CT or MRI, EKG, and carotid Doppler. These should be done within 24 to 48 hours if they are not done in an emergency room. If they are done and are normal, a longer period of up to 7 days may be appropriate for further work-up. 3) Patients with TIA within 2 weeks who are not admitted should be worked up within 24 to 48 hours (ie, carotid Doppler, blood work, cardiac evaluation such as EKG, rhythm strips, and echocardiography). 4) Medical assessment should at least include EKG, CBC, electrolytes, creatinine, glucose, and lipid studies. 5) Imaging should include CT or MRI for all patients to rule out structural lesions such as acute stroke, subdural hemorrhage, and brain tumor (25% or more of patients with a clinical TIA may actually have had a small stroke). Some form of vascular imaging (ie, ultrasound, CTA, or MRA) should also be performed. Catheter angiography remains the gold standard, but should be used for diagnostic purposes primarily when the other tests are discordant or cannot be performed. 6) Cardiac evaluation with transthoracic or transesophageal echocardiography and testing for right to left shunting is advised in patients younger than 45 years of age if other studies do not identify a cause for the TIA.

The guidelines go on to make specific recommendation for antithrombotic therapy and for treatment of other specific risk factors that are identified during the work-up. These are important and emphasize the need for antiplatelet therapy for most patients, anticoagulation when indicated, and aggressive management of risk factors including carotid stenosis, hypertension, hyperlipidemia, and diabetes. The recommendations are largely similar to those of the American Heart Association's 2006 statement on stroke prevention (*Stroke.* 2006;37:577-617). Those guidelines, however, did not address the importance of rapid evaluation of TIA patients. The main importance of the new NSA guidelines is that they stress the need for rapid evaluation and treatment of TIA patients. ■

CME Questions

4. In the study on community-acquired Listeria meningitis by Brouwer et al:
   a. the majority of cases had a subacute presentation with more than 4 days of symptoms.
   b. Gram stain of the CSF was most often negative despite culture positivity.
   c. the CSF biochemical and cellular pattern was pathognomonic.
   d. meningitis due to Listeria only occurred in immunocompromised individuals.

5. According to Segers et al, application of chlorhexidine to the oropharynx and nasopharynx to patients undergoing cardiac surgery led to:
   a. an increase in hospital length of stay.
   b. an increase in colonization with *Staphylococcus aureus.*
   c. an increase in colonization with Gram-negative rods.
   d. a decrease in perioperative nosocomial infections.

6 . Transient ischemic attacks (TIA):
   a. do not pose an imminent neurological threat.
   b. are only worrisome if associated with crescendo symptomatology.
   c. may be an indication for hospitalization and aggressive evaluation.
   d. should be treated with thrombolysis.

Answers: 4. (b); 5. (d); 6. (c)

CME Objectives

The objectives of *Hospital Medicine Alert* are to:

• review pertinent safety, infection control, and quality improvement practices;

• discuss diagnosis and treatment of acute illness in the hospital setting; and

• review current data on diagnostic and therapeutic modalities for common inpatient problems. ■

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CUMULATIVE INDEX

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