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INSIDE

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MRI or CT: Which is Best for Acute Stroke Imaging?

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.

Synopsis: *MRI is more sensitive than CT for detecting acute ischemia and can detect acute hemorrhage with equal sensitivity to CT.*

Source: Chalela JA, et al. Magnetic resonance imaging and computed tomography in emergency assessment of patients with suspected acute stroke: A prospective comparison. *Lancet.* 2007;369:293-298.

MAGNETIC RESONANCE IMAGING (MRI) CAN VISUALIZE ACUTE strokes with great sensitivity and can also identify acute and chronic intracranial hemorrhage. Computed tomography (CT), nevertheless, is still the first study obtained on stroke patients at almost all hospitals because of its greater availability and because of concerns about the ability of MRI to diagnose acute hemorrhage. To compare the utility of MRI and CT, Chalela and colleagues performed a blinded prospective comparison of CT and MRI in 356 acute stroke patients at a single hospital.

All patients referred to the hospital's stroke team were eligible. Patients were excluded if either CT or MRI were not done. Reasons for not doing both studies included contraindication to MRI, clinical syndrome strongly suggestive of subarachnoid hemorrhage, initiation of antithrombotic or thrombolytic therapy before completion of both scans, or inability to complete both scans quickly enough to permit intravenous thrombolysis within 3 hours of symptom onset. Of the 450 patients who were screened, 94 were excluded from the study.

A panel of 4 experts reviewed the images for the study. Positive findings were considered to be present if 3 of the 4 readers agreed. The readers did not have access to clinical information.

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The primary result was that MRI detected acute ischemic stroke in 52% of the patients, and CT only in 17% (P <0.0001). The greater sensitivity of MRI is not surprising as all patients underwent diffusion-weighted imaging, which can detect acute stroke within one hour of onset.

Of importance, although MRI is more sensitive than CT, there were still 33 false negative MRI results among the 356 studies reviewed by the panel of experts. In other words, the expert panel did not identify an acute stroke on the MRI of 33 patients who had a final diagnosis of acute ischemic stroke. Of note, the treating physicians who had access to clinical information (unlike the panel of experts) identified acute strokes in 23 of these 33 MRI studies. This finding suggests that communication between clinicians and radiologists is important in interpretation of acute stroke imaging.

With regard to false negative MRI studies, it is important to emphasize that imaging confirmation of acute stroke is not necessary to initiate intravenous thrombolytic therapy or other conventional stroke treatments. It is only necessary to rule out acute hemorrhage before intravenous thrombolysis. Nevertheless, imaging confirmation of stroke is important in some settings-for example, if a patient presents with a seizure and an acute deficit that may be ischemic or may be a post-ictal Todd's paralysis, or if a patient is being considered for intra-arterial treatment.

With regard to acute hemorrhage, MRI and CT had similar sensitivities. MRI found intracranial hemorrhage in 6% and CT in 7%. CT identified 4 patients with hemorrhage that was not seen on MRI, and MRI identified 2 patients with CT scans that were negative. Among the 90 patients imaged within 3 hours, MRI missed 2 acute hemorrhages that were seen on CT while CT missed one acute hemorrhage seen on MRI. Thus, neither test is 100% accurate for diagnosis of hemorrhage; in the past, one of the reasons for preferring CT over MRI has been the belief that CT is the gold standard for detection of acute hemorrhage. Additional information about the clinical significance of the hemorrhages that were not detected by CT or by MRI might be helpful but was not provided.

MRI was found to detect chronic hemorrhages in 26% of patients, whereas CT, which is poor in detecting chronic blood products, did not identify any chronic bleeds. The extent to which the presence of old hemorrhage is clinically important is not certain, but it may influence choice of thrombolytic or antithrombotic treatment in some cases.

COMMENTARY

In view of all of these findings, the authors conclude that MRI should be the imaging modality of choice for patients suspected of having an acute stroke. MRI's high sensitivity and inter-rater reliability are in its favor, but the results with expert readers do not necessarily apply to community practice where specialists may not be available to interpret scans acutely. This especially remains a concern with regard to identification of acute hemorrhage in patients being considered for intravenous thrombolysis.

In addition, it should be noted that 20% of patients were excluded from the study primarily because of contraindications to MRI or lack of time, so the results of the study do not apply to all acute stroke patients. The advantages of MRI should not be taken as reason to perform MRI in unstable or uncooperative patients whose treatment may be excessively delayed by attempts to do it. Indeed, for any patient who is a candidate for intravenous thrombolysis, MRI may introduce significant delay. This paper, nevertheless, demonstrates that there are substantial advantages to MRI. Its use in acute stroke ought to be considered instead of CT in many patients. In addition, when new emergency departments are being designed, rapid access to MRI should be incorporated as a design feature that will facilitate the care of stroke patients. ■

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Prediction and Diagnosis of HIV Dementia

ABSTRACT & COMMENTARY

By Michael T. Lin, MD

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Dr. Lin reports no financial relationships relevant to this field of study.

Synopsis: *Several CSF biomarkers, sphingomyelin, sphingomyelinase, ceramide, 4-hydroxynonenal, and vitamin E, are associated with the development of HIV dementia in patients being treated with highly active antiretroviral therapy (HAART).*

Source: Bandaru VV, et al. Associative and predictive biomarkers of dementia in HIV-1-infected patients. *Neurology.* 2007,68:1481-1487.

HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY (HAART) has changed the nature of HIV dementia: the degree of cognitive impairment is milder, the course may improve as well as worsen, and traditional biomarkers such as CSF viral load or levels of monocyte chemotactic protein 1 (MCP-1) are less likely to be associated with dementia. The objective of this study was to identify new CSF biomarkers that are associated with or predictive of HIV dementia in the setting of HAART.

The study involved 48 patients from the North Eastern AIDS Dementia cohort, assessed cognitively at 0, 6, and 12 months. CSF was drawn at the 6 month time point, and analyzed for biochemical markers. Biochemical markers correlating with cognitive change over the preceding 6 months (between 0 and 6 months) were said to be biomarkers associated with cognitive change; biochemical markers correlating with cognitive change over the subsequent 6 months (between 6 and 12 months) were said to be biomarkers predictive of cognitive change. Based on previous work showing accumulation of sphingomyelin, ceramide, sterol, and lipid peroxidation products in brains of HIV dementia patients, these were the primary biomarkers the authors investigated.

Considering first the cognitive changes occurring before the CSF draw (between the 0 and 6 month time points), the authors divided the cohort into 3 groups: those who were not demented at both time points ("nondemented"), those who were initially demented and remained stably so ("inactive dementia"), and those who were initially not demented but became demented ("active dementia"). Those with inactive dementia over the preceding 6 months had 3-5 fold elevations of CSF sphingomyelin compared to nondemented or active dementia subjects. Those with active dementia over the preceding 6 months had increased CSF ceramide levels and sphingomyelinase activity, increased levels of lipid peroxidation products (4-hydroxynonenal), and decreased levels of the lipid antioxidant vitamin E.

Considering, next, the cognitive changes occurring after the CSF draw (between the 6- and 12-month time points), the authors divided the cohort into 3 groups, based on whether scores improved, remained stable, or worsened. The group that subsequently worsened had increased CSF levels of triglyceride C52 and vitamin E. Sphingomyelin, ceramide, and hydroxynonenal levels were not predictive of subsequent worsening.

COMMENTARY

These are interesting findings, consistent with the known biology of HIV. In tissue culture, the HIV-1 coat protein gp120 and the trans acting protein Tat can increase sphingomyelin levels in 6 hours, followed by activation of neutral sphingomyelinase (Haughey et al. 2004; Jana et al. 2004). In response to inflammatory mediators, sphingomyelinase cleaves sphingomyelin to produce ceramide, which induces apoptosis and increases oxidant stress. Additionally, cleavage of sphingomyelin by sphingomyelinase disrupts the association between cholesterol and sphingomyelin. The cholesterol released can then accumulate in lipid droplets containing cholesterol esters and triglycerides. This sequence could explain the increases in sphingomyelin in stably demented subjects; the increased sphingomyelinase, ceramide, and lipid peroxidation seen in actively demented subjects; and the increased triglyceride C52 seen in subjects who subsequently worsened. The authors interpret the elevated vitamin E levels initially seen in subjects who subsequently worsened as a secondary compensatory response to ongoing pathology. When the pathology overwhelms defensive systems, decreased vitamin E levels would then be found in actively dementing subjects.

Several potential follow-up studies should be considered. Although the design of this study cleverly minimized the number of CSF draws, true biomarkers should be shown to vary over time in parallel with the process being followed. The results of this study should thus be confirmed with serial determinations of biomarkers in parallel with cognitive assessments. Additionally, with at least one key biomarker of active pathogenesis, ceramide, the magnitude of difference between groups, although statistically signifi-

cant, was small, and it is not clear that such a biomarker could usefully discriminate between groups. The sensitivity, specificity, and ability to discriminate between groups should be characterized. Finally, the pathogenetic sequence identified could lead to new potential therapy of HIV dementia, targeting the HIV-induced perturbations of sphingomyelin/ceramide metabolism. ■

Background:

Haughey NJ, et al. Perturbation of sphingolipid metabolism and ceramide production in HIV-dementia. *Ann Neurol.* 2004;55:257-267.

Jana A, Pahan K. Human immunodeficiency virus type 1 gp120 induces apoptosis in human primary neurons through redox-regulated activation of neutral sphingomyelinase. *J Neurosci.* 2004;24:9531-9540.

Celiac Disease and Myopathy

ABSTRACT & COMMENTARY

By Michael Rubin, MD

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Dr. Rubin is on the speaker's bureau for Athena Diagnostics, and does research for Pfizer and Merck.

***Synopsis**: Celiac disease is a cause of treatable inflammatory myopathy, and is easily diagnosed with serum antibody studies.*

Source: Hadjivassiliou M et al. Myopathy associated with gluten sensitivity. *Muscle Nerve*. 2007;35;443-450.

Clinical manifestations of gluten sensitivity encompass diverse organ systems. When restricted to the gastrointestinal tract and associated with villous atrophy, crypt hyperplasia, and small bowel intraepithelial lymphocytosis, the term celiac disease is appropriate. Skin involvement defines dermatitis herpetiformis, while neuropathy or ataxia remain its most common neurologic expression. Myopathy, hitherto not well characterized, may also occur. Among 300 patients referred over 12 years to the Gluten Sensitivity/Neurology Clinic at The Royal Hallamshire Hospital, Sheffield England, 13 presented with myopathy, 4 of which additionally demonstrated neuropathy alone (=2) or ataxia and neuropathy (n=2). Only 1 was previously known to have celiac disease at the time of presentation. Workup failed to reveal any cause for myopathy other than gluten seropositivity in 12 patients, including positive IgG or IgA antigliadin (n = 12) or antiendomysial (n = 2) antibodies. Electrodiagnostic studies, duodenal biopsy, and muscle biopsy was performed following serologic diagnosis.

Mean age of onset was 54 years, with females outnumbering males (8:5). Weakness was proximal in 8 (62%), both proximal and distal in 4 (31%), and predominantly distal in 1 (8%). Creatine kinase (CK) was elevated in 11 (range 221-4380 IU/L, normal < 190), 10 had the HLA-DQ2 genotype, and 6 each had duodenal biopsy-proven enteropathy or associated autoimmune diseases included high thyroid antibodies (n = 3), hypothyroidism (n = 2), or inflammatory arthropathy (n = 1). Electrodiagnostic studies yielded normal nerve conduction studies in 10, with 3 showing loss of evoked motor potential amplitude. Needle electromyography revealed myopathic features in 10, demonstrating short-duration, small amplitude motor unit potentials in at least 1 proximal muscle, with fibrillation potentials seen in 2 of these patients. Inflammatory myositis was seen on biopsy in 6, 1 patient also having features of inclusion body myositis with basophilic rimmed vacuoles. Nonspecific myopathy was evident in the remaining biopsies.

Of 6 patients on a gluten-free diet and immunosuppressive therapy, 5 improved and one normalized serum CK values while remaining clinically unchanged. Of 7 patients solely on dietary management, 4 improved clinically with reduction or normalization of serum CK. Refusal to adopt a gluten free diet was associated with progressive myopathy in a single patient. Myopathy is a manifestation of gluten sensitivity, appears to be immune mediated, and may be positively affected by dietary control.

■ COMMENTARY

Screening for celiac disease, an immune non-IgE-mediated enteropathy, requires a blood test for measurement of anti-gliadin and anti-endomysial antibodies. Measurement of IgA autoantibodies to tissue transglutaminase (tTG), or endomysial antibody, has 95-100% sensitivity and specificity (*Allergy Asthma Proc* 2007,28:20-24). Concomitant measurement of serum IgA levels excludes the possibility of IgA deficiency and increases the validity of a negative test. Small bowel biopsy is then recommended to exclude the marginal likelihood of an alternative diagnosis. Among patients with screening positive serology, 25-30% will have negative biopsies and it remains unclear whether these represent false positive results, mild celi-

ac disease, or autoantibody production of undetermined significance. Genetic testing is not useful for confirming the diagnosis. ■

Treatment of High-Grade Gliomas in Elderly Patients

ABSTRACT & COMMENTARY

By Adília Hormigo, MD, PhD

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Dr. Hormigo reports no financial relationships relevant to this field of study.

Synopsis: *Elderly patients with glioblastoma, who are independent in activities of daily living, will have a longer survival with good quality of life if treated with radiotherapy rather than supportive care, alone.*

Source: Keime-Guibert F, et al. Radiotherapy for glioblastoma in the elderly. *N Eng J Med*. 2007;356:1527-1535

Most of the protocols for treatment of brain tumors exclude the elderly population. A concern for those that treat these patients is a potential increase in toxicity related to the treatment with cognitive deterioration and decrease of quality of life. A multicenter study was conducted in France, to compare radiotherapy treatment to supportive care in elderly patients with a high-grade glioma. Patients at the age of 70 or older with newly diagnosed anaplastic astrocytoma or glioblastoma multiforme, who underwent a resection, and had a Karnofsky performance score of 70 or higher were eligible to enroll. Diagnosis was confirmed by central review. Patients were randomized to focal radiotherapy in a daily fraction of 1.8 Gy, 5 days a week, to a total dose of 50 Gy or to supportive care alone, consisting of corticosteroids, anti-convulsant agents, physical and psychological support, and palliative care treatment. All patients who received radiotherapy tolerated it well and had no severe adverse effect from radiotherapy. Eighty-one patients with glioblastoma and 2 patients with anaplastic astrocytoma were enrolled. The median age was 73 for those patients who received supportive care alone and 75 for those who received radiotherapy. The median length of time from diagnosis to the start of radiation was 5.3 weeks. The median survival for the 39 patients who received radiotherapy was 29.1 weeks and 19.9 weeks for 42 patients who received supportive care alone. The median progression-free survival was 14.9 weeks with radiotherapy and supportive care and 5.4 weeks with supportive care alone. The median survival benefit for the group who received radiotherapy was 12.2 weeks greater than the group that received supportive care alone. Through their statistical analysis, the authors also showed that the survival benefit of radiotherapy was independent of the extent of the surgery. The Mini-Mental examination score declined over time in both groups, but there was no significant difference between the 2. Measures of quality of life also showed no significant differences. The trial was discontinued at the first interim analysis because of the advantage of radiotherapy over supportive care alone. The authors conclude that there was improvement in median survival for older patients with glioblastoma multiforme who underwent radiotherapy without reducing the quality of life or cognition.

■ COMMENTARY

This multi-center trial conducted in France compared radiotherapy to supportive care alone in patients 70 or older with high grade glioma. Since they only accrued two patients with anaplastic astrocytoma, their recommendation is for patients with glioblastoma multiforme. A significant benefit of radiotherapy was found at first interim analysis and thus the study was stopped. The study showed a similar decline in Karnofsky performance status over time within the 2 groups and no difference in quality of life measures. The conclusion from this study is that treatment with radiotherapy should be offered to the elderly patients who are able to care for themselves because it is well tolerated and has significant survival benefit.

In younger patients, the current standard treatment for a high-grade glioma is radiotherapy with concurrent temozolomide chemotherapy, followed by chemotherapy with temozolomide alone. One would think that a potential follow up study in the elderly with glioblastoma multiforme, would be to compare this regimen to radiotherapy alone, using the same primary endpoint of overall survival and secondary endpoints of progression-free survival, tolerance of the combined treatment, quality of life and cognition. ■

Background:

Stupp R, et al. *N Eng J Med* 2005;352:987-996.

Do Migraines Increase a Man's Stroke Risk? Yes, If He is Young at Heart

ABSTRACT & COMMENTARY

By Dara G. Jamieson, MD
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Dr. Jamieson is a consultant for Boehringer Ingelheim and Merck, and is on the speaker's bureau for Boehringer Ingelheim, Merck, Ortho-McNeil, and Pfizer.

Synopsis: *Men with migraine are at increased risk of myocardial infarction. But, risk of ischemic stroke is increased only in younger male migraineurs.*

Source: Kurth T, et al. Migraine and risk of cardiovascular disease in men. *Arch Intern Med*. 200;167:795-801.

THE DIAGNOSIS OF MIGRAINE HEADACHES MAY PORtend a more complicated medical course than just years of episodic disabling headaches. Migraine with aura has been associated with an adverse vascular risk profile and prothrombotic factors. Studies of patients with migraine headaches have tended to focus on this common disease in women. The known correlation between migraine and vascular risk was recently analyzed in data from the Women's Health Study (WHS). This study confirmed that women with migraine with aura have a greater risk of cardiovascular, as well as cerebrovascular, disease. Women with active migraine with aura had an increased risk of ischemic stroke, myocardial infarction (MI), myocardial revascularization, angina, and vascular death. Increased risk was noted after approximately 6 years of follow-up. Women with migraine without aura did not have an increased risk of any vascular events.

However, men make up about a quarter of the 28 million Americans with migraine headaches. The vascular risk of male migraineurs is less well characterized than in women with migraine. Kurth et al report the results of a prospective cohort study of participants in the Physicians' Health Study (PHS), a randomized placebo-controlled trial designed to test the benefits and risks of low dose aspirin and beta carotene in the primary prevention of cardiovascular disease and cancer in apparently healthy male physicians. Between 1981 and 1984, over 22,000 men were randomized to receive one of the two therapies or placebo. Questionnaires were used to collect baseline and follow-up data. For this analysis of migraine headaches and vascular risk, information was collected through February 2005 with a mean follow-up of 15.7 years. Men were classified as having migraine if they had a migraine headache in the first 5 years of follow-up, with frequent migraine defined as 4 or more reports of migraine during this period. Non-migraine headaches were reported, but data was not available for the International Headache Society classification or for the determination of migraine with aura versus migraine without aura. The first occurrence of the combined outcome of nonfatal ischemic stroke, nonfatal MI, or cardiovascular death was determined by follow-up questionnaires and examination of medical records. Cox proportional hazard models evaluated the association between migraine and outcomes. Multivariable models adjusted for multiple vascular risk factors.

For the analysis, 20,084 men were free of vascular disease at 5-year follow-up. About 7.2% (1449) of men reported migraine on the 60 month questionnaire, with frequent migraine reported in 434 men. Migraineurs were younger and more likely to have hypertension or elevated cholesterol. Compared with men without migraine, those men who reported migraine were at significantly increased risk of cardiovascular disease and myocardial infarction. The multivariable-adjusted hazard ratios (95% confidence intervals) were 1.24 (1.06-1.46; $P = 0.008$) for combined major cardiovascular events, 1.12 (0.84-1.50; $P = 0.43$) for ischemic stroke, 1.42 (1.15-1.77; $P < 0.001$) for myocardial infarction, and 1.07 (0.80-1.43; $P = 0.65$) for ischemic cardiovascular death. While there was no association in older age groups, there was an association between migraine and ischemic stroke (age-adjusted HR 1.84; 95% CI, 1.10-3.08; $P = 0.03$) for migraineurs younger than 55 years old, as compared to men without migraine. Unlike for ischemic stroke, age did not significantly modify the association between migraine and major cardiovascular disease and MI. No statistically significant increase in coronary revascularization or angina was noted in men with migraine. There was no association between men who reported only nonmigraine headaches and vascular outcomes.

In this study of initially healthy men, free from vascular disease at study entry and during the 5 year migraine ascertainment period, migraine was associated with a significantly increased risk of major cardiovascular events, driven by an increased risk of MI.

After adjustment for cardiovascular risk factors, men who reported migraine had a 24% increased risk of major cardiovascular disease and a 42% increased risk of MI. Migraine was not statistically associated with increased risk of ischemic stroke, death from ischemic cardiovascular disease, coronary revascularization, or angina. However there was an increased risk of ischemic stroke for men with migraine who were 40 to 54 years of age, as compared to older men with migraine.

COMMENTARY

In a previous report from the PHS, migraine was not associated with an increased risk of cardiac disease during a mean of 12 years of follow-up. These more recent results, with almost 16 years of follow-up, show increased risk of MI. The duration of follow-up of a disease with relatively low prevalence in men may account for the disparate results. The WHS indicated an ischemic stroke and cardiac risk, but only in women with active migraine with aura. More information was accumulated for the women in the WHS, allowing analysis of vascular risk as a function of headache characteristics. However, the PHS was not designed to assess men with migraine headaches, which limited the ability of the analysis to assign detailed headache characteristics to specific vascular outcomes. While the PHS had many participants prospectively followed for a long period, headaches were self-reported without information on migraine type. Details of migraine drug use and confounding conditions were not reported. The participants in the PHS were healthy, male, middle-aged, mostly white physicians; although the study results are probably applicable to other male groups. There are still unanswered questions about migraines and vascular disease; but, the increased vascular risk of men, and women, with migraine headaches indicates the need for vigilance in managing their other vascular risk factors.

Background:

Kurth, et al. Migraine and risk of cardiovascular disease in women. *JAMA*. 2006;296:283-291.

Stenting for Intracranial Atherosclerotic Disease: An Option Beyond Aspirin

ABSTRACT & COMMENTARY

By Alan Z. Segal, MD
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Dr. Segal is on the speaker's bureau for Boehringer-Ingelheim.

Synopsis: *Intracranial stenting is a promising new technology for secondary stroke prevention, but needs to be studied in a randomized trial against best medical therapy.*

Source: Bose A, et al. A novel, self-expanding, nitinol stent in medically refractory intracranial atherosclerotic stenoses: The Wingspan Study. *Stroke*.2007;38:1531-1537.

Surgical treatment of atherosclerotic stenoses in the intracranial circulation has been limited to unproven surgical procedures, such as EC-IC (extracranial to intracranial) bypass. Medical management is limited to anti-platelet therapy with aspirin, since the results of the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial showed that warfarin therapy provided no added benefit for stroke prevention and significantly increased the risk of major bleeding. Reports of endovascular treatment for intracranial stenosis have included case series using coronary angioplasty balloons and balloon expandable stents. The Wingspan device was designed specifically for the cerebral vasculature, and thus may offer a superior safety and efficacy profile for these high-risk patients.

Bose et al treated 45 patients with the Wingspan device. Each had intracranial stenosis and were refractory to medical therapy. The degree of stenosis was reduced from 75% to 32% post procedure, and 28% at 6-month follow up. It was notable that the vessels further improved over time post-stenting indicating a process of stent-associated vascular remodeling. The rates of adverse events were low, with a 4.5% composite ipsilateral stroke/death rate at 30 days and a 6-month stroke/death rate of 7%. Physician reported follow up over an average of 13 months showed comparable results, with one additional stroke reported. Stents were most commonly placed in the middle cerebral artery M1 segment (n = 10), petrous carotid (n = 5) or the vertebral artery (n = 13). Eighteen procedural related complications were reported in 12 patients, but none of these

resulted in permanent sequelae.

The authors' discussion elucidates how the Wingspan device is different from balloon-expandable stents. Because the angioplasty balloon for Wingspan is undersized and inflated at a much lower pressure, there is much less risk of trauma to the atherosclerotic vessel. The self-expanding Wingspan stent is flexible and can navigate through and conform to tortuous vessels. In contrast, a balloon expandable stent must be oversized in order to properly appose to the vessel wall.

COMMENTARY

This study confirms that the Wingspan stent can be safely and effectively deployed to treat atherosclerotic lesions in the intracranial vasculature. Even without a head-to-head comparison, this device appears to be favorable to stents designed for the cardiac circulation, not the brain. These data also compare favorably to the data from the WASID study, which showed a 12% per year stroke rate in these high-risk patients. Among patients with the most severe stenoses in WASID (>70%), one-year stroke risk was 23%. Overall WASID patients had milder stenoses (mean 64%) than in the present study (mean 75%). In conclusion, although the Wingspan results certainly appear tantalizing, randomized comparison between stenting and medical management will be needed to confirm these results.

What about stenting for extracranial vertebral artery stenosis?

In a sub-study to the much larger CAVATAS trial for stenting of carotid stenosis, (Coward LJ, McCabe DJH, Ederle J et al. *Stroke* 2007; 38: 1526), the investigators included 16 cases of symptomatic vertebral artery stenosis. Eight patients with vertebral artery origin stenosis were treated with stenting, while eight patients were treated medically (of these, one had distal disease). During a mean follow-up period of 4.7 years, no patient in either treatment arm had a stroke. Three patients in each treatment arm died of myocardial infarction or carotid territory stroke and one endovascular patient had a non-fatal carotid territory stroke.

As the authors conclude, this trial was unable to prove a benefit for vertebral artery stenting, but the numbers were quite small. More importantly, these patients were at risk for other types of vascular events thus mandating a broad approach to atherosclerotic risk reduction.

Unlike the patients in Wingspan and WASID, who had severe intracranial atherosclerotic disease, these CAVATAS patients, with vertebral artery origin disease, appeared to be at quite low stroke risk. The vertebral circulation has a built-in redundancy, with one dominant vertebral feeding the basilar and a smaller non-dominant vessel. Therefore, atherosclerotic lesions at one vertebral origin may not warrant as aggressive intervention and may be, in most cases, managed medically. ■

CME Questions

21. Which of the tests below is best to screen for gluten sensitivity (celiac disease):

A). IgA antibodies to transglutaminase
B) IgG antibodies to transglutaminase
C) IgM antibodies to transglutaminase
D) IgA antibodies to gliadin
E) IgG antibodies to gliadin

22. Men with migraine:

A) have an increased risk of myocardial infarction.
B) have an increased ischemic stroke risk with increased age.
C) have an increased risk of vascular events only associated with migraine with aura.
D) have the same vascular risk as women with migraine.
E) have an increased risk of angina and coronary revascularization.

23. Which of the following is true for elderly patients with glioblastoma multiforme?

A) Radiotherapy should not be given to patients over 70.
B) Elderly patients should receive chemotherapy before radiotherapy.
C) Radiotherapy should not be given to patients who require substantial assistance.
D) Supportive care is the treatment choice for elderly patients with glioblastoma multiforme.

Answers: 21.(a) 22.(a) 23.(c)

CME Objectives

The objectives of *Neurology Alert* are:

• To present the current scientific data regarding diagnosis and treatment of neurological disease, including stroke, Alzheimer's disease, transient ischemic attack, and coma;

• To discuss the pathogenesis and treatment of pain;

• To present basic science lessons in brain function;

• To discuss information regarding new drugs for commonly diagnosed diseases and new uses for traditional drugs;

• To discuss nonclinical issues of importance to neurological, such as the right to die and the physician's legal obligation to patients with terminal illness. ■

In Future Issues: **Update on Neuromyelitis Optica (Devic's disease)**

PHARMACOLOGY WATCH

Supplement to Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Infectious Disease Alert, Internal Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports, Travel Medicine Advisor.

Risk With Preventative Antibiotics Outweighs Benefit for Most

Sweeping new changes have been made to the guidelines for prevention of endocarditis in patients undergoing dental procedures. The new recommendations dramatically reduce the indications for dental prophylaxis and reduce the number of patients who need preprocedure antibiotics. The guideline was issued by the American Heart Association in conjunction with the American Dental Association, Infectious Diseases Society of America, and the Pediatric Infectious Diseases Society and was published online April 19, 2007, in *Circulation*. The guidelines reflect evidence that the risk of taking preventative antibiotics outweighs the benefit for most patients. It is also been found that infectious endocarditis (IE) is more likely to result from frequent exposure to random bacteremias from activity such as flossing and brushing than from dental work. Specifically, the guidelines say that prophylactic antibiotics are no longer required for patients with mitral valve prolapse, rheumatic heart disease, bicuspid valve disease, calcified aortic stenosis, or congenital heart conditions such as ventricular septal defect, atrial septal defect, and hypertrophic cardiomyopathy. There are still patients who are at extremely high risk of IE who should continue to receive prophylactic antibiotics: patients with artificial heart valves, a history of infective endocarditis, congenital heart disease including unrepaired or incompletely repaired cyanotic congenital heart disease, including those with palliative shunts and conduits, those with a completely repaired congenital heart defect with prosthetic material during the first 6 months after the procedure, repaired congenital heart defect with residual defect at the site or adjacent to the site of a prosthetic patch or prosthetic device, or a cardiac transplant patient with a cardiac valvulopathy. Antibiotic prophylaxis is no longer recommended for any other form of congenital heart disease. Dosing regimens are essentially the same as previous recommendations and include oral amoxicillin 2 gm 30 to 60 minutes prior to procedure. Oral alternatives include cephalexin, clindamycin, azithromycin or clarithromycin. Parenteral regimens include ampicillin, cefazolin, ceftriaxone, and clindamycin. The guideline also no longer recommends antibiotics to prevent IE in patients undergoing genitourinary or gastrointestinal tract procedures (*Circulation* 2007, doi:10.1161/CIRCULATIONAHA.106.183095). The full guideline is available at http://www.ada.org/prof/resources/ topics/infective_endocarditis_guidelines.pdf. ■

Gonococcal Infections, CDC's Updated Treatment

The CDC has issued updated treatment recommendations for gonococcal infections and associated conditions due to the high level of resistance of gonorrhea to fluoroquinolones. The agencies Gonococcal Isolate Surveillance Project demonstrates that fluoroquinolone-resistant gonorrhea is continuing to spread and is now widespread

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throughout United States. Therefore, fluoroquinolones such as ciprofloxacin, ofloxacin, or levofloxacin are no longer recommended. Current recommended regimens for gonococcal infections of the cervix, urethra, and rectum are ceftriaxone 125 mg IM and a single dose or cefixime 400 mg orally in a single dose plus treatment for chlamydia if chlamydial infection is not ruled out. Uncomplicated gonococcal infections of the pharynx should be treated with ceftriaxone 125 mg IM plus treatment for chlamydia, if chlamydial infection is not ruled out. Disseminated gonococcal infection should be treated with ceftriaxone 1 g IM or IV every 24 hours. Pelvic inflammatory disease may be treated with parenteral and oral therapy. Parenteral therapy regimens include cefotetan or cefoxitin plus doxycycline or clindamycin plus gentamicin. An alternative regimen is ampicillin/sulbactam plus oral doxycycline. Oral therapy can be considered in women with mild to moderate disease. With the loss of fluoroquinolones, cephalosporins are the mainstay of most regimens. For patients who are highly allergic to cephalosporins, spectinomycin may be considered although it is not generally available in this country. Another option is azithromycin, however, prescribing should be done in consultation with an infectious disease specialist due to concerns over emerging antimicrobial resistance to macrolides. The CDC's full recommendations are available online at www.cdc.gov/std/treatment/2006/updated-regimens.htm. ■

Head Lice — Malathion First-Line Treatment

Malathion should be first-line treatment for children who have lice according to a new review in the journal *Pediatrics*. Head lice have become resistant to nearly all first-line treatments in United States including permethrin, which has been considered first-line treatment for years. Malathion, in the formulation containing isopropyl alcohol and terpineol, is safe and effective for lice and all existing points within the life cycle, and generally requires a single treatment, reducing the duration of infestation, and lost time from school and work. Concern about flammability seems to be over emphasized, as there have been no reported cases of bodily injury related to burns (*Pediatrics* 2007. 119:965-974).

Statins, May Cut the Risk of Cataracts

Statins, the cholesterol wonder drugs, have been associated with a number of other benefits including reduction of inflammation within the arteries, improved bone density, reduction in the risk of colon cancer, renoprotective effects, and reduction in the risk of Alzheimer's disease and other dementias. Now, a new study suggests that the drugs may also cut the risk of cataracts by 50%. Researchers from Australia reviewed the rate of cataract development in 3,654 elderly patients. After 10 years, after controlling for age, gender and others factors, the hazard ratio for any type of cataract in statin users was 0.52. In subgroups, there was a decreased risk of nuclear cataracts (HR = 0.66) and cortical cataracts (HR =0.76), but neither of these reached statistical significance. The authors conclude that there may be a protective influence of statins on cataracts and this needs to be further explored (*Am J Ophthalmol* 2007; 143:687-689). ■

FDA Actions

Sanofi Aventis has been approved to produce a vaccine to prevent bird flu in humans. The vaccine against the H5N1 virus will not be produced commercially, but will instead be stockpiled by the U.S. government for distribution in case of the outbreak. The FDA admits that the vaccine is not optimal, requiring a higher dose than normal flu vaccine, and 2 shots which must be given 28 days apart. But until other vaccines are developed, this vaccine will be used as the "interim measure."

The FDA is recommending updating black box warning regarding suicidality in young adults (under age 24) starting on antidepressants, calling for appropriate monitoring and close observation. The new recommendation should also include the statement that there was no increase in suicidality in adults over the age of 24, and a decrease in the risk in adults over the age of 64.

The FDA has approved generic versions of 2 of the most popular drugs of the last decade, Ambien (zolpidem) and Zoloft (sertraline). Zolpidem will be available in 5 mg and 10 mg immediate-release tablets. Thirteen manufactures have received approval to market the product. Sertraline is approved in the 25 mg, 50 mg and 100 mg strengths, and will be produced by Ranbaxy Laboratories.

The FDA has issued a warning about the health risks of dietary supplements touted as sexual enhancement products and treatments for erectile dysfunction that have been distributed under the trade names True Man and Energy Max. Both drugs have been sold throughout United States. Energy Max was found to contain an analogue of sildenafil, the active ingredient in Viagra, while True Man was found to contain an analogue of sildenafil and vardenafil, the active ingredient in Levitra. Both drugs can have serious interactions with nitrates. ■