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Japanese Encephalitis Vaccine

ABSTRACT & COMMENTARY

Synopsis: *Although Japanese encephalitis rarely occurs in travelers, certain groups and subsets of individuals have a risk of infection that can reach 1 in 5000 travelers per week. It is crucial to recognize those with increased risk, and to seriously consider immunizing them in order to prevent the potentially devastating sequelae of Japanese encephalitis.*

Source: Shlim DR, Solomon T. Japanese encephalitis vaccine for travelers: Exploring the limits of risk. *Clin Infect Dis*. 2002;5:183-188.

THIS EXCELLENT REVIEW HIGHLIGHTS A NUMBER OF IMPORTANT issues regarding Japanese encephalitis (JE) infection. The CDC estimates the risk of acquiring JE to be < 1 in 1,000,000 travelers visiting endemic areas. However, for travelers spending significant periods of time in risk areas during transmission season, the risk greatly increases from 1 in 5000 to 1 in 20,000 travelers per week. Mortality from the disease is 30-40%, and 50% of survivors will likely have permanent neuropsychiatric sequelae.

JE virus is carried by *Culex* mosquitoes. The infection rates among mosquitoes found in areas of known hyperendemicity is 3% at most. While symptomatic illness usually occurs in < 1 in 250 persons when bitten by infected mosquitoes, during a study of American service personnel in Korea, 1 in 25 infections did lead to symptomatic illness.

Cases that have occurred in tourists include the following data:

March 1994	Bali	Swedish woman	nonfatal
January 1995	Bali	Danish man	fatal
1989	Thailand	Israeli woman	nonfatal

The JE vaccine that is used in travelers is the Biken product, an inactivated mouse brain-derived vaccine. Vaccine efficacy is 91% and 2 doses provide 80% seroconversion rates. Severe neurological reactions have been reported in 1-2.3 per 1,000,000 recipients of the vaccine in Japan. Mucocutaneous reactions

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INSIDE

occur in approximately 1-17 per 10,000 recipients, and neurological symptoms in 0.1-2.3 per 10,000 recipients in Denmark. One fatality occurred in a vaccine recipient from among more than 10,000,000 recipients in the United States and Japan. The sum of all types of adverse events is estimated at 15 per 100,000 recipients in the United States. Urticaria and angioedema are estimated to occur in 6.3 per 100,000 recipients, also in the United States.

COMMENT BY LIN H. CHEN, MD

JE is a mosquito-borne flavivirus infection closely related to the West Nile virus, Saint Louis encephalitis, and Murray Valley encephalitis viruses. More than 10,000 cases of JE occur annually.[1] Epidemics occur more frequently in temperate regions of east Asia, but southern and southeast Asia also continue to be endemic regions for this disease. JE is transmitted by *Culex* mosquitoes, and the risk of being bitten is greatest around rice paddies where the mosquitoes breed. Following an incubation period of 1-2 weeks, a small proportion of infections (1 in 25 to 1 in 1000) become symptomatic.[1] Presenting symptoms include fever, headache, and malaise, followed by neurologic signs including seizures, paralyses, paresis, ataxia, cranial nerve defects, and sensory derangements. As pointed out by Shlim and Solomon, about one third of all *symptomatic* cases are fatal, and half of the remainder develop long-term neurologic sequelae.

Twenty-four cases of travelers and expatriates who acquired JE from 1978-1992 were summarized in Recommendations of the Advisory Committee on Immunization Practices (ACIP) in 1993.[2] From these data the CDC derived the overall risk of JE in travelers visiting endemic areas to be < 1 in 1,000,000.

The JE vaccine has been shown to be immunogenic and safe using the 0, 7, 14-day or 0, 7, 30-day schedule,[3] but need for booster doses of JE vaccine is not clearly defined. Antibodies following immunization with JE vaccine have been shown to persist for 3 years.[4] A booster dose is generally considered after 3 years if the traveler continues to be at risk, although the ACIP recommendations state that boosters may be given after 2 years.[2] Since there are no studies to define the need for further booster doses, Shlim and Solomon suggest the options of giving another booster after 3 years or measuring the serum JE neutralizing antibody levels to ensure protection is still present.

Initial reports of adverse reactions to the JE vaccine commonly described urticaria and angioedema, but there were also cases that showed respiratory distress.[5,6] Some reactions occurred several days to 2 weeks following immunizations. Two patterns of systemic immediate-type reactions have emerged. One type presents as urticaria and angioedema and is associated with the presence of IgE antibodies directed against gelatin.[7] The other type presents with cardiovascular symptoms including hypotension and cyanosis.[7] There appears to be a correlation between adverse reactions to the JE vaccine and a predisposition to allergies in the recipient, younger age, and female gender.[8]

Reported rates of adverse events have been quite variable from country to country. Post-marketing surveillance data noted total adverse events to be 2.8 per 100,000 doses in Japan compared with 15 per 100,000 doses in the United States.[9] Systemic hypersensitivity reactions were reported in 0.8 per 100,000 doses in Japan, compared with 6.3 per 100,000 doses in the United States. Serious neurological adverse events were reported in 0.2 per

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100,000 doses in Japan, significantly lower than the rates reported from Denmark.

Shlim and Solomon's succinct statement concerning those populations for whom the travel medicine practitioner might consider the JE vaccine most relevant is as follows: "persons who will be spending time living in a village setting near rice paddies and farm animals during a season of transmission; soldiers who will be on maneuvers in an area of endemicity during the season of risk. . . aid workers, missionaries, students, and researchers whose work will involve spending time in an area of endemicity during the season of risk; bicyclists, backpackers, and other adventure travelers whose itinerary is uncertain but may include significant time in areas of endemicity; expatriates taking up residence in a country in which JE is endemic. . . and travelers who request the vaccine after the risk of JE has been discussed, even if the travel medicine practitioner feels the risk is low." ■

References

1. Shope RE. Other flavivirus infections. In: *Tropical Infectious Diseases*. Guerrant RL, Walker DH, Weller PF, eds. Philadelphia, Pa: Churchill Livingstone; 1999: 1275-1279.
2. CDC. Inactivated Japanese encephalitis virus vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep*. 1993;42(RR-1):1-15.
3. Defraites RF, et al. Japanese encephalitis vaccine (inactivated, BIKEN) in US soldiers: Immunogenicity and safety of vaccine administered in two dosing regimens. *Am J Trop Med Hyg*. 1999;61:288-293.
4. Gambel JM, et al. Japanese encephalitis vaccine: Persistence of antibodies up to 3 years after a 3-dose primary series. *J Infect Dis*. 1995;171:1074.
5. Andersen MM, Ronne T. Side-effects with Japanese encephalitis vaccine. *Lancet*. 1991;337:1044.
6. Ruff TA, Eisen D, Fuller A. Adverse reactions to Japanese encephalitis vaccine. *Lancet*. 1991;338:881-882.
7. Sakaguchi M, Inouye S. Two patterns of systemic immediate-type reactions to Japanese encephalitis vaccines. *Vaccine*. 1998;16:68-69.
8. Plesner AM, Ronne T, Wachmann H. Case-control study of allergic reactions to Japanese encephalitis vaccine. *Vaccine*. 2000;18:1830-1836.
9. Takahashi H, et al. Adverse events after Japanese encephalitis vaccination: Review of post-marketing surveillance data from Japan and the United States. *Vaccine*. 2000;18:2963-2969.

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Macrophage Apoptosis by Anthrax Lethal Factor Through p38 MAP Kinase Inhibition

ABSTRACT & COMMENTARY

Synopsis: *The bacterium Bacillus anthracis causes the death of macrophages, which may allow it to avoid detection by the innate immune system.*

Source: Park JM, et al. Macrophage apoptosis by anthrax lethal factor through p38 MAP kinase inhibition. *Science*. 2002;297:2048-2051.

THERE IS ALREADY A GOOD BIT KNOWN ABOUT THE pathogenesis of anthrax, interest obviously being piqued by the mini-bioterror epidemic propagated through the US mail just 1 year ago. Now new evidence comes from The Department of Pharmacology at UC San Diego shedding light on the mechanism of a major virulence factor in *Bacillus anthracis*.

One major question in anthrax research has been what happens to anthrax spores after consumption by pulmonary macrophages? Without an evasion mechanism, the spores would be engulfed and killed. Park and colleagues pick up the story of pathogenesis after protective factor (PA) assists translocation of edema factor and lethal factor (LF). The other existing knowledge is that metalloprotease with ability to cleave mitogen-induced kinases (MAPK), LF combines with PA to produce lethal toxin (LT), which is highly toxic for macrophages.

That macrophage toxicity, some evidence suggests, is due to either necrosis or programmed cell death—apoptosis—of macrophages. Put in a nutshell, this study found that LT produces apoptosis of macrophages but some other factors are needed. The present experiment used classic LPS but also lipoteichoic acid from *Staphylococcus aureus* and *Bacillus subtilis* to prime purified macrophages for the apoptotic and necrotic action of LT. Some cell types were more sensitive to the apoptosis effect of LT, some the necrosis effect.

LPS causes signal transduction in macrophages through p38 MKK, glowing, and other kinases. LT was shown to block the activation of p38 map kinase

(MAPK) and that blockage allows apoptosis to occur. NFkB and p38 normally act together to inhibit apoptosis. Experimentally produced MKK was cleaved by LF and that LT with either LPS or lipopeptide produced 3-5 times as much apoptosis as LPS or SB alone.

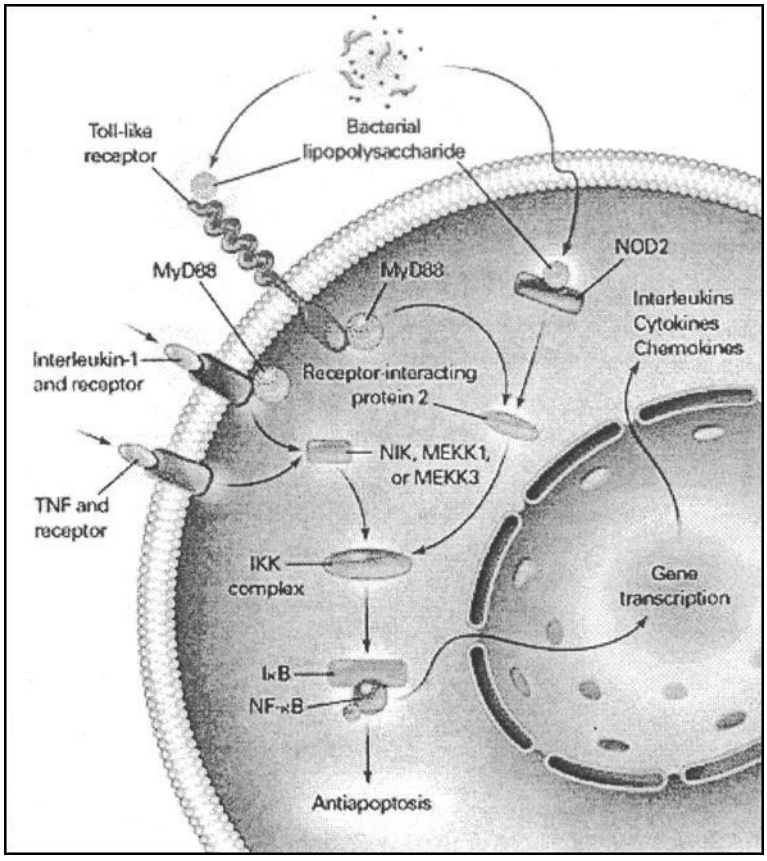
It is important to realize that in order for macrophages to survive LPS, NFkB must be activated. NFkB combined with effects of p38 jointly produce another factor(s) that protect macrophages from apoptosis. In their final experiment Park et al actually tested activation of a number of NFkB targets to show that the activation is p38 dependent. This experiment was performed by measuring total cellular RNA after 4 hours of LT or SB treatment of such NFkB targets as IL-1α, cyclooxygenase, and IKBA.

On a more clinical note, in a late-breaker session at the recent Infectious Diseases Society of America held in Chicago 24-27 in October, the infectious diseases clinical team at the Capitol reported data on the dynamics of spread of anthrax spores from the infamous Senator Daschle letter.[1] Dr. Gregory Martin, the infectious diseases physician for the Senate, gave a superb summary of the epidemiology of spore release in October 2001 at the Hart Senate Building. Nasopharyngeal cultures were performed on 58 exposed individuals throughout the building: 28 were positive, 13 of 13 in the immediate vicinity, and 9 of 45 from persons more adjacent and 6 first responders. There were nasopharyngeal cultures of 6000 additional persons with "less definite exposure" and none were positive.

Based on the positive individuals and their location, it was surmised that spores spread very quickly—in 1 to 4 minutes—and could spread quickly also to adjacent floors. Exposed individuals were offered 100 days of antibiotic prophylaxis and anthrax vaccination. There was a higher frequency of symptoms in exposed volunteers compared to nonexposed. No clearcut inhalation anthrax developed, but a milder form of the illness could not be ruled out in culture-positive individuals.

Figure

NFkB



Source: Podolsky D. N Engl J Med 2002;347:417-429.

COMMENT BY JOSEPH F. JOHN, MD

Infectious disease physicians usually think of the deleterious effects of NFkB production including the activation of tumor necrosis factor (TNF), IL-1B, and COX-2. Yet it is known that these lymphokines may have a biphasic cellular response, the first phase often assisting in cell-mediated immune microbial killing. This current work shows with elegance that age-old toxins now revisited on man, like those of *B anthracis*, inhibit that sentinel system, and, once inhibited, allows programmed cell death to occur that may itself be sufficient for morbidity and mortality in humans or may be combined with the cell necrosis effects of EF and LT. It is the very lack of cytokine expression by macrophages in anthrax that may allow a relative "silent" infection to rage.

Readers may consider the foregoing sequence a space age product, far from the bedside. Analysis of cytokine responses—both supportive and deleterious—may be at hand in severe acute infections. Indeed we have entered an age of use of biological modifiers and we will need to have working knowledge of cytokine perturbation and the fundamentals of the NFkB crosstalk to recommend and evaluate these new therapies.

Anthrax may be a special case because of its ability to produce intense morbidity and mortality. Antibiotic therapy alone, as in LPS induced SIRS, is unlikely to be curative in far-advanced cases. The salvage of

many of the 17 recent victims of terroristic anthrax has had one apparent downside. Recent news, yet to be supported in peer-review publications, apparently found that several of the anthrax victims have evolved an illness reminiscent chronic fatigue syndrome, perhaps suggesting that the effects of the toxins of *B anthracis* are not simply short acting.

The experience in the Hart Senate Building is sobering. As Dr. Martin related on October 27 in Chicago, there were many incorrect assumptions. What was apparent is that weaponized spores can be quickly and easily spread and exposure can be high, certainly for those in the immediate proximity and even adjacent inside locations.

It is my opinion that anthrax remains the ideal bioweapon for many reasons. All physicians led by those experts in infectious diseases need to remain current in their knowledge and skills concerning disease due to *B anthracis*. The thoughtful response by Dr. Greg Martin and his team at the Capitol demonstrates the versatility and capability of infectious diseases physicians faced with a bewildering problem of microbial exposure. The abstract reported by him and his colleagues provides substantial new information to help other infectious diseases physicians respond to an anthrax attack. ■

Widening the Meningitis Belt

ABSTRACT & COMMENTARY

Synopsis: *Careful evaluation of epidemiologic data from recent African outbreaks of meningococcal disease suggests that significant risks now extend beyond the sub-Saharan "belt" through the Rift Valley and Great Lakes regions into Mozambique, then into Namibia and Angola.*

Source: Molesworth AM, et al. Where is the meningitis belt? Defining an area at risk of epidemic meningitis in Africa. *Trans R Soc Trop Med Hyg*. 2002;96:242-249.

SINCE 1963, PEOPLE HAVE RECOGNIZED THE PRESENCE of a belt-like band across Africa wherein meningococcal epidemics are common. Over the past 2 decades, however, there have been several waves of severe epidemics in African regions outside the "belt." British researchers thoroughly reviewed outbreak reports of Neisseria meningitidis disease in Africa from 1980 through mid-2001. They both mapped outbreaks and calculated incidence rates.

A total of 114 outbreaks were identified. Group A meningococcus was most commonly the cause, and clone III-1 has been predominant since 1988. Figure 1 shows the traditional "Meningitis Belt," while Figure 2 demonstrates the areas in which the current study found high incidences of meningococcal disease. While the brunt of the meningitis burden still occurs in the traditional "belt," there is significant disease in other parts of Africa. Interestingly, the mapping of meningitis epidemics corresponds to areas with annual rainfall rates ranging from 30-110 cm. Alterations in climate and forests during the past 2 decades might be changing the epidemiology of meningococcal disease in Africa.

COMMENT BY PHILIP R. FISCHER, MD, DTM&H

Meningococcal disease can be devastating both to individuals and to populations. While it is difficult to extrapolate from indigenous reports of disease risk for travelers, the report from Dr. Molesworth and colleagues suggest we might need to enlarge our view of risk areas in Africa. Outbreaks of meningitis (*N meningitidis* serogroup A) in the "Great Lakes Region" of Burundi, Rwanda, and Tanzania were reported in September 2002[1] and confirm that the risk for meningitis epidemics extends well beyond the original geographic "belt."

Travel medicine practitioners use a variety of resources to guide their advice to travelers. While commercial groups and organizations such as CDC and WHO periodically update their recommendations, all

Figure 1
Traditional Meningitis Belt

Countries included in the epidemic belt (WHO)

individuals providing pretravel care should be aware that there is a growing risk of meningococcal disease outside the traditional "belt" across Africa. Especially for those travelers anticipating contact with at-risk groups (crowded villages and refugee camps, dormitory populations, health care settings), there could be consideration given to meningococcal vaccination prior to any trip within the widened meningitis "belt" of Africa.

Meningococcal vaccines vary in different parts of the world. Americans have had access to the quadrivalent (A, C, Y, W135) vaccine, and others have sometimes used vaccines that "only" cover serogroups A and/or C. While most African outbreaks are caused by serogroup A, there has been an increase in serogroup W135 infection in travelers to Saudi Arabia. Some Hajj pilgrims received vaccinations, but without W135 protection, and then transmitted meningococcus to contacts following their trips.[2] When available, the quadrivalent vaccine should be used for travelers to Saudi Arabia (and is indeed now required).[3]

Pretravel consultations also provide an opportunity to review the adequacy of "routine" immunizations, and such "routine" schedules have changed in recent years. Meningococcal vaccine is now recommended by some groups for American college freshmen who will be living in dormitories.[4] In the United Kingdom, a conjugate meningococcal C vaccine that is more effective than the older polysaccharide vaccine, when used in young children, is now part of the primary immunization program.[5] ■

References

1. WHO CSR and Epidemiological Bulletin (e-mail), 4 September 2002 as reported on www.who.int/disease-outbreak-news/
2. Wilder-Smith A, et al. Acquisition of W135 meningococcal carriage in Hajj pilgrims and transmission to household contacts: Prospective study. *BMJ*. 2002;325:365-366.
3. Memish ZA. Meningococcal disease and travel. *Clin Infect Dis*. 2002;34:84-90.
4. Rosenstein NE, et al. Meningococcal vaccines. *Infect Dis Clin North Am*. 2001;15:155-169.
5. Soriano-Gabarro M, et al. Vaccines for the prevention of meningococcal disease in children. *Semin Pediatr Infect Dis*. 2002;13:182-189.

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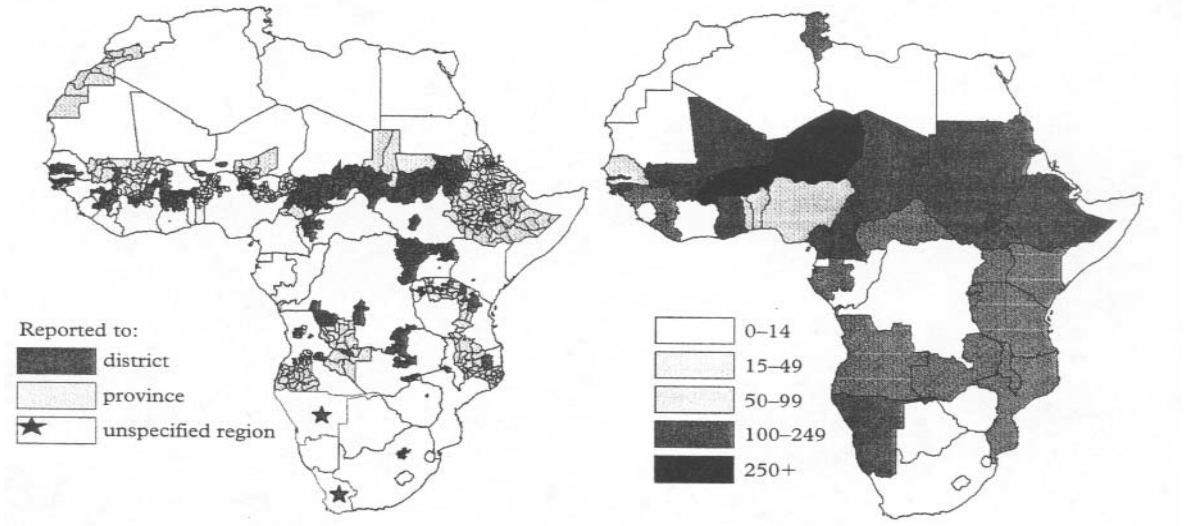
Figure 2

Widened Meningitis Belt



Chronic Infection May Contribute to Stroke Risk

ABSTRACT & COMMENTARY

Synopsis: *The association between H pylori and acute cerebrovascular disease seems to be due to a higher prevalence of more virulent H pylori strains in patients with atherosclerotic stroke.*

Source: Pietroiusti A, et al. Cytotoxin-associated gene-a-positive *Helicobacter pylori* strains are associated with atherosclerotic stroke. *Circulation*. 2002;106:580-584.

IT IS WELL KNOWN THAT CHRONIC INFLAMMATION IS A significant contributor to atherosclerotic disease. Serologic positivity for *Chlamydia pneumoniae* and

Helicobacter pylori have been associated with atherosclerosis independent of other vascular risk factors. These organisms have been linked to disease in the coronary arteries, carotid system, and peripheral vasculature. Although *H pylori* often presents as peptic ulcer disease and chlamydia rarely produces pneumonia, these chronic infections are usually entirely asymptomatic and thus are rarely treated.

In the current report, Pietroiusti and colleagues present data linking a particularly virulent *H pylori* strain (bearing the cytotoxin-associated gene A [CagA]) with stroke due to atherosclerosis. Dividing stroke patients into etiologic subtypes, 138 patients with large vessel stroke were compared to 61 patients with cardioembolic infarcts and 151 healthy controls. *H pylori* infection in general was highly prevalent in all groups, occurring in approximately 70% of patients. The prevalence of CagA-positive strains, however, was much higher in patients with large vessel strokes (43%) than among patients with cardioembolism (20%) or controls (18%)—$P < 0.001$ for either comparison. C-reactive protein levels, indicating an inflammatory state, were also significantly higher in the presence of *CagA*.

COMMENT BY ALAN Z. SEGAL, MD

By dividing infarcts into specific subtypes, rather than treating them as a lump sum, Pietroiusti et al were able to make significant insights into stroke pathophysiology. These data indicate that inflammation appears to play a role in strokes mediated by atherosclerosis, but not strokes related to cardiac thrombi. Similarly, stroke is not associated with all *H pylori* infections (an exceedingly common phenomenon), but rather with a specific more virulent (and less common) strain.

In a related article, Franceschi and colleagues (*Circulation.* 2002;106:430-434) further elucidate this interesting link. In an ex vivo, immunochemical model, they demonstrate that Anti-CagA antibodies specifically bind to epitopes on atherosclerotic blood vessels. *H pylori* may, therefore, promote atherosclerosis through a much more discrete process than merely nonspecific inflammation. Antibodies made against CagA may cross react with antigens expressed by cells involved in atherogenesis such as vascular smooth muscle, fibroblasts, or endothelial cells.

While mass treatments with antibiotics to prevent stroke and myocardial infarction are not yet justified, there is compelling evidence that particular chronic infections may significantly contribute to vascular disease.

Dr. Segal is Assistant Professor, Department of Neurology, Weill-Cornell Medical College, Attending Neurologist, New York Presbyterian Hospital.

CME Questions

18. Which of the following is true regarding chronic infection and stroke risk?

a. Infection is related to strokes of any subtype.
b. Any *H Pylori* seropositivity increases stroke risk.
c. C-reactive protein is elevated in all patients with *H Pylori.*
d. Antibodies against *H Pylori* may cross react with blood vessel walls.
e. Mass antibiotic campaigns should be waged to eradicate *H Pylori.*

19. Which of the following statements is true?

a. African outbreaks of meningococcal disease are confined to a belt-like strip across sub-Saharan Africa.
b. Routine meningococcal vaccination is now recommended for some pediatric patients in the United States and the United Kingdom.
c. A single meningococcal vaccine (monovalent, bivalent, or quadrivalent) is adequate for travel to Saudi Arabia during the Hajj.
d. Meningococcal disease is extremely rare in the Great Lakes Region of Africa (Rwanda, Burundi, Uganda, Tanzania, Democratic Republic of Congo).

20. Japanese encephalitis is:

a. a universally fatal disease process.
b. carried by *Culex* mosquitoes, which breed near rice paddies.
c. preventable by a vaccine which has no known serious side effects.
d. None of the above

Readers are Invited

Readers are invited to submit questions or comments on material seen in or relevant to *Infectious Disease Alert*. Send your questions to: Rob Kimball—Reader Questions, *Infectious Disease Alert*, c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. ■

In Future Issues:

Group A Streptococcal Infection

UPDATES

By Carol A. Kemper, MD, FACP

Polio-Like Paralysis: What Next from West Nile Virus?

Source: MMWR Morb Mortal Wkly Rep. 2002;51(37):825-828.

THIS REPORT FROM THE CDC describes the occurrence of a newly recognized illness associated with West Nile Virus (WNV) infection: an acute flacid paralysis (AFP), similar to polio, which occurred in 6 adults in Mississippi and Louisiana in August of this year. All 6 patients had acute onset of painless, asymmetrical weakness without evidence of sensory abnormalities. The initial diagnosis in 2 patients was acute stroke, and the other patients were variously diagnosed with meningoencephalitis, postviral demyelinating syndrome, and Guillain-Barré Syndrome (GBS). Several received IVIG and/or corticosteroids. However, electrophysiologic studies confirmed a severe, asymmetric process involving anterior horn cells and/or their axons, similar to poliomyelitis. In addition, CSF pleocytosis was evident in all but 1 case. WNV infection was subsequently confirmed in all 6 cases based on IgM and neutralizing antibodies.

Of the 1641 laboratory-confirmed cases of WNV as of September, 2002, only these 6 cases have resulted in AFP (0.37%). Nevertheless, the CDC cautions that clinicians should be aware of the potential for WNV to cause AFP, and be quick to distinguish it from GBS. Unlike AFP, GBS generally causes an ascending, symmetric, paralysis with both motor and sensory changes; the CSF protein is increased in the absence of pleocytosis. Because these 6 cases only recently occurred, it remains unknown whether the paralysis will be permanent. Residual paralysis lasting greater than 60 days is one of the diagnostic criteria for possible polio—which could create confusion in countries where polio remains endemic. ■

Cat Scratch Disease: Not Just for Kids

Source: Ridder GJ, et al. *Clin Infect Dis.* 2002;35:643-649.

RIDDER AND COLLEAGUES FROM Germany, who were especially interested in cat scratch disease (CSD), surveyed all causes of cervical lymphadenopathy in 454 patients referred to the Head and Neck Service at the University of Freiberg from 1997 to 2001. Patients were screened with a battery of serologic studies (eg, bartonella, toxoplasma, EBV, CMV, mumps, lyme, brucellosis, and tularemia), and TST. CSD was defined based on 2 of 3 criteria (clinical symptoms, serologic conversion, or molecular evidence of Bartonella DNA in lymph node tissue). FNA or biopsy was performed in patients with a suspected malignancy or a lack of evidence of infection.

Overall, about one third of the patients had evidence of infection, one third had benign or malignant neoplasms, and one third remained undiagnosed. CSD was the leading cause of infection, occurring in 61 persons (13.4%), although 4 of these were also diagnosed with concomitant malignant tumors. All 61 cases were confirmed by serology, and 10 of 21 patients with lymph node specimens had Bartonella DNA detected.

Interestingly, Bartonella DNA was found in lymphatic tissues only during the first 6 weeks of illness, suggesting that methods to identify a cat scratch organism, whether by molecular, pathologic or microbiologic techniques, beyond 6 weeks are not likely to be successful.

Of those patients with CSD, there were a similar number of children and adults compared with those with lymphadenopathy due to other causes, and the median age for both groups was about 35 years. Slightly more than half (59%) of the CSD cases had bilateral cervical disease and the remainder had unilateral disease. Eleven (18%) had lymphadenopathy present for 3 or more months. Similar to other studies of CSD, only half of the patients could recall contact with cats. The diagnosis of CSD may therefore solely depend on serologic evidence of recent infection.

An obvious limitation to this study was that fully one third of cases remained undiagnosed, and there was no mention of mycobacterial infection (or studies to look for such, other than a screening TST). However, this study does suggest that CSD serologies should be performed more commonly in the evaluation of cervical lymphadenopathy in both children as well as adults. ■