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Human Illness Associated with Veterinary Vaccines

ABSTRACT & COMMENTARY

Synopsis: *Use of veterinary vaccines has decreased disease and illness in animals, but inadvertent human exposure to these vaccines, in particular live vaccines, actually has the potential to cause human infections and illness.*

Source: Berkelman RL. Human illness associated with use of veterinary vaccines. *Clin Infect Dis*. 2003;37:407-414.

THE UNITED STATES DEPARTMENT OF AGRICULTURE (USDA) CURRENTLY licenses more than 2000 vaccines for use in animals. Many of these vaccines are inactivated formulations, but at least 500 are live vaccine formulations, with a potential for inadvertent infections of humans. At highest risk for exposures are veterinarians, animal workers, and pet owners. Reports from the literature as well as personal communications with health officials, veterinary schools, and universities were the basis for this article.

Brucellosis

In 1934, the US Brucellosis Eradication Program was begun to eliminate brucellosis in cattle. An early live bacterial vaccine, called S19, was administered for many years and later replaced with a modified live culture vaccine, RB51, in 1996. In unpublished data from the CDC's passive surveillance registry between 1998 and 1999, 26 individuals reported exposure to RB51 vaccine either via needlestick injury (21 patients), splashes to the eye (4 patients), or a splash to an open wound (1 patient). Most exposed patients received prophylactic antibiotics (73%), yet a pro-

portion of those so affected still had persistent symptoms for over 6 months (27%). One patient required surgery and *Brucella abortus* strain RB51 was isolated from the surgical wound.

In other countries, human illness has been reported from accidental exposure to the live vaccine, *Brucella melitensis* strain Rev-1, which is used worldwide. Two such cases, reported from Spain, were female veterinarians with febrile, systemic illnesses after inadvertent needlestick injuries while vaccinating sheep. Brucellosis was confirmed by serology and culture of the vaccine strain of *Brucella melitensis* in both cases. Treatment with doxycycline and rifampin resulted in complete recovery.[1]

Oral Rabies Wildlife Vaccine

Recombinant vaccinia-rabies glycoprotein virus vaccine within oral baits has been used in Europe for 20 years, and in the United States (10 years), to control the spread of rabies in wildlife populations. Humans may have inadvertent exposure to vaccinia virus through contact with these baits. A 26-year-old woman with epidermolytic hyperkeratosis, who was also 15 weeks pregnant, was bitten on the arm by her dog while removing the bait from its mouth. Several days later she developed vesicular lesions with pain, erythema, and swelling of her forearm. The skin lesions progressed to necrotic lesions with axillary adenopathy. Electron microscopy of tissue from the lesions revealed typical orthopoxvirus morphology, and genetic evaluation confirmed the source as vaccinia-rabies glycoprotein virus.[2] Toll-free numbers to report exposures are often included on the baits, and simple procedures such as hand washing after any handling of these baits can help prevent exposures. As the use of these bait vaccines continue to increase, it would seem prudent to ask about possible exposure to such baits in any patient presenting with vesicular lesions.

Bordetella bronchiseptica

Bordetella bronchiseptica is a cause of tracheobronchitis in dogs, atrophic rhinitis in swine, and disease in rabbits and other mammals. Human illness from *B bronchiseptica* can occur in healthy and immunosuppressed patients ranging from a pertussis-like illness to pneumonia, sepsis, and death.[3] Vaccines for "kennel cough" in dogs can contain *B bronchiseptica* live vaccine and parainfluenza virus for intranasal aerosol administration. In one case, a 14-year-old boy, holding his dog's head during administration of the intranasal vaccine, was accidentally sprayed directly in the face with the vaccine. The boy later developed a persistent paroxysmal cough with post-tussive vomiting that eventually responded to antibiotic treatment. Although cultures from the patient were not done, the CDC was later able to grow 2 morphologically different colonies of *B bronchiseptica* representing vaccine of the same lot to which the boy had been exposed (Sanden G. CDC. Unpublished data).

Intranasal administration of live vaccines to animals is convenient, yet it can result in inadvertent exposure to humans, especially if the animals sneeze, which often occurs if liquid is delivered intranasally. For children or adults presenting with a pertussis-like illness, physicians should inquire about exposure to veterinary clinics or recently vaccinated or sick animals.

COMMENT BY MARY-LOUISE SCULLY, MD

The topic of animal vaccines and their risk to humans is intriguing and timely, especially as significant numbers of HIV, cancer, and transplant patients may also be pet owners. The licensing and regulation of animal vaccines is under the USDA but is less stringent than the regulation and licensing of human vaccines under the auspices of the FDA. Adverse reactions or illness to animal vaccines can be reported to the Center for Veterinary Biologics, within the USDA's Animal and Plant Health Inspection Service (APHIS), either by using the toll-free telephone hotline (800-752-6255), or by their web site (www.aphis.usda.gov/vs/cvb). Berkelman's article is insightful and highlights the need for more careful monitoring, reporting, and possibly better packaging instructions to veterinarians, regarding the ability of live animal vaccines to cause disease in humans.

Animal vaccine production is a large, successful industry in the world market of veterinary animal health. In the United States, Fort Dodge Animal Health (a division of Wyeth Corporation) recorded net sales of $653 million in 2002. Sales in part may reflect the recent license approval for the Fort Dodge Animal Health West Nile Virus vaccine, a killed vaccine product. Despite some concerns that the vaccine may cause pregnant mares to abort or give birth to deformed foals, the APHIS feels the vaccine is safe for horses and strongly recommends its use. In 2002, West Nile virus caused 14,717 equine cases, with another 2168 equine cases so far in 2003. As the veterinary vaccine is a *killed* vaccine, there is less potential for human illness with accidental exposure. Unfortunately, the time frame for development and subsequent approval of a human vaccine for West Nile virus is not as close at hand.

Vaccination programs for animals have had an overall beneficial effect in reducing disease in domestic and farm animals. In addition, the rabies bait vaccine program has helped arrest the spread of rabies in terrestrial animals in the United States and Europe. However, the lines of communication need to remain open between the government agencies, vaccine manufacturers, veterinarians, and physicians, to ensure adequate exchange of information about the potential effects of these veterinary vaccines on public health. ■

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Atovaquone/Proguanil-Resistant *Plasmodium falciparum* Malaria Appears

ABSTRACT & COMMENTARY

Synopsis: *A returning traveler from West Africa developed falciparum malaria, which was treated with the combination agent atovaquone/proguanil. Relapse provided an opportunity to use molecular techniques to confirm parasite resistance due to a genetic mutation affecting parasite cytochrome b in the original infecting strain of* Plasmodium falciparum. *When such a mutation occurs in a strain of* P falciparum, *which has already experienced a mutation conferring resistance to folic acid antagonists, it spells potential trouble for atovaquone/proguanil.*

Source: Schwartz E, et al. Genetic confirmation of atovaquone-proguanil-resistant *Plasmodium falciparum* malaria acquired by a nonimmune traveler to East Africa. *Clin Infect Dis*. 2003;37:450-451.

A 24-YEAR-OLD ISRAELI WOMAN ACQUIRED FALCIparum malaria during a 1-week vacation to Mombassa, Kenya, in January 2002. She had not taken malaria chemoprophylaxis, and her symptoms developed 10 days after return home, with her admission blood smears showing 3% *Plasmodium falciparum* parasitemia. She was treated with atovaquone 1000 mg and proguanil 400 mg daily for 4 days, with resolution of fever. Her malaria smears showed parasite clearance by day 4. Fever recurred 30 days later, and malaria blood smears again showed *P falciparum*. The patient recovered with administration of oral quinine 600 mg t.i.d. for 3 days and doxycycline 100 mg b.i.d. for 7 days.

Molecular techniques were used to compare the malaria parasites observed during her initial presentation and at recurrence. This included extraction of DNA from malaria parasites, PCR amplification of the gene encoding the merozoite surface protein-1, and genetic fingerprinting with single-strand conformational polymorphism analysis, which showed the isolates to have identical genetic fingerprints. The initial isolate had wild-type sequence of cytochrome b, but the recrudescent isolate had a mutation at position 268 resulting in a substitution of tyrosine with serine. Both isolates had mutations in the dihydrofolate reductase gene associated with resistance to cycloguanil, the active metabolite of proguanil. These techniques confirmed the true basis for this malaria treatment failure.

■ COMMENT BY LIN H. CHEN, MD

Drug resistance occurring among *P falciparum* organisms are well-recognized problems that arise from chromosomal mutations. Polymorphisms in the *pfcrt* gene, which lead to impaired parasite vacuole uptake of chloroquine and polymorphisms in the *pfmdr1* gene, are both associated with chloroquine resistance.[1,2] Point mutations in the *dhps* gene and the *dhfr* gene lead to reduced drug-binding affinities for dihydropteroate synthetase and dihydrofolate reductase, respectively, and are associated with sulfadoxine-pyrimethamine resistance.[2] Mefloquine resistance is quite significant in Southeast Asia and appears to be associated with mutations in the *pfmdr1* gene, as does quinine resistance.[2] Doxycycline had been the only chemoprophylactic option in areas with multidrug resistance until the combination of atovaquone and proguanil became available. Atovaquone/proguanil is also a recent addition to the therapeutic options for falciparum malaria, with cure rates > 96% at the dose of 1000 mg/400 mg daily for 3 days.[3,4]

Atovaquone acts on malaria parasites by inhibiting mitochondrial electron transport at the cytochrome b level.[3] Treatment of *P falciparum* with atovaquone alone unfortunately results in rapid emergence of resistance. Proguanil, with its metabolite cycloguanil, is a parasite dihydrofolate reductase inhibitor. Proguanil enhances atovaquone's effect on mitochondrial membrane potential, and the combination is synergistic.[5] However, point mutations in the parasite *dhfr* gene lead to proguanil resistance, which is well established.[2]

Resistance to atovaquone is attributed to point mutations in the *P falciparum* cytochrome b gene. Resulting amino acid substitutions caused by such gene mutations lead to decreased drug binding to malaria parasite cytochrome b, thereby reducing atovaquone's ability to

inhibit the cytochrome b complex role in electron transport.[6] Mutations at codon 268 of the cytochrome b gene produce the amino acid change from tyrosine to serine and have been associated with atovaquone/proguanil treatment failure.[7] The case report by Schwartz and associates documents clinical failure of atovaquone/proguanil in the treatment of a traveler with *P falciparum* malaria and clearly demonstrates the genetic alteration.

Travelers have played significant roles as both couriers and disease transmitters in the history of infectious diseases.[8] The dramatic increase in the movement of people across international borders provides opportunities for travelers to be sentinels of emerging infections, including drug-resistant malaria. Surveillance networks such as GeoSentinel and TropNetEurope collect and analyze data on travel-related illnesses, especially imported infectious diseases.[9,10] Analysis of imported falciparum malaria in the TropNetEurope database from 1999 to 2000 showed that the majority of European travelers (58.8%) and immigrants (68.2%) acquired their malaria infections in West Africa, and only 40% of European travelers and 28% of the immigrants used malaria chemoprophylaxis during travel.[10] Such information is useful in focusing preventive strategies on travelers going to West Africa and reaching more immigrants traveling to visit friends and relatives.

Another informative study assessed the efficacy of malaria chemoprophylaxis in returning Danish travelers with malaria from 1997 to 1999.[11] Breakthrough malaria occurred in travelers taking atovaquone/proguanil, as well as other chemoprophylactic regimens. The incidence of imported malaria differed greatly according to the country visited, from 1 per 140 travelers to Ghana to almost 1 per 40,000 in travelers to Thailand; the estimated failure rates against *P falciparum*, based on cases per prescription, in compliant patients, were: chloroquine/proguanil (1:599), mefloquine (1:2232), and atovaquone/proguanil (1:1943).[11] Thirty-seven percent of the malaria cases took all doses of their chemoprophylactic regimen, indicating a combination of poor compliance and significant failures. This particular study in travelers demonstrated a lower efficacy of chloroquine/proguanil against *P falciparum*, likely from increasing parasite resistance.[11]

Other case reports of travelers with *P falciparum* malaria resistant to atovaquone/proguanil have been published in travelers returning from the Ivory Coast (Reviewed in *Travel Medicine Advisor Update* May/June 2003) and Nigeria.[12,13] Molecular studies showed mutations that led to changes from tyrosine to serine[12] or tyrosine to asparagine[13] in codon 268 of cytochrome b. The case report is further evidence that *P falciparum* can rapidly develop resistance to atovaquone and proguanil following treatment and provides an example of travelers as sentinels for the emergence of drug resistance. Malaria should remain in the differential of febrile returning travelers even in those receiving atovaquone/proguanil for prophylaxis. Travel medicine specialists should be watchful for the possible emergence of atovaquone and proguanil resistance in the evaluation of travelers, if use either as malaria chemoprophylaxis or as malaria therapy. ■

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Postmalarial Neurological Syndrome Revisited

ABSTRACT & COMMENTARY

Synopsis: *Observations of those patients recovering from* Plasmodium falciparum *malaria in Vietnam and Thailand who developed a discrete neurological syndrome led to a prospective study, which described the clinical features and associations of postmalarial neurological syndrome (PMNS). A fascinating report of a PMNS case from Baylor College of Medicine, published in* Clinical Infectious Diseases (CID), *represents the first patient identified with PMNS in the United States.*

Source: Falchook GS, et al. Postmalarial neurological syndrome after treatment of *Plasmodium falciparum* malaria in the United States. *Clin Infect Dis*. 2003;37:e22-e24.

Neurological infections and their complications, particularly the cerebral form of severe

Plasmodium falciparum malaria, are perhaps among most feared entities known to physicians who take care of travelers. The postinfectious syndrome described by this recent CID case report is consistent with the other such cases described by Nguyen and associates in 1996.[1] These cases were specifically noted as *not* due to cerebral malaria. Common features among the 1996 Asian cases included: 1) having a negative malaria blood smear at the onset of neurological or neuropsychiatric symptoms; 2) a preceding severe case of malaria infection; 3) a recent complete recovery from *P falciparum* malaria; and 4) complete recovery from PMNS without specific treatment within 10 days.

The most recently described patient was a 50-year-old Ghanaian woman who was visiting friends and relatives in the United States and presented with intermittent dyspnea during physical exertion. Her examination was consistent with pulmonary edema. She was treated with quinine sulfate and doxycycline when her peripheral blood smear revealed *P falciparum* parasites at a 0.2% level of parasitemia. Her hemoglobin was 5-6 g/dL, and other pertinent admission labs were serum sodium level of 122 meq/L and serum potassium of 6.4 meq/L and creatinine of 2.5 mg/dL. These values were corrected. However, on day 5 of treatment, this antimalarial regimen was altered when her blood sugar level decreased to 31 mg/dL. Malaria treatment was completed with a 3-day course of atovaquone/proguanil. Following treatment, *P falciparum* was no longer detected in peripheral blood smears. The patient required endotracheal intubation on day 6 to treat pulmonary edema, which was not responding to large doses of loop diuretics. Echocardiogram showed mild concentric LVH with normal ejection fraction and normal LVEDP, and the pulmonary edema was felt to be noncardiac in origin but secondary to *P falciparum* infection.

Eleven days following resolution of parasitemia and 9 days after completing antimalarial therapy, the patient was found to have an abnormal mental status and the new onset of upper and lower extremity myoclonus, jerking, and tremors. She was awake but disoriented, unable to answer questions or follow commands. Verbal response consisted only of incomprehensible responses to pain. She was neither hypoxic, nor hypoglycemic, and there were no acute changes noted on head CT scan although multiple old lacunar infarcts were seen. Subsequent brain MRI showed nonspecific increased signal in the pons, posterior internal capsule, thalamus, corona radiata, and periventricular areas. CSF analysis was normal, and CSF cultures for bacteria, fungi, and mycobacteria were all unrevealing. All potentially offending medications were discontinued the day after symptoms developed; yet the patient's abnormal mental state became progressively worse. Eight days later, she developed both visual and auditory hallucinations, but within 2 days her mental status began to improve; she was able to both understand and answer questions, and her mental status returned to normal. Although she exhibited a slight expressive aphasia, this resolved 2 days later and she subsequently had no further neurological episodes or complications.

COMMENT BY MARIA D. MILENO, MD

The mechanism(s) and reasons for the development of PMNS are unknown. The brain sequestration of parasitized RBCs in persons with cerebral malaria has been documented in several necropsy series and remains the accepted pathogenesis of neurological syndromes occurring *during* falciparum-associated cerebral malaria. This finding is not limited to persons who die with cerebral malaria and could be a factor in the development of PMNS. Cerebral malaria is fatal in 15-20% of cases; in most other cases, recovery from coma is complete. Additional factors contributing to neurological symptoms can include hypoglycemia as well as use of mefloquine or chloroquine for prophylaxis or treatment. Both have been associated with an acute self-limited neuropsychiatric syndrome. Clinically significant neurological events have also been described with use of artemisinin compounds for the treatment of malaria.

Importantly, the patient who was reported in CID did not receive mefloquine, an agent that has been associated with neuropsychiatric side effects such as seizures and psychosis. Nor did she receive any other antimalarials commonly associated with adverse neurological events. One-fourth of the patients in Nguyen et al's study also had not received mefloquine. The combination atovaquone/proguanil has rarely been associated with neuropsychiatric effects, largely among patients with predisposing neuropsychiatric medical histories. There has been speculation about whether PMNS is a distinct clinical entity and not simply a consequence of either cerebral damage from malaria or the adverse effects of antimalarial therapy; this case report offered no evidence of cerebral malaria or drug-induced adverse events. It appears to be a disturbing, yet self-limited, syndrome characterized by bizarre derangement in mental status without long-term sequelae. More cases of what is a fairly recently described neurological syndrome will probably be recognized if travel medicine practitioners are simply aware of it. They are likely to be the major source of additional cases. ■

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A Young Girl Returns From Senegal with Dysentery

CASE REPORT

The patient was a previously healthy 5-year-old girl who had returned 3 days prior to admission from a 1-month stay in Senegal, West Africa, after visiting relatives. She had stayed in a suburban area and eaten local foods. She had not been swimming, and there were no known direct exposures to animals. She had been well in Senegal until 6 days prior to admission when she began to develop multiple episodes of watery, then bloody, stools and tactile fever. Over the next few days she continued to have bloody diarrhea and also had decreased activity, diffuse abdominal pain, and poor oral intake. She was seen by a physician in West Africa who started her on metronidazole (Flagyl) and amoxicillin/clavulanate (Augmentin). Her symptoms persisted, however, and her father ultimately decided to bring her home to Connecticut.

Upon return, her pediatrician discontinued the antibiotics she had received in Africa, sent off laboratory studies, and offered supportive treatment. She appeared fairly well in the doctor's office and she was sent home with instructions to return if symptoms worsened. That evening, her parents decided to bring her to the pediatric emergency department because of persistent diarrhea and fever. In the emergency department, she was febrile to 39.2°C, and on examination she had diffuse periumbilical tenderness without rebound. She had neither lymphadenopathy nor hepatosplenomegaly. Lung and heart sounds were normal. There were no rashes. She was found to be dehydrated (5-10%) with significant hyponatremia (serum Na^+ 119 meq/l). White blood cell count was 28,700/ul with 21% segmented neutrophils and 32% band forms. Platelets were 368,000/ul, and she had a normal hemoglobin and hematocrit. She was started empirically on intravenous cefotaxime at 200 mg/kg/d. Blood and stool cultures were positive by the second day of hospitalization for *Shigella dysenteriae*. Antibiotics were changed to Ceftriaxone (75 mg/kg/d) based on the susceptibility pattern of the isolated organisms. She finished a 1-week course of intravenous therapy; her symptoms slowly resolved without additional complications and she was discharged to home.

COMMENT BY MELISSA HELD, MD

Diarrhea is a common problem, often affecting travelers to developing countries. Bacterial agents may be identified in up to 85% of travelers with diarrhea lasting for less then 2 weeks. Destination represents one of the major risk factors for the development of diarrhea. People who visit friends or relatives during international travel are at increased risk over other travelers for becoming ill.[1] They are more likely to stay in small towns or villages, to eat local food, and to drink from the local water supply. These travelers are also more likely than traditional tourists to be exposed to pathogens in the environment and are less likely to obtain their recommended vaccinations or medications. In assessing risk, the health care provider should consider the length of stay in the area, areas of exposure (jungle, rural, urban), and level of accommodations (camping, hotels, backpacking).[2] Younger adults may be at higher risk of acquiring an infection secondary to a more adventurous itinerary and style while traveling. Children may be especially vulnerable since they likely have not been previously exposed to pathogens in the foreign environment and have an increased risk of fecal-oral contamination.[6] Parents who are foreign-born may already have both disdain and immunity to a number of pathogens they may be exposed to while traveling.

Shigella spp. are some of the most common causes of bloody diarrhea or dysentery. In the United States, *Shigellae* are most often isolated from children younger than 5 years of age who have symptoms of bacillary dysentery. Organisms are easily transmissible, and only a small number are required to cause disease. There are 4 general species, with at least 41 major serotypes overall. *Shigella sonnei* is the most common species encountered within industrialized countries, followed by *S flexneri*. *S boydii* and *S dysenteriae* are less commonly found. A population-based study of the incidence of *Shigella* infections and causative serotypes in Santiago, Chile, among 7489 children younger than 60 months of age, showed that 4 serotypes, *S sonnei* (45%), *S flexneri 2b* (19%), *S flexneri 2a* (14%), and *S flexneri*) *serotype 6* (11%) accounted for 89% of all cases. In this study, no isolations of *S dysenteriae* were made.[4] *Shigella* organisms are able to bypass the gastric acid barrier and colonize the terminal ileum and colon. These organisms secrete proteins, which facilitate invasion of the intestinal epithelium. Mucosal invasion of the gut is associated with an intense inflammatory response resulting in mucosal edema with both PMN and mononuclear infiltration, leading to microabscess formation and mucosal ulcerations.[8]

S dysenteriae infections predominate within non-industrialized nations, and they can be particularly

virulent. This species has been associated with large outbreaks of disease, especially in developing countries,[11] and will often cause septicemia, especially in young infants. *S dysenteriae* is the species most associated with severe dehydration and electrolyte imbalances as well as renal, gastrointestinal, and neurologic complications. *S dysenteriae*, type 1, produces the Shiga toxin, which is capable of affecting renal epithelial cells and causing the hemolytic uremic syndrome (HUS).[5] It is also associated with some less common complications such as toxic megacolon. Seizures have been reported in hospitalized children with Shigellosis with some degree of frequency.

Severe *Shigella* infection is one of the diarrheal diseases in which antimicrobials can be of benefit.[5] Use of appropriate antibiotics can help reduce severity and duration of disease. However, the use of antimicrobials in bloody diarrhea relies on the health care provider's knowledge of the relative frequency of pathogens in different areas of the world and the emerging resistance to antimicrobials.[9] In many developing countries, there are little sensitivity data available to help in guiding antimicrobial therapy. Trimethoprim-sulfamethoxazole, nalidixic acid, and amoxicillin are inexpensive antibiotics widely available for use in the treatment of *Shigella* dysentery. Treatment of shigellosis, however, has become complicated by the emergence of strains resistant to these antibiotics.[3,11] High-level resistance has been demonstrated among all *Shigella* species but varies according to geographic location. When available, susceptibility results should be used to guide therapy. Current guidelines recommend limiting treatment to more severe cases of *Shigella* infection and use of ceftriaxone or a fluoroquinolone when resistance to other antibiotics is suspected or confirmed. Although use of fluoroquinolones in children remains controversial, experience has shown that short courses of this antimicrobial class should still be considered for severe infections resistant to other antimicrobials.[10] ■

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A Tourist From Thailand Loses Her Vision

ABSTRACT & COMMENTARY

Synopsis: *An unusual manifestation of dengue fever serves as a warning about its potential ocular complications.*

Source: Haritoglou C, et al. *Lancet*. 2002;360:1070.

A 25-YEAR-OLD WOMAN HAD BEEN ON HOLIDAY IN Thailand during 2002. Two days before her return to Germany, she developed aching muscles and decreased visual acuity. She then went on to develop fever, maculopapular rash, hepatosplenomegaly, and thrombocytopenia (69, 000/m L). On ophthalmological examination visual acuity was reduced to 20/500, bilaterally. Evoked potential measurements were abnormal as well as color vision testing. Funduscopic examination revealed bilateral exudative maculopathy and small hemorrhages. Visual acuity eventually improved over 8 weeks to 20/100 in the right eye and 20/30 in the left eye. The reduction of vision in the right eye was due to intraretinal lipid deposits, presumably as sequelae of exudation initially observed. A serum IgM antibody titer of 1:640 confirmed dengue fever.

■ COMMENT BY MICHELE BARRY, MD

This is an unusual presentation for dengue fever in a traveler who had returned from Thailand. Although ocular manifestations of dengue fever have been described before, this case is a sober reminder that increased vascular permeability and breakdown of the inner retinal blood barrier can occur, even in nonhemorrhagic cases of dengue fever. Microinfarctions of the nerve fiber layer, as well as an optic neuritis, have been described in

dengue fever. Of interest, the patient flew home in a pressurized plane where pressure inequities might have exacerbated exhudation from leaky capillaries in the eye. Although steroids are generally used in optic neuritis, this patient was not given steroids due to Haritoglou and colleagues' discomfort in administrating steroids during dengue viremia—a controversial point. Usually, ocular alterations do resolve in dengue without specific treatment, but this tourist was left with impaired visual acuity in her right eye. ■

CME Questions

13. Which of the following statements regarding veterinary vaccines is *incorrect*?

a. Pertussis-like symptoms in a child or adult may be due to inadvertent exposure to *B bronchiseptica* live intranasal animal vaccine.
b. Simple procedures such as hand washing may decrease the risk of illness after handling recombinant vaccinia-rabies glycoprotein bait vaccine.
c. Inadvertent human exposure and subsequent illness has been reported with *Brucella* RB51, *Brucella melitensis* Rev-1, and *B bronchiseptica* animal vaccines.
d. Intranasal live veterinary vaccines do not result in accidental exposure to pet owners.
e. Knowledge of pet owner immune status is useful information for veterinarians to have prior to initiating animal vaccination with live vaccines.

14. Which one of the following statements regarding drug-resistant malaria is correct?

a. There has been no confirmation of malaria resistance to atovaquone and proguanil therapy.
b. Malaria drug resistance is not yet widespread.
c. A traveler cannot develop malaria while on prophylaxis with atovaquone and proguanil.
d. Atovaquone resistance results from mutations in codon 268 of the parasite cytochrome b gene.
e. Proguanil resistance is exceedingly rare and only occurs after prolonged treatment with the folic acid antagonists.

15. Which of the following statements about postmalarial neurologic syndrome (PMNS) is correct?

a. PMNS only occurs in the setting of cerebral malaria.
b. Persons with persistently positive malaria smears at time of onset of neurological symptoms are candidates for development of PMNS.
c. The use of mefloquine anteceded three-quarters of all cases of patients described with PMNS.
d. Complete recovery from PMNS occurs within 10 days without specific treatment.
e. c and d

Answers: 13.(d); 14.(d); 15.(e)

Readers are Invited. . .

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