

Prophylaxis Still Essential After Rabies Exposure

BY JANE SALODOF MACNEIL
Southwest Bureau

SCOTTSDALE, ARIZ. — Despite the first known survival of an unvaccinated rabies patient, prophylaxis still is the only proven defense after rabies exposure, Dr. L. Barry Seltz told physicians at a pediatric update sponsored by Phoenix Children's Hospital.

"There is no established, effective treatment," Dr. Seltz of the University of Arizona in Tucson warned in a talk that addressed misconceptions about human rabies risk and why current thinking discourages vaccination in the gluteal area.

The treatment that saved the Wisconsin teenager (*N. Engl. J. Med.* 2005;352:2508-14) needs to be duplicated, according to Dr. Seltz. Vaccination can be before or after exposure, he said, but it must be done whenever exposure to the rabies virus is suspected.

Exposure may not be easy to document, however. For Dr. Seltz, a key lesson from the survival of the 15-year-old girl is the importance of taking a good patient history.

"She said she had been bitten by a bat. She didn't think anything of it," he said, crediting careful questioning by the



teenager's primary care physician with unearthing this crucial piece of information after the patient became ill. She had not previously reported the bite.

Despite public fear of rabid dogs and widespread rabies in wild raccoons on the Eastern seaboard, Dr. Seltz said that most human rabies cases in the United States involve bats. From 1990 to 2004, he said there were 47 cases, including 10 cases acquired abroad. Of the 37 infections that originated in this country, 34 were deter-

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DR. SELTZ

he would vaccinate in the absence of certain exposure, he cited the person who was asleep when a bat flew into a room or a child who cannot give a reliable history.

Other than a bite, he said the virus can be transmitted via "contamination of non-intact skin or mucous membranes with saliva from a rabid animal."

"Petting a rabid animal is not an exposure. Contact with blood, urine, or feces of an infected animal is not exposure," he said.

The virus has a 20- to 60-day incubation period in humans. Ten days is adequate

for observation of a dog that appears healthy after it has bitten someone in the United States, according to Dr. Seltz. If the dog has been infected, the virus will present itself quickly.

To control rabies in humans, he urged preexposure vaccination of veterinarians, animal handlers, lab workers, people moving to areas where dog rabies is common, and those who make frequent contact with wildlife.

The postexposure protocol is three-pronged, he said: local wound care, active immunization, and passive immunization with immune globulin. "Cleaning [the wound] is critically important," he said. "Animal studies show that wound cleaning can reduce the risk of rabies by 50%."

The vaccines available in the U.S. are all inactivated viruses. Do not inject them in the gluteal area, he warned, as it has been associated with prophylaxis failure.

Exposed patients should receive a dose of 20 IU/kg—no more, no less—of immune globulin prepared from the plasma of immunized human donors, Dr. Seltz added.

In five cases of children who died despite receiving the full postexposure protocol for multiple bites, their wounds were not sufficiently infiltrated with immune globulin, according to Dr. Seltz. If a child has multiple wounds, he said to dilute the 20-IU/kg dose in normal saline solution and use the extra volume to make sure all the wounds are infiltrated. ■

Bats vs. Raccoons

Dogs are the first animal that comes to mind when most people think about rabies, but Dr. Seltz said they are not much of a threat in the United States.

In 2004, only 94 rabid dogs were reported in this country, according to Dr. Seltz. Among domestic animals, there were more cases of rabid cats and rabid cattle: 281 and 115 animals, respectively.

Dog bites do account for most of the 50,000 human rabies cases worldwide each year, he said. In the United States, however, 92%-94% of animal rabies comes from wild animals.

The largest concentration of infected animals has been identified to date on the East Coast, Dr. Seltz reported. Nationwide, in 2004, there were 2,400 rabid raccoons, 1,800 skunks, and 1,300 bats. Because bats are more likely to come in contact with people, they are most often implicated in human infections. Squirrels are rarely found to be rabid, he said, as they generally do not survive the initial attack of a rabid animal.

Rabies has been found throughout the country, he continued, except for Hawaii. It is the only state with no reports.

Antidepressants May Bolster Immune Function in HIV-Positive Patients

BY DAMIAN McNAMARA
Miami Bureau

SAN JUAN, P.R. — A selective serotonin reuptake inhibitor can enhance killer lymphocyte activity against HIV infection, according to preliminary study findings.

Depression may raise the risk of morbidity and mortality in patients with many medical conditions, including HIV infection. In addition, depression has been linked to immune function deficits, such as decreased natural killer cell activity, according to a presentation at the annual meeting of the American College of Psychiatrists.

In normal physiology, natural killer cells defend against viral infections and eliminate neoplastic cells. Natural killer cells are a focus of the ongoing HIV in Women: Depression and Immunity study, funded by the National Institute of Mental Health.

In this study of 40 women, a blood sample was obtained from each subject, and the researchers then treated the sample with citalopram and/or a substance P antagonist (an experimental agent); they then measured natural killer cell activity in vitro. They found that such treatment could reverse the detrimental effect of HIV on natural killer cell activity.

These preliminary data are "hot off the press," Dr. Dwight L. Evans said. "Next we need to look at this in a real in vivo situation."

"These findings ... suggest that killer lymphocyte antiviral activity is enhanced by an

SSRI and the substance P antagonist," said Dr. Evans, the Ruth Meltzer Professor and chair of psychiatry at the University of Pennsylvania in Philadelphia.

"The reason we focused on natural killer cells—or killer lymphocytes as they are now known—is they kill or lyse HIV-1 infected cells and secrete chemokines and cytokines," Dr. Evans said.

Cytotoxic T lymphocytes also lyse HIV-infected cells and secrete HIV-suppressive factors. Severe life stress decreases both these natural killer cells and cytotoxic T lymphocytes, he added.

In another study, Dr. Evans and his associates found that resolution of major depression was associated with increased natural killer cell activity in HIV-seropositive women (*Am. J. Psychiatry* 2005;162:2125-30).

The investigators assessed 57 women over 2 years and found that variations in natural killer cell levels corresponded to changes in depression status and ratings on the 17-item Hamilton Depression Rating Scale. Major depression in 11 participants resolved over time, with a simultaneous and significant increase in natural killer cell activity, which returned to normal levels.

"This study suggests that depression may impair certain aspects of innate cellular immunity relevant to delaying the progression of HIV disease and that these alterations are reversible with the resolution of a depressive episode," the authors wrote. ■

HIV Neurocognitive Impairment Underrecognized, Study Shows

SAN DIEGO — Physicians at a university-based infectious disease clinic are not routinely screening for HIV-associated neurocognitive impairment in patients infected with HIV, results from a small, single-center study has shown.

"Although the incidence of HIV neurocognitive impairment per year is decreasing, it's still very prevalent,"

Dr. Kristin M. Brousseau said in an interview during a poster session at the annual meeting of the American Neuropsychiatric Association. Cognitive impairment has significant implications for patients' ability to adhere to their medications, she noted.

She and her associates randomly reviewed the charts of 50 HIV-positive patients who visited a university-based infectious disease clinic. They used 15 search terms to identify whether physicians recorded HIV-associated neurocognitive impairment (HNCI) as a clinical problem.

The mean age of the 50 patients was 45 years, and most (78%) were

male, said Dr. Brousseau, of the department of psychiatry at the University of Colorado at Denver and Health Sciences Center. More than half (56%) had a coexisting psychiatric diagnosis, and 48% had a co-

existing substance abuse diagnosis.

HNCI was documented in the medical records of only three patients (6%), even though

the reported prevalence in the medical literature is 30%-40%. Only one patient underwent formal cognitive screening.

Physicians are "not doing a screening test for cognition," which can be performed in 5-7 minutes, she said.

The researchers noted that hepatitis C coinfection and a history of interferon treatment were seen in the patients with documented HNCI.

"Further studies are needed to determine the true prevalence of HNCI and explore the long-term effects of HCV coinfection and interferon treatment in this population," they wrote in their poster.

—Doug Brunk



Cognitive impairment has significant implications for patients' ability to adhere to their medications.

DR. BROUSSEAU