vCJD May Be More Widespread Than Projected

Prion diseases have long incubation periods, possibly approaching or even exceeding the human life span.

BY JONATHAN GARDNER
London Bureau

Variant Creutzfeldt-Jakob disease could have an incubation time of 30 years or longer and could affect a wider population than currently forecast, according to new research on patients with a similar human prion disease.

Researchers examined 11 recent cases of kuru, a prion protein disease that became an epidemic in the mid-1900s among several groups of Papua New Guinea natives, resulting from their ritual cannibalism, reported John Collinge, Ph.D., a professor of neurology at University College London, and his colleagues (Lancet 2006;367:2068-74).

Cannibalism practices were banned by the Australian authorities in the mid-1950s, and researchers are confident they have been nonexistent since 1960. However, because kuru disease still affects Papua New Guinea natives, researchers have been able to determine long incubation times.

Dr. Collinge and his colleagues monitored 11 cases of kuru disease in Papua New Guinea beginning in 1996, with disease onset between November 1994 and October 2001. The average age of patient onset was 46 years or older.

The oldest patient at disease onset was a 63-year-old man in 1996. The minimum incubation time for the patient was 36 years. However, because young boys traditionally stopped participating in the cannibalism ritual around the age of 7 years, the likely incubation period was 56 years, the researchers reported.

The mean incubation period for kuru is currently estimated to be about 12 years.

Of the 11 patients, 8 were heterozygous for valine and methionine at codon 129 of the human prion protein gene. That distribution of heterozygous genotypes within the kuru patients did not, however, differ markedly from the surrounding population.

Although kuru disease's lethality arose from intraspecies recycling of infectious prions, the results of the latest research suggest that prion diseases, such as variant Creutzfeldt-Jakob disease (vCJD), may have longer incubation times than current models now pose.

Genetic transmission barriers may limit the number of people who acquire vCJD by consuming meat infected with bovine spongiform encephalopathy (BSE). Those who have already suffered from the disease may have been genetically predisposed to have shorter incubation times. Meanwhile, the research on kuru patients demonstrates that prion diseases can also have very long incubation times, "approaching (and perhaps exceeding) the typical human life span," according to the researchers.

"Therefore, a human BSE epidemic may be multiphasic, and recent estimates of the size of the vCJD epidemic based on uniform genetic susceptibility could be substantial underestimations," they wrote.

"Genes implicated in species-barrier effects, which would further increase both the mean and range of human BSE incubation periods, are also probably relevant. In this context, a human epidemic will be difficult to accurately model until such modifier loci are identified and their gene frequencies in the population can be measured." ■

Study Finds FDG-PET 93% Accurate In Diagnosing Chronic Osteomyelitis

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Fluorodeoxyglucose PET scan results reflected a diagnosis of chronic osteomyelitis with 93% accuracy in a single-center study.

"Chronic osteomyelitis is a big area of morbidity for our society," Dr. Abass Alavi said in an interview at the annual meeting of the Society of Nuclear Medicine. "A test that can accurately detect and monitor these patients is needed" because current modalities, including structural imaging and combined nuclear medicine techniques, are either insensitive or not specific.

"Therefore, a lot of people are not getting treatments that are needed," Dr. Alavi added.

He and his associates at the University of Pennsylvania Medical Center, Philadelphia, studied 57 patients with suspected chronic osteomyelitis who underwent fluorodeoxyglucose (FDG) PET imaging in full-ring PET scanners.

The researchers then compared the images with the final diagnosis based on surgical findings, microbiology, and clinical follow-up.

Dr. Alavi, chief of the division of nuclear medicine at the medical center, reported that FDG-PET correctly diagnosed the presence or absence of chronic osteomyelitis in 53 of the 57 patients.

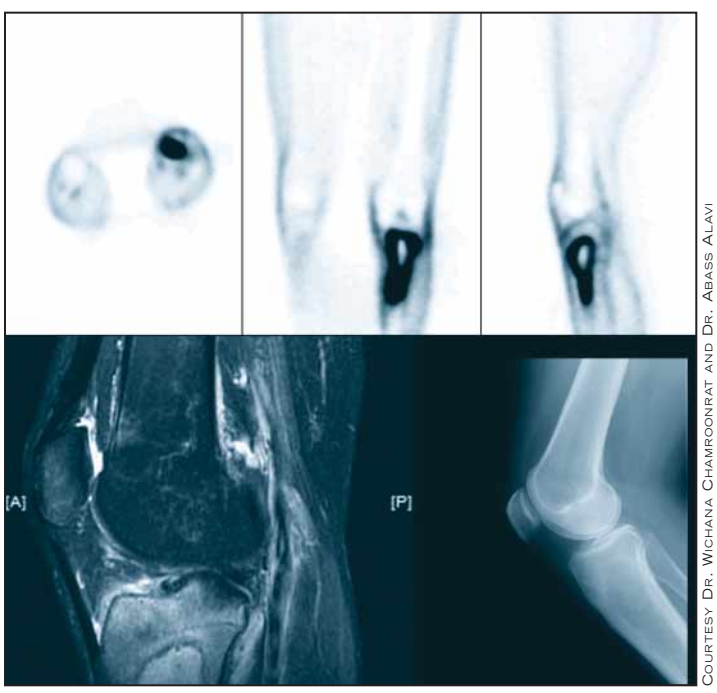
Among the 57 patients, 27 had chronic osteomyelitis and 30 were free of bone infection. The procedure correctly identified 26 of the 27 patients with chronic osteomyelitis, but there were false positives in 3 patients.

FDG-PET had a sensitivity of 96.3%, a specificity of 90%, and an accuracy of 93%. The positive predictive value was 90% and the negative predictive value was 96.4%, he reported.

The potential cost advantages of FDG-PET for diagnosing osteomyelitis "are clearly there, because we have a test that has an accuracy of better than 90%," said Dr. Alavi, who was the first clinician to apply FDG-PET technology in humans. "Before I started this technique, we had to do white cell imaging, which costs about $2,000. Then we had to a bone scan [and] a bone marrow scan. A patient had to do these over 2 days. The cost of FDG-PET should not be more than $1,500."

He predicted that FDG-PET will become the diagnostic tool of choice for other common inflammatory diseases, such as rheumatoid arthritis and ulcerative colitis.

Dr. Alavi described a recent case in which FDG-PET was used in a patient who was in and out of the hospital for 6 weeks with a fever of unknown origin. "One single FDG-PET showed an infection in the mediastinum," he said. "It looks like FDG-PET is going to be the way to go whenever there's infection." ■



COURTESY DR. WICHANA CHAMROONRAT AND DR. ABASS ALAVI

At top, images show abnormal intense FDG uptake in the left proximal tibia. At bottom left, MRI T2 image shows abnormal signal intensity in the proximal left tibia. At bottom right, plain radiograph of the left knee shows no detectable abnormality.

Summer Menactra Shortage Expected to Echo Last Year's

WASHINGTON — Despite a recommendation to prioritize 11- to 12-year-olds, distribution of the meningococcal conjugate vaccine was especially high among 18-year-olds and was evenly distributed among 11- to 17-year-olds during its first year on the market, Dr. Gregory Wallace reported at a meeting of the National Vaccine Advisory Committee.

The rationale for the recommendation was to help establish an adolescent vaccine visit, and was not generated because of an increased disease risk among 11- to 12-year-olds, explained Dr. Wallace, chief of the Vaccine Supply & Assurance Branch at the Centers for Disease Control and Prevention.

The vaccine is also recommended for adolescents entering high school who have not been previously vaccinated, as well as for college freshmen living in dorms.

Demand for the meningococcal conjugate vaccine (MCV4), marketed as Menactra, was high starting in June 2005 after the publication and promotion of the vaccination recommendations by the CDC's Advisory Committee on Immunization Practices, the American Academy of Pediatrics, and the American Academy of Family Physicians.

The demand was initially highest for 18-year-olds, and the peak months were June and July 2005. The high demand then decreased during the fall of 2005, as did patients' and parents' concerns about the vaccine supply.

The overall vaccine distribution rate from March 2005 to March 2006 was approximately 10% for 11- to 17-year-olds, but it approached 16% among 18-year-olds, based on physicians' billing-claims data provided by the vaccine's manufacturer, Sanofi Pasteur USA.

About 4.2 million doses were distributed between March 2005 and March 2006. Although the manufacturer projects that 6 million doses will be available for 2006-2007, the amount currently available for the summer months of 2006 is approximately the same as last year, Dr. Wallace said.

Sanofi Pasteur expects the demand for the vaccine to exceed supply this summer. To handle the anticipated summer rush among 18-year-olds, the CDC and other organizations have recommended that physicians defer the vaccination of 11- to 12-year-olds until further notice from the manufacturer that the shortage has been resolved.

The current supply projections should be sufficient to cover adolescents entering high school, dorm-dwelling college freshmen, and other high-risk groups, including military recruits and travelers to areas where the risk of meningococcal disease is high.

For periodic vaccine supply updates, visit www.cdc.gov/nip/news/shortages/default.htm.

—Heidi Splete