Objective: To describe 2 patients with rapidly progressive dementia and risk factors for exposure to chronic wasting disease (CWD) in whom extensive testing negated the possible transmission of CWD.

Design/Methods: We describe the evaluation of 2 young adults with initial exposure histories and clinical presentations that suggested the possibility of CWD transmission to humans.

Patients: A 52-year-old woman with possible laboratory exposure to CWD and a 25-year-old man who had consumed meat from a CWD endemic area.

Interventions: Clinical evaluation, neuropathological examination, and genetic testing.

Results: Neuropathological and genetic assessment in the 2 patients proved the diagnoses of early-onset Alzheimer disease and a rare genetic prion disease.

Conclusion: No convincing cases of CWD transmission to humans have been detected in our surveillance program.

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Spongiform encephalopathies are a family of degenerative disorders affecting a variety of human and mammalian species. Issues concerning possible cross-species transmission have captured scientific and public attention following the outbreak of a form of Creutzfeldt-Jakob disease with unusual clinical and histopathological features. Now known as variant Creutzfeldt-Jakob disease, the disease was identified in young adults in the United Kingdom and linked to consumption of meat from cattle infected with bovine spongiform encephalopathy.1 Two other spongiform encephalopathies affecting mammals whose meat is consumed regularly by humans are scrapie in sheep and chronic wasting disease (CWD) in some cervid species. Despite more than 200 years of exposure to the scrapie agent in sheep, no evidence of scrapie transmission to humans exists, although this risk cannot be completely excluded.2 Whether humans are susceptible to CWD is not known. As with all spongiform encephalopathies, CWD is marked by accumulation of an abnormal isoform of the normal brain protein known as the prion protein.3 Infectious prions have also been demonstrated in other tissues, including skeletal muscle, saliva, and blood of clinically ill CWD-infected deer.3,4 Exposure to CWD prions could potentially occur through consuming meat or tissues from infected animals; while processing game; or through unusual pathways such as ingesting antler velvet, which is used in Asian cultures as a traditional medicine.

Chronic wasting disease was first described as an endemic disease in free-ranging herds of mule deer (Odocoileus hemionus), white-tailed deer (Odocoileus virginianus), and mountain elk (Cervus elaphus nelsoni) in a contiguous area encompassing northeastern Colorado, southwestern Nebraska, and southeastern Wyoming, where disease prevalence averages 5% in mule deer.7 Subsequently, CWD has been found in wild deer in Illinois, Kansas, Minnesota, New Mexico, New York, South Dakota, Utah, West Virginia, Wisconsin, Alberta, and Saskatchewan and in captive, ranched deer and elk in 10 American states and 2 Canadian provinces. The origins of the disease are obscure. The earliest recognized cases of CWD occurred in captive deer in a research facility in Colorado in 1967, and indirect evidence indicates that the dis-
and electroencephalography demonstrated mild diffuse volume loss, dementia and other neurologic disorders. Brain magnetic resonance imaging showed mild diffuse neuritic plaques and tau-positive neurofibrillary tangles (Figure). Further analysis of brain tissue at the National Prion Disease Pathology Surveillance Center was negative for prion disease by Western blot analysis. Subsequent investigation by the state department of health revealed the patient had worked in an area of the laboratory that conducted necropsies on domestic animals and had never been assigned to the CWD testing laboratory. The Colorado Department of Public Health and Environment could not confirm that the technician had ever worked with deer and elk tissues.

CASE 2

This 25-year-old right-handed man had a 4-month history of progressive gait disturbance, myoclonus, hallucinations, slowed cognition, impaired attention, and memory loss. He had hunted deer and elk in a CWD endemic area of southern Wyoming and cooked and ate the field-dressed meat. His family history was significant in that his mother had died of a dementing disease at age 40 years, although there was neither a clinical diagnosis nor an autopsy. Brain magnetic resonance imaging findings were unremarkable, and electroencephalography demonstrated 1-Hz high-amplitude periodic sharp wave complexes. Other laboratory studies had negative results. Testing for the 14-3-3 protein had positive results, but the cerebrospinal fluid was otherwise unremarkable. The diagnosis of Gerstmann-Sträussler-Scheinker syndrome, a familial prion disease, was confirmed with a detailed autopsy examination and referral of the brain to the National Prion Disease Pathology Surveillance Center. Autopsy brain tissue showed the presence of protease-resistant prion protein by Western blot analysis. Genetic evaluation revealed the P102L mutation in the prion protein gene with methionine/valine heterozygosity at codon 129.

No cases of CWD transmission to humans have been detected to date. Colorado has implemented a multifaceted program to assess the human health risk, if any, of exposure to CWD. This includes making human prion disease a physician-reportable condition, conducting investigations and autopsies on all suspected prion disease cases, and initiating epidemiological studies on the incidence of human prion disease. Several cases with atypical features investigated as part of this project have been previously reported, including our second case in a review of prion disease in young patients. This patient was presented in an abstract by our group in 2003 and

Figure. High-power photomicrograph illustrating the numerous neuritic plaques, silver-positive neuropil threads, and neurofibrillary tangles seen on brain biopsy in patient 1 (modified Bielschowsky silver stain, original magnification, ×600).
was then included in a review article published in 2004, prior to completion of our 5-year summary report; this case is presented here with updated information. Our group recently completed an epidemiological study that did not reveal any unusual patterns in neurological and neuropsychiatric mortality associated with areas of Colorado where CWD is endemic. In this report, we describe 2 patients in whom the possibility of human CWD transmission was considered high based on the clinical presentation and exposure history. Despite reported exposures to potentially CWD-positive tissues, alternate diagnoses were confirmed by clinical, neuropathological, and genetic evaluation. Both patients were found to have rare neurological diagnoses: early-onset Alzheimer disease in one and a familial form of prion disease, proven by identification of an established gene mutation, in the other. These cases underscore the importance of a thorough clinical, neuropathological, and genetic evaluation before a neurological or neuropsychiatric disorder in persons exposed to potentially infected game can be attributed to CWD. Although significant barriers can exist to obtaining autopsies on suspected Creutzfeldt-Jakob disease cases, postmortem brain examinations with referral to the National Prion Disease Pathology Surveillance Center are crucial to evaluating patients with prion disease.

Our experience over a 5-year period is consistent with previously described human case investigations and laboratory studies that also support the absence of human CWD to date. However, proving the absence of a rare transmission event to a person is exceedingly difficult. Still, while not conclusive, our results are reassuring from a clinical perspective. These cases support the need for a coordinated surveillance effort, including epidemiologic investigation, clinical evaluation, and neuropathological and genetic examination for all suspect cases. Further surveillance of the possibility of human transmission of CWD is warranted, particularly among persons with cervid exposure in endemic states.

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