PUBLIC HEALTH SERVICE

Interagency
Coordinating Committee on
Human Growth Hormone and Creutzfeldt-Jakob Disease

November 28, 2023, 2:00 PM

- Virtual Meeting -
Hosted by the National Institutes of Health
Bethesda, Maryland

Committee Members Attending
Dr. William Cefalu, NIDDK
Dr. Ellen Leschek, NIDDK
Dr. James Mills, NICHD
Dr. Avindra Nath, NINDS
Dr. Griffin Rodgers, NIDDK, Chair
Dr. Lawrence Schonberger, CDC
Dr. Aida Kuzucan, FDA

Also Attending
Dr. Joe Abrams, CDC
Dr. Erica Bizzell, NIDDK
Ms. Leslie Curtis, NIDDK
Dr. Gregory Germino, NIDDK
Dr. Ryan Maddox, CDC
Dr. Heather Rieff, NIDDK
Dr. B. Tibor Roberts, NIDDK
Dr. Robert Tilghman, NIDDK
Ms. Alyssa Voss, NIDDK

Westat Contract
Dr. Leschek reported that a new 5-year contract with Westat—to collect and analyze critical information about CJD onset and progression to help inform the Committee's work—began in July.

National Hormone and Pituitary Program (NHPP) Cohort Update
Dr. Leschek reported that there have been no additional confirmed cases of CJD within the cohort since the 2021 meeting, and there are no new clinically suspicious cases. The total number of official cases (*i.e.*, clinically or neuropathologically confirmed) remains at 35.

However, Dr. Leschek alerted the Committee that an additional case is expected to be confirmed. A physician contacted the National Prion Disease Pathology Surveillance Center in July to say that he was treating a cohort member in his or her late 50s, who has since died. The individual presented with progressive tremor and ataxia, and magnetic resonance imaging, electroencephalograph, and RT-QuIC tests were all consistent with prion disease. The Surveillance Center worked with the physician to arrange an autopsy. When the Committee receives the death certificate, this will officially be counted as the 36th case. When the autopsy results are available, it will presumably be listed as neuropathologically confirmed.

The individual's physician thought the symptoms may have begun as recently as May of 2023, about 51.5 years after initiation of treatment with hGH. If so, this would increase the longest known incubation time for a cohort case by more than 5 years.

Dr. Rodgers wondered how many living cohort members were 50 years or more beyond their treatment period. Apropos of this, Dr. Schonberger noted that the cohort is now aging to the point that sporadic CJD is becoming more of a risk. Dr. Abrams suggested that it may be possible to develop a model that predicts how many future cases we might expect to see by making certain assumptions based on dates of treatment and expected incubation times. He and Dr. Leschek planned to consider the question and work together to develop the idea, as appropriate.

Dr. Leschek discussed three cases under investigation. Regarding the first of these, a 64-year-old who died from unspecified dementia in hospice, the Committee considered all data available and concluded there was too little evidence for concern to consider this a potential case. She also discussed a 69-year-old whose death certificate did not list any CJD-indicative causes, but the executor of whose will contacted Dr. Leschek to let the Committee know this cohort member had developed dementia prior to death. There was no autopsy and no next of kin are available, so the CDC is working to obtain medical records. In addition, there was a 59-year-old whose death certificate listed dementia as a secondary cause, and Dr. Leschek is currently reaching out to next of kin.

Dr. Leschek noted that the data on suicide risk in the cohort discussed at the 2022 meeting had been assembled into a paper that is now published, and she thanked Dr. Abrams for his efforts in getting that accomplished.

Dr. Leschek reminded the Committee that she had learned a few years ago that some cohort members had donated their bodies or organs, despite Committee recommendations that they should not do so because of the risk of transmitting pre-symptomatic CJD to tissue recipients. She had spent some time following up and learned that no organs had been transplanted from those donors.

Since then, she noted, the FDA modified its blood donation guidance with our input, and we modified our website to say organs and tissues from pituitary growth hormone recipients may be donated, but the potential donor should disclose to the recipient organization, in advance, that he or she had received pituitary hGH and may be at increased risk for the development of CJD. Dr. Leschek, who discovered that despite these changes five more cohort members had donated their bodies, expressed concern that these notifications of donor CJD risk may not be happening. She contacted the recipient organizations, which confirmed they had not inquired about growth hormone therapy but that none of the individuals had CJD-indicative symptoms at death, also assured her that no tissues from the cadavers were transplanted into patients.

Updates on Fact Sheet and Public Inquiries

Ms. Curtis stated that the fact sheet resource list was updated to reflect the new scientific papers discussed at the 2022 meeting. For reference, the comprehensive fact sheet is here, and the resource list is here.

Ms. Curtis also reported that there were 8 inquiries regarding hGH and CJD over the past year, compared to 12 the year before. Two were from confirmed cohort members. None of the inquiries were suggestive of potential new cases of CJD.

Recent Progress in CJD Research

Drs. Schonberger and Nath noted four recent publications of interest:

1. Pritzkow S, Ramirez F, Lyon A, et al. Detection of prions in the urine of patients affected by sporadic Creutzfeldt-Jakob disease. Ann Clin Transl Neurol. 10:2316-2323, 2023.

2. Zhao J, Rostgaard K, Lauwers E, et al. Intracerebral hemorrhage among blood donors and their transfusion recipients. JAMA 330:941-950, 2023

3. Zou W-Q, Gambetti P. (2023). Prions and Diseases, 2nd Edition. Biomedicine, Springer Nature, Cham, Switzerland.

4. Thomas S, Roberts B, Domanović D, et al. Safety profile of plasma for fractionation donated in the United Kingdom, with respect to variant Creutzfeldt-Jakob disease. Vox Sang. 118:345-353, 2023.

Report on CJD in Foreign and Commercial Growth Hormone Recipients

Dr. Schonberger reported that during the last year he learned of one new foreign case of CJD in a non-U.S. growth hormone recipient. This was in a citizen of the United Kingdom who had an incubation period of approximately 44 years. The total number of foreign cases therefore increases to 217. Dr. Nath noted anecdotal reports of increased likelihood of CJD diagnosis following COVID infection. Recent research suggests that components of the viral protein coat might increase the risk for or rate of protein aggregation not only for CJD but also for other neurodegenerative protein aggregation diseases. If so, this would suggest that COVID has the potential to accelerate pathogenesis but not that it causes the disease itself. Dr. Maddox noted that at least in the U.S. through 2021, death certificate data do not show either a clear increase in the number of CJD cases, or a reduction in average age of onset.

Griffin P. Rodgers, M.D.
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