PUBLIC HEALTH SERVICE

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

November 18, 2020, 10:00 AM

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

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

Also Attending
Ms. Emily Back, NIDDK
Dr. Greg Germino, NIDDK
Dr. Ryan Maddox, CDC
Ms. Amy Reiter, NIDDK
Dr. B. Tibor Roberts, NIDDK
Dr. Robert Tilghman, NIDDK
Ms. Alyssa Voss, NIDDK

Westat Contract
Dr. Leschek reported that Westat is in the second year of the current 5-year contract.

National Hormone and Pituitary Program (NHPP) Cohort Update
Dr. Leschek reported that there had been two additional cases of CJD within the cohort: one neuropathologically confirmed by autopsy, and one clinically confirmed by death certificate matching (*i.e.*, no biopsy or autopsy was performed). These cases bring the total number of official cases to 35. There have not been any new clinically suspicious cases, and there is one case under investigation.

The new neuropathologically confirmed case was a person in the cohort who had been treated with pituitary human growth hormone (hGH) from approximately 1972 to 1983 and died in 2020 with symptoms of CJD. Autopsy results and cerebrospinal fluid analysis were consistent with CJD. The period between midpoint of hormone treatment and onset of CJD symptoms was about 42 years. To date, however, no CJD has been reported in an individual who began treatment with NHPP hormone after 1977, when Dr. Albert Parlow's laboratory began purifying hGH for the Program. This suggests the new case of CJD was likely to have resulted from treatment received no later than 1977. Of note, this case represents the longest time from start of hormone therapy to onset of symptoms (47 years).

The new case that was clinically confirmed by a death certificate diagnosis was a person in the cohort who had been treated with pituitary hGH from 1975 to 1976, with treatment lasting less than 14 months. The death certificate states that this individual died in 2018 of CJD. No autopsy was performed, there is no living next-of-kin, and the CDC has thus far been unable to get the state's health department to retrieve the individual's medical records to determine when

onset of symptoms occurred. However, assuming symptoms began no more than 2 years prior to death, the period between midpoint of treatment and onset of symptoms is estimated to be about 40 years.

The case under investigation was a person in the cohort who received pituitary hGH from 1962 to 1965 and died in 2016. The death certificate does not mention CJD but lists dementia as the cause of death. There is no living next-of-kin, so the CDC is requesting assistance from the appropriate state health department in retrieving medical records to determine if the cohort member may have developed CJD or Alzheimer's disease.

Organ and Body Donations for Research

The NIDDK comprehensive and summary information web pages were revised to include guidance for cohort members who wish to donate their bodies to science (*i.e.*, they should disclose to the recipient organization, in advance, that they have received pituitary hGH and may be at increased risk for developing CJD).

The Committee is not aware of any additional organ or body donations from cohort members since the 2019 meeting.

Modification of FDA Guidance on Blood, Organ, and Tissue Donations

In April 2020, the FDA released revised guidance that recommended the removal of hGH from medication deferral lists for blood donations. The Committee supplied feedback and suggested edits to the guidance to reflect information from recent cases of CJD in the cohort. The FDA incorporated these edits and released updated guidance in August 2020. The NIDDK comprehensive and summary information web pages were revised to include this updated guidance, which states that the FDA still recommends that pituitary hGH recipients refrain from donating blood and requires that potential organ and tissue donors disclose to the recipient organization, in advance, that they have received pituitary hGH and may be at increased risk for the development of CJD.

Suicide, Accident, and Trauma Rates in Cohort

Dr. Leschek noted that the rates of suicide, accident, and trauma-related deaths appear to be considerably higher in the cohort compared to the general U.S. population. The Committee plans to analyze these data further and determine whether such an assessment could suggest preventative strategies for cohort members.

Updates on Fact Sheet and Public Inquiries

Ms. Back stated that the comprehensive and summary fact sheets were updated to reflect the updated blood/tissue/organ/body donation guidelines (as discussed above) and the new foreign case of CJD. Scientific papers discussed at the 2019 meeting were added to the resource list. For reference, the comprehensive fact sheet is here, the summary version is here, and the resource list is here.

Ms. Voss reported that there were seven inquiries regarding hGH and CJD over the past year, the same number as the year before. Five were from confirmed cohort members. None of the calls were suggestive of potential new cases of CJD.

Recent Progress in CJD Research

Dr. Schonberger and Dr. Nath noted six recent publications of interest:

1. Recommendations to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease and Variant Creutzfeldt-Jakob Disease by Blood and Blood Components. U.S. Food and Drug Administration, August 2020.

2. Brandel JP, Vlaicu MB, Culeux A, *et al*. Variant Creutzfeldt-Jakob Disease Diagnosed 7.5 Years after Occupational Exposure. *N Engl J Med*. 2020; 383: 83-85.

3. Asher DM, Belay E, Bigio E, *et al.* Risk of Transmissibility from Neurodegenerative Disease-Associated Proteins: Experimental Knowns and Unknowns. *J Neuropathol Exp Neurol.* 2020; 79: 1141-1146.

4. Bizzi A, Pascuzzo R, Blevins J, *et al*. Evaluation of a New Criterion for Detecting Prion Disease with Diffusion Magnetic Resonance Imaging. *JAMA Neurol*. 2020; 77: 1141-1149.

5. Rhoads DD, Wrona A, Foutz A, *et al*. Diagnosis of Prion Diseases by RT-QuIC Results in Improved Surveillance. *Neurology.* 2020; 95: e1017-e1026.

6. Sánchez-González L, Maddox RA, Lewis LC, et al. Human Prion Disease Surveillance in Washington State, 2006-2017. *JAMA Netw Open*. 2020; 3: e2020690.

Report on CJD in Foreign and Commercial GH Recipients

Dr. Schonberger reported one new 2019 case from the United Kingdom (bringing the U.K. total to 80 for hGH-related cases). This brings the total to 215 foreign cases.

Griffin P. Rodgers, M.D.
Director, NIDDK