

# Prions for Neuropathy Fellows (and Friends)

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## Case-Based Questions (please see page 3 for answers)

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| 1. | You get a phone call from a family member whose neurologist just told them that they have prion disease based on a positive CSF 14-3-3 protein result, obtained from the reference lab with the highest sensitivity (90%) and specificity (80%) in the country, where one out of every 20 CSFs come from a patient with prion disease. What is the likelihood that your relative has prion disease? |
| a. | Zero. Nobody believes that test.  |
| b. | Not likely.   |
| c. | About 50/50.  |
| d. | More likely than not.   |
| e. | 100%. Listen to your doctor.  |

  

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| 2. | You're asked to evaluate the brain of a 46-year-old woman who had several months of forgetfulness and confusion followed by hallucinations and delusions of persecution. CSF RT-QuIC was negative, and brain biopsy showed no spongiform degeneration or protease resistant prion protein. Which subcortical region must be examined to exclude prion disease? |
| a. | Cerebellar dentate nucleus   |
| b. | Cerebellar hemisphere  |
| c. | Midbrain   |
| d. | Striatum   |
| e. | Thalamus   |

  

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| 3. | Cerebellar Kuru plaques are most often encountered in patients with which type of prion disease? |
| a. | Gerstmann-Straussler-Scheinker Disease   |
| b. | Iatrogenic CJD   |
| c. | Kuru (duh)   |
| d. | Sporadic CJD   |
| e. | Variant CJD  |

**Scroll to Page 3 for answers**

Question 1 Correct answer and rationale: The correct answer is “b”. With a pretest probability of 5%, a sensitivity of 90%, and specificity of 80%, the likelihood of a patient with a positive test actually suffering from prion disease is about 20%.

Question 2 Correct answer and rationale: The correct answer is “e”. Both familial and sporadic fatal insomnia spare cortical regions until late in the disease course. Therefore, a negative brain biopsy does not exclude the possibility of this diagnosis, which is better assessed by MRI and/or polysomnography. Fatal insomnias are characterized by neuronal loss with reactive astrocytosis involving predominantly thalamic and inferior olivary nuclei, with positive immunohistochemical staining often restricted to the entorhinal cortex.

Question 3 Correct answer and rationale: The correct answer is “d”. Although cerebellar kuru plaques were seen in over 50% of patients dying from Kuru, abolition of endocannibalism in the early 1960s has cut way back on the number of Kuru cases encountered in the 21<sup>st</sup>-century. About 5 to 10% of patients with sporadic CJD will show cerebellar kuru plaques. Gerstmann-Straussler-Scheinker Disease is characterized by multicentric prion plaques, while variant CJD is characterized by prion plaques surrounded by vacuoles, resembling flowers. Very rare cases of iatrogenic prion disease showing cortical prion plaques have been reported.