**Update on ALS and Related Neurodegenerative Disorders**

*Brent T. Harris, MD, PhD, FCAP*

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

<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
</table>
| 1. Which of the following proteins are found to be aggregated most commonly in both sporadic ALS and FTLD-MND? | a. Alpha-synuclein  
b. Beta-amyloid  
c. Phosphorylated-tau  
d. TDP-43 |
| 2. What is the most common gene associated with genetic alteration found in familial ALS and FTLD-MND? | a. *APOE*  
b. *C9orf72*  
c. *Presenilin*  
d. *SOD1*  
e. *TDP43* |
| 3. Which of the following is the only way to a diagnosis of FTLD or ALS?   | a. Autopsy and neuropathological evaluation  
b. Biofluid evaluation of CSF or blood  
c. Muscle biopsy  
d. Surgical biopsy of the spinal cord or frontal lobe  
e. *<INSERT ANSWER CHOICE>* |
Scroll to Page 3 for Answers
Question 1: Correct answer and rationale: <D: Atypical TDP43 aggregates are found in glia and neurons in the motor cortex and spinal cord for both ALS and FTLD.> 

Question 2: Correct answer and rationale: <B: Increased numbers of hexanucleotide repeats in the C9orf72 gene is the most common familial genetic alteration in ALS and FTLD-MND.> 

Question 3: Correct answer and rationale: <A: Autopsy with appropriate sampling of brain, spinal cord, and muscle with H&E, special stain histopathology and immunohistochemical evaluation for TDP43 and possibly other markers of disease is the only current way to pathologically diagnose ALS and/or FTLD-MND.