

## Study Questions

Choose the ONE best answer.

- 2.1 Which one of the following statements concerning protein structure is correct?
- Proteins consisting of one polypeptide have quaternary structure that is stabilized by covalent bonds.
  - The peptide bonds that link amino acids in a protein most commonly occur in the cis configuration.
  - The formation of a disulfide bond in a protein requires the participating cysteine residues to be adjacent in the primary structure.
  - The denaturation of proteins leads to irreversible loss of secondary structural elements such as the  $\alpha$ -helix.
  - The primary driving force for protein folding is the hydrophobic effect.
- 2.2 A particular point mutation results in disruption of the  $\alpha$ -helical structure in a segment of the mutant protein. The most likely change in the primary structure of the mutant protein is:
- glutamate to aspartate.
  - lysine to arginine.
  - methionine to proline.
  - valine to alanine.
- 2.3 In comparing the  $\alpha$ -helix to the  $\beta$ -sheet, which statement is correct only for the  $\beta$ -sheet?
- Extensive hydrogen bonds between the carbonyl oxygen (C=O) and the amide hydrogen (N-H) of the peptide bond are formed.
  - It may be found in typical globular proteins.
  - It is stabilized by interchain hydrogen bonds.
  - It is an example of secondary structure.
  - It may be found in supersecondary structures.
- 2.4 An 80-year-old man presented with impairment of higher intellectual function and alterations in mood and behavior. His family reported progressive disorientation and memory loss over the last 6 months. There is no family history of dementia. The patient was tentatively diagnosed with Alzheimer disease. Which one of the following best describes Alzheimer disease?
- It is associated with  $\beta$ -amyloid, an abnormal protein with an altered amino acid sequence.
  - It results from accumulation of denatured proteins that have random conformations.
  - It is associated with the accumulation of amyloid precursor protein.
  - It is associated with the deposition of neurotoxic amyloid  $\beta$  peptide aggregates.
  - It is an environmentally produced disease not influenced by the genetics of the individual.
  - It is caused by the infectious  $\beta$ -sheet form of a host-cell protein.

Correct answer = E. The hydrophobic effect, or the tendency of nonpolar entities to associate in a polar environment, is the driving force of protein folding. Quaternary structure requires more than one polypeptide, and, when present, it is stabilized primarily by noncovalent bonds. The peptide bond is almost always trans. The two cysteine residues participating in disulfide bond formation may be a great distance apart in the amino acid sequence of a polypeptide (or on two separate polypeptides) but are brought into close proximity by the three-dimensional folding of the polypeptide. Denaturation may be reversible or irreversible.

Correct answer = C. Proline, because of its secondary amino group, is incompatible with an  $\alpha$ -helix. Glutamate, aspartate, lysine, and arginine are charged amino acids, and valine is a branched amino acid. Charged and branched (bulky) amino acids may disrupt an  $\alpha$ -helix.

Correct answer = C. The  $\beta$ -sheet is stabilized by interchain hydrogen bonds formed between separate polypeptide chains and by intrachain hydrogen bonds formed between regions of a single polypeptide. The  $\alpha$ -helix, however, is stabilized only by intrachain hydrogen bonds. Statements A, B, D, and E are true for both of these secondary structural elements.

Correct answer = D. Alzheimer disease is associated with long, fibrillar protein assemblies consisting of  $\beta$ -pleated sheets found in the brain and elsewhere. The disease is associated with abnormal processing of a normal protein. The accumulated altered protein occurs in a  $\beta$ -pleated sheet configuration that is neurotoxic. The amyloid  $\beta$  that is deposited in the brain in Alzheimer disease is derived by proteolytic cleavages from the larger amyloid precursor protein, a single transmembrane protein expressed on the cell surface in the brain and other tissues. Most cases of Alzheimer disease are sporadic, although at least 5% of cases are familial. Prion diseases, such as Creutzfeldt-Jakob, are caused by the infectious  $\beta$ -sheet form (PrP<sup>Sc</sup>) of a host-cell protein (PrP<sup>C</sup>).