Chapter 43
Alzheimer's Disease
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Questions

1. What are the 2 main neuropathological hallmarks of Alzheimer’s disease? Compare and contrast their anatomical location and protein composition.

2. Describe the major types of genetic mutations that are associated with Alzheimer’s disease.

3. Why is the incidence of Alzheimer’s disease increasing?

4. What is the “Amyloid Hypothesis” of Alzheimer’s disease?

5. Review 3 proposed mechanisms of action for how anti-b-amyloid antibodies might remove amyloid deposits.

6. What is the difference between active and passive vaccination?

7. List 3 barriers to the use of active vaccination clinically.

8. List 2 advantages of passive immunotherapy over active immunotherapy?

9. List 2 disadvantages of passive immunotherapy over active immunotherapy?

10. Which of the following is a risk factor of Alzheimer’s disease?
    a. head trauma
    b. cancer
    c. education
    d. schizophrenia
    e. all of the above

11. Which of the following is NOT a proposed mechanism to explain the anti-Ab action of active immunization?
    a. catalytic dissolution of amyloid plaques
    b. microglial activation and amyloid degradation
    c. clearance of amyloid through a peripheral sink
    d. suppression of APP processing
    e. all of the above

12. Amyloid associated with cerebral blood vessels is called:
    a. argyrophilic Alzheimer vasculature
    b. congophilic amyloid angiopathy
    c. senile plaques
    d. neurofibrillary tangles
    e. all of the above
Answers

1. **What are the 2 main neuropathological hallmarks of Alzheimer’s disease? Compare and contrast their anatomical location and protein composition.**
   The two main neuropathological hallmarks of Alzheimer’s disease are amyloid plaques and neurofibrillary tangles. Amyloid plaques are extracellular, and are composed of the β-amyloid peptide, while neurofibrillary tangles are intracellular in neurons, and are composed of abnormally phosphorylated tau protein.

2. **Describe the major types of genetic mutations that are associated with Alzheimer’s disease.**
   Mutations in the amyloid precursor protein, presenilin-1 or presenilin-2 can be inherited in some families. These genes are dominant, so inheritance of one gene copy causes the symptoms of Alzheimer’s disease. The gene apolipoprotein-E has been identified as a risk factor. Inheritance of the apolipoprotein-E4 allele is associated with an increased probability of developing Alzheimer’s disease.

3. **Why is the incidence of Alzheimer’s disease increasing?**
   The risk of developing Alzheimer’s disease increases with aging, and a larger percentage of the population is surviving to these ages of increased risk.

4. **What is the “Amyloid Hypothesis” of Alzheimer’s disease?**
   The “Amyloid Hypothesis” posits that the symptoms of Alzheimer’s disease result from the accumulation of extracellular amyloid in the brain of affected individuals.

5. **Review 3 proposed mechanisms of action for how anti-β-amyloid antibodies might remove amyloid deposits.**
   The 3 proposed mechanisms include (1) catalytic dissociation of amyloid fibrils by the antibodies directly, (2) activation of brain microglial cells causing phagocytosis of β-amyloid and (3) efflux of β-amyloid from the brain to the circulation as antibodies in the circulation bind β-amyloid, which reduces free β-amyloid concentrations in the blood and causes a change in the equilibrium between brain and blood β-amyloid concentrations.

6. **What is the difference between active and passive vaccination?**
   In active vaccination, a protein is injected together with an adjuvant (a molecule that enhances immunity), leading to the activation of the host immune system and the production of antibodies against the injected protein. In passive vaccination, the antibodies are injected directly.

7. **List 3 barriers to the use of active vaccination clinically.**
   (1) The production of antibodies is variable, resulting in different numbers and types of antibodies in different individuals. (2) There may be side effects due to activation of undesired components of the immune system. (3) Once the protein is injected into the host, the immune response cannot be stopped if adverse events ensue.

8. **List 2 advantages of passive immunotherapy over active immunotherapy?**
   (1) Because a therapeutic agent is administered directly in passive vaccination, its pharmacokinetics can be measured, controlled and standardized. (2) If adverse events ensue, injections of the therapeutic antibody may be stopped. Neither is true of active vaccination.

9. **List 2 disadvantages of passive immunotherapy over active immunotherapy?**
   (1) Production and storage of the therapeutic antibody for passive immuno-therapy is more complicated and expensive than active vaccination. (2) Administration of passive immunotherapy must be repeated over long durations as symptoms continue. In contrast, active vaccination is administered once, or in a short series of boosters.

10. a

11. d
12. b