

# Concurrent Neocortical Borreliosis and Alzheimer's Disease

## Demonstration of a Spirochetal Cyst Form

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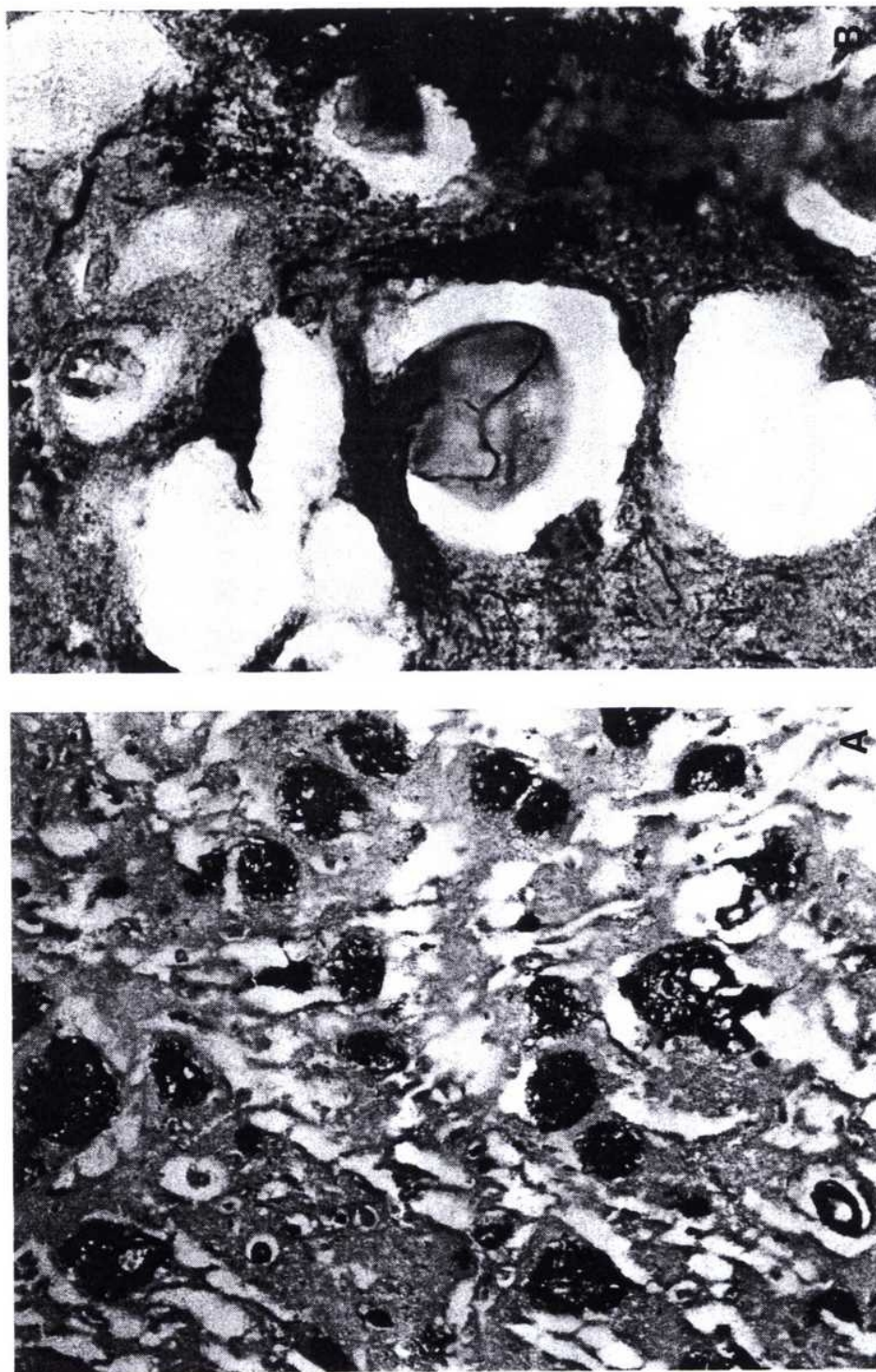
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A 71-year-old man died in Arizona 3 years after the onset of progressive dementia. A diagnosis of probable Alzheimer's disease was based on clinical criteria. The brain was removed at autopsy, frozen (unfixed), and transported to the Department of Pathology, University of California, San Diego, School of Medicine where it was stored at  $-70^{\circ}\text{C}$  for further study. The author received the frozen brain and utilized methods previously described<sup>1</sup> for *in vitro* culture, cytologic, immunohistochemical, and silver impregnation studies. Argyrophilic plaques and neurofibrillary tangles were found in the frontal lobe and hippocampal formation in sufficient number to establish the neuropathologic diagnosis of Alzheimer's disease (FIG. 1A). Spirochetes were visualized in imprint preparations of freshly thawed frontal lobe cortex with monoclonal antibody H5332, which specifically binds to the outer surface membrane of *Borrelia burgdorferi* (FIG. 2). *Borrelia* spirochetes were recovered from cultures of freshly thawed cerebral cortex and hippocampus in Barbour-Stoenner-Kelly medium. An unexpected observation was the identification of cystic forms of the *Borrelia* spirochete in dark-field preparations of cultured hippocampus, and in imprints of hippocampus using the monoclonal antibody H9724, which binds to class-specific axial filament proteins of *Borrelia* spirochetes. Oil immersion examination of sections from the hippocampus impregnated with silver disclosed a rare cystic structure (FIG. 1B). Previous workers have identified spirochetal cyst forms in cultures of nonpathogenic treponemal spirochetes and have suggested that spirochetes have a complex life cycle.<sup>2-5</sup> Dark-field examination of aged cultures of the B31 reference strain of *Borrelia burgdorferi* disclosed cystic structures similar to the cysts found in the autopsy brain culture.

The following hypothesis is offered based on these observations. *Borrelia* spirochetes have a complex life cycle which includes corkscrew-shaped forms, uncoiled filamentous forms, L-forms lacking a cell wall, cystic and ameboid forms, and granular forms. These forms may exist as either extracellular or intracellular pathogens. The cystic form of *Borrelia* may explain the Pick body, which is found in Pick's disease, and the granular form of *Borrelia* may explain granulovacuolar degeneration of nerve cells in the hippocampal formation in Alzheimer's disease. A cystic form of the *Borrelia* spirochete would explain the ability of the microbe to persist in the host during a prolonged period of asymptomatic clinical latency, which spans the period between primary infection and the expression of tertiary manifestations of neuroborreliosis.

### REFERENCES

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**FIGURE 1.** Autopsy hippocampus, ammoniacal silver stain. (A) Argyrophilic plaques; magnification: 100x. (B) Cyst form near plaque; magnification: 500x.



**FIGURE 2.** *Borrelia* spirochete in imprint of unfixed frontal lobe of brain, revealed using murine monoclonal antibody H5332 for outer surface membrane of *Borrelia burgdorferi*. Magnification: 1000 $\times$ .

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