

Preface

Chronic Inflammation and Amyloidogenesis in Alzheimer's Disease: The Emerging Role of Infection

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The realization that pathogens can produce slowly progressive chronic diseases has resulted in new concepts of infectious diseases. A number of chronic diseases are caused by one or more infectious agents: e.g., stomach ulcer is caused by *Helicobacter pylori*; chronic lung disease in newborns and chronic asthma in adults are both caused by Mycoplasmas; and, *Chlamydia pneumoniae* and some other pathogens have been associated with atherosclerosis.

It has been known from a century that dementia and amyloidosis can be caused by chronic bacterial infection, namely by *Treponema pallidum* in the atrophic form of general paresis in syphilis. Alzheimer's disease (AD), the most frequent cause of dementia, is a form of amyloidosis. The pathological mechanisms driving the accumulation of amyloid remain unclear. Pathogens (e.g., bacteria, viruses) are powerful stimulators of inflammation and were suggested to be one of the contributors in generating and sustaining chronic inflammation and amyloid deposition in AD. The concept is not new as it was discussed by Alzheimer and his colleagues a century ago. The fact that pathogens may suppress, subvert or evade host defenses and establish chronic or latent infection has received little attention in the past. During infection, active oxygen and nitro-

gen species generated by inflammatory cells may cause DNA damage, induce apoptosis, and modulate enzyme activities and gene expression. Depending upon the biology of the pathogen and the host defense mechanisms the organism can persist in the infected tissues, resulting in chronic inflammation. Pathogens may also elicit an autoimmune response without persistence of the initiating agent. The outcome of infection is as much determined by the genetic predisposition of the patient as by the virulence and biology of the infecting agent. Environmental factors and nutrition are critical determinants of disease expression as well.

The goal of this special issue is to bring together a few of those scientists who have contributed significantly to this emerging field of research in order to guide new researchers toward highly productive investigations. Highest priority should be given for such research in the future. It may have major implications for public health, treatment, and prevention as adequate anti-bacterial and anti-viral drugs are available. Treatment of a bacterial infection and associated viral infection may result in regression and, if started early, prevention of disease. The impact on reducing health-care costs would be substantial.