Microorganisms resident in our bodies participate in a variety of regulatory and pathogenic processes.Dysbiosis may promote immunoregulatory dysfunction due to inadequate education of the immune system, chronic inflammation, and epithelial barrier permeability.We postulate that each of these lifestyle transitions engendered progressive depletion of microbial diversity and enhancement of virulence, thereby enhancing AD risk pathways.We propose that microbiota of the gut, oral cavity, nasal cavity, and brain may modulate AD pathogenesis, and that changes in the microbial composition of these body regions across history suggest escalation of AD risk.Furthermore, the composition of symbiotic microbes has changed dramatically across human history alongside the rise of agriculturalism, industrialization, and globalization.It is likely that the human life span extended into the eighth decade tens of thousands of years ago, yet little is known about premodern geriatric epidemiology.Subsequently, proinflammatory agents--and occasionally microbes--may infiltrate the brain and promote AD .pathogenic processes.APOE genotypes appear to moderate the effect of dysbiosis on AD risk