

Brain tissue affected by Alzheimer's disease prepared for microscope examination.

the aggregation of amyloid interferes with neuronal signalling and causes dementia. Since they formulated their amyloid-cascade hypothesis, this has been the dominant view on the cause of AD.

The need to understand the mechanisms of the disease, and find targets for preventing it, is becoming urgent. With the greying of society, it is predicted that some 66 million people worldwide will have dementia in 2030. Funded by governments and the pharmaceutical industry, studies are being undertaken that are unprecedented in terms of sample size, follow-up and comprehensiveness. By tracking genetics, brain structure and cerebrospinal fluid, almost all the studies aim to localize the pathways and mechanisms proposed by the amyloid-cascade hypothesis. Most assume that this research roller coaster will reveal what causes AD. But will it?

Lock invites readers to look at alternatives to our current path. She delivers key concepts in epidemiology, neuroscience and genetics in a way that is both scholarly and free of unnecessary technical details. Lock's bird's-eye view and mix of diverging sources of information is refreshing. For example, she writes of the astonishing reluctance of individuals screened for biomarkers to change their convictions about their risk of developing AD. Just pages later, she recounts the very similar reluctance of scientists to change their convictions about the mechanism by which the condition develops — even when faced with findings that contradict the amyloid-cascade hypothesis.

Lock calls for a paradigm shift. She hopes that careful investigation of lifestyle and environmental exposure, and their effects on gene expression, will reveal opportunities for intervention. But if we find them, will we be able to implement them? Our ability to change unhealthy behaviours lags far behind our recognition of them as unhealthy, and we have only begun to touch on ways to help people take pleasure in healthy lifestyles. Moreover, restrictive measures on the marketing of temptations may become a major issue for industry and economies. Lock invites us to face such challenges and take responsibility for implementing preventive measures worldwide, irrespective of national and personal incomes. For its wide scope and balanced critical evaluation, *The Alzheimer Conundrum* is an inspiring read for everyone working in the field. ■

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ANTHROPOLOGY OF MEDICINE

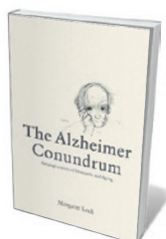
Where we are now with Alzheimer's

Eus Van Someren welcomes a call to critically evaluate progress in research on this form of dementia.

In the Mini Mental State Examination, a questionnaire used worldwide to evaluate the severity of dementia, an early question is “Where are we now?” That is also the primary question of Margaret Lock's *The Alzheimer Conundrum*. This anthropological study peers back at a century of grappling with Alzheimer's disease (AD) and surveys the quest to understand its mechanisms and the scientific enterprise needed to unravel them.

Lock dares to pose big questions, and is well prepared to do so. For ten years, she intensively studied epidemiological and neurobiological research on AD, went to meetings, and interviewed experts, people at risk and carers. The result reads like a travel diary, with a balance between engagement and objectivity. Lock highlights how scientific progress can be both accelerated and impeded by paradigms, the entangled interests of the pharmaceutical industry, the media and personal beliefs. She covers the history of AD, prominent views on its cause, risk factors such as mild cognitive impairment, and biomarkers.

Along the way, Lock dissects three fundamental tensions. The first is between the ‘localization’ approach that attributes dementia to specific neuropathological changes, and the ‘entanglement’ approach that includes complex interactions between mind, environment, ageing and life events. The second is between the view that AD is intrinsic to ageing, and the understanding that it is a distinct pathology. The third is between deterministic genomics, and the view that adds epigenetics.



The Alzheimer Conundrum: Entanglements of Dementia and Aging
BY MARGARET LOCK
Princeton University Press: 2013.

The AD trail that Lock follows began in Germany more than a century ago. The discovery of the disease by neuropathologist Alois Alzheimer in 1906, and its naming by his colleague, the psychiatrist Emil Kraepelin, rested on a new technique for which neurologists Camillo Golgi and Santiago Ramón y Cajal received a Nobel prize. Their staining

techniques for brain tissue made the invisible visible and revealed the amyloid plaques and neurofibrillary tangles that have come to be regarded as key players in dementia.

After decades of dormancy, AD research reappeared on stage in 1966. Psychiatrist Martin Roth and his colleagues reintroduced Alzheimer's idea, describing autopsies of patients diagnosed with dementia that showed not arteriosclerosis — then the primary suspect — but numerous plaques and tangles. In 1992, neuroscientists John Hardy and Gerald Higgins proposed that



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