CHAPTER 20

Animal Research for Alzheimer Disease: Failures of Science and Ethics

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1 Introduction

This is a uniquely human disease, with impairments in abstract reasoning and judgment. We’ve cured mice engineered with this disease over 500 times. The mouse models don’t translate into humans. We know for a fact that mice don’t write books.

Howard Fillit, Chief Science Officer, Alzheimer’s Drug Discovery Foundation,
in Shakoor et al., 2017

Perhaps the most impactful and foreboding development in chronic diseases in recent decades has been the increasing prevalence and awareness of dementia. The various dementias, especially Alzheimer disease (AD), have derailed and ended the lives of tens of millions in America and worldwide. It is a truism that AD patients die twice. First the mind dies, and only later does the body. AD uniquely and unremittingly affects not only patients, but their families, caregivers, and communities. In recent years, AD may have displaced cancer as the most feared disease among Americans. As with other diseases that have no meaningful methods for prevention and treatment, research targeting AD has primarily focused on preclinical approaches, predominantly using animals. Nonetheless, decades of animal research have failed to translate into significant advances in the prevention or treatment of AD. In view of this failure, a different and human-relevant approach is critically needed.
This chapter addresses the epidemiology and current understanding of AD as a scientific and societal challenge, reviews the uses and results of animal research in basic science and drug development, and discusses risk factors and funding. Important follow-up topics, including current and in-development, human-relevant approaches for replacement of the failed animal research paradigm, deserve comparable treatment and hence are not addressed here. The reader is referred to the list of recommended readings at the end of the chapter for further discussion of these topics.

The ethics of continued use of the animal-based approach in AD is troublesome in at least two respects. First, regardless of where one stands on the ethical spectrum of animal use for medical research, certainly the inhumane and lethal use of animals for demonstrably faulty research is unethical. Second, the ethical responsibility to AD patients, their families, and the larger community demands reliable and useful results, which in turn demand a revised research approach, emphasizing human-relevant methods.

2 Epidemiology and Current Status

Dementia can be defined as a disorder of mental capabilities caused by brain disease or injury and marked by memory disorders, impaired thought and reasoning, diminished judgment, social withdrawal, and altered personality. Except for several reversible causes, dementia is a chronic and unremitting disease with a fatal outcome. AD is the most common form of dementia, accounting for 60%–80% of all dementia diagnoses in the United States (US) (Alzheimer’s Association, 2017). The next four most prevalent categories of dementia (vascular dementia, dementia with Lewy bodies, frontotemporal dementia, and mixed dementia) account for all but a small percentage of the other diagnoses. Vascular and mixed dementia overlap considerably with AD; nearly all cases of vascular dementia display characteristics of AD (Thal, Grinberg and Attems, 2012), and prevalence figures do not include the AD precursor, mild cognitive impairment (MCI), making the percentage of dementia and incipient dementia attributable to AD even higher (Lopez et al., 2012; Mitchell and Shiri-Feshki, 2009; Roberts et al., 2014a; Ward et al., 2013). AD prevalence increases with age and varies based on diagnostic criteria and death records. It can only be definitively diagnosed by postmortem examination of the brain, though recent advances in neuroimaging and cerebrospinal fluid analysis offer strong clinical evidence and presumptive diagnosis. AD is almost certainly underdiagnosed and underreported, both among persons who die of AD and