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Fighting Alzheimer's disease: is there a chance to conquer?

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Being a complete pessimist [1], I always try to avoid overly enthusiastic responses to scientific articles that report the emergence of new promising means of preventing or treating a particular disease. This also applies to research on Alzheimer's disease (AD). Therefore, to the question posed in the title, in my opinion, the following answers are possible, among others: 1) the pathogenesis of AD is still unclear; 2) we do not yet know how to treat AD; 3) the first and second together; 4) AD is not a disease at all; 5) if AD is still a consequence of aging, then we must keep in mind that we also still know almost nothing about the process. In the late 1980s, at a symposium on brain aging in Moscow, D.R. Crapper McLachlan told us about his concept [2] of the occurrence of AD, according to which its pathogenesis is based on aluminum that enters the body with food and drinking water, in particular, when using aluminum utensils. However, in subsequent years, there was no confirmation of this hypothesis. Moreover, in many investigations the inconsistency of this concept was proved. At the same time, numerous works were published in which the leading role in this process of free radicals was postulated (for example, [3]), which were proposed to be combated with the help of antioxidants. However, this idea was later found to be wrong. The Alzheimer's Society website has a dedicated page on the possible role of antioxidants in the prevention and treatment of AD.

It notes that to date there are no reliable clinical data on the advisability of using such drugs against AD. And here is the most important thing: on the same page it is said that data from laboratory studies on model animals, on the contrary, indicate that antioxidants help with AD. However, this is not real AD, but a kind of "surrogate" that is similar to it in some signs and symptoms. After analyzing a fairly large number of articles on this issue, I got the impression that almost all the achievements in the search for means of preventing or treating AD are based on work with model animals. Most often, these are mice with genetic abnormalities in the functioning of the nervous system, which in their manifestations are similar to the symptoms of AD in humans. Unfortunately, experiments on such model animals very often lead researchers to incorrect conclusions. This is well illustrated by the story that I called the "bexarotene saga." Bexarotene (Targretin) is an FDA-approved anti-cancer drug, so there are no problems with its research even in humans. However, attempts to use this drug against AD began precisely with experiments on model animals. In particular, in the sensational work of 2012 [4] published in the prestigious journal Science, the authors found that bexarotene removes beta-amyloid from the brain of mice with model AD, and also restores their cognitive capabilities, which is reflected in the restoration of the lost ability to build nests from pieces of paper. Unfortunately, a large number of papers later appeared (for example, [5]), which refuted these results. The same applies to clinical studies of the effectiveness of bexarotene in the

treatment of AD. In my opinion, the correct choice of control objects [6] when conducting such experiments is paramount, and the wrong strategy in this matter almost always leads to incorrect conclusions. At the same time, almost all modern work aimed at finding means to combat AD is carried out on model animals, since this requires much less money and time than clinical experiments. And no one has canceled the ethical requirements for research in humans – as a rule, we cannot administer drugs to healthy people and monitor whether they develop AD. Apparently, this is precisely why we have not made any progress so far in surveys of the prevention and treatment of this scourge of modern humanity, the demographic aging of which (an increase in the proportion of older people in the population) has led to a sharp increase in the number of individuals with AD in almost all developed countries. It is also possible (see the beginning of this text) that, however paradoxical it may sound, AD is not a disease at all, but only a set of signs of non-specific senile brain degradation leading to senile dementia, on the study of which, in this case, efforts should be focused both by gerontologists and neuroscientists.

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