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New drugs show promise, and research finds value in vaccines, antivirals, exercise and probiotics.

LIFE SCIENCE

Scientists Are Finally Making Progress Against Alzheimer's

Buck up, baby boomers. Sixty may not be the new 40, but 80 could soon be the new 60. A trove of new Alzheimer's research suggests that medicines and lifestyle changes can not only slow but prevent, even reverse, the debilitating disease.

Alzheimer's is characterized by a buildup of amyloid plaque and tangles of tau proteins in the brain. They trigger inflammation, which in turn causes cognitive decline and neuron death. Scientists don't know exactly what causes this destructive cascade. The disease's complexity stymied the quest for treatments for decades, but no more. Scientists are learning quickly.

The only two approved treatments for Alzheimer's that can slow progression—developed by Eli Lilly and Biogen-Eisai—work by removing amyloid plaque. They reduce cognitive decline by 25% to 36% over 18 months compared with a placebo group in clinical trials. Those in the earliest stages of the diseases saw bigger benefits, and nearly half of those in the Lilly trial showed no progression after a year.

Some back-bench scientists who don't treat Alzheimer's patients dismiss such benefits as not meaningful. But the medications could mean more years when your mother recognizes you. Who wouldn't find that meaningful?

Recent follow-up studies have also shown that the benefits grow over time—doubling over three years for Eli Lilly's treatment and quadrupling over four years for Biogen- Eisai's. Drugmakers are studying whether eliminating amyloid can ward off Alzheimer's in preclinical patients—those without cognitive symptoms—as statins can prevent cardiovascular disease.

Lifestyle changes can augment the benefits. A recently published randomized trial found that a "treatment" of regular physical and cognitive exercise, nutritious diet and social engagement improved cognitive performance among previously sedentary older adults at risk of dementia. A smaller study earlier this summer found such lifestyle interventions improved metal acuity of early-stage Alzheimer's patients, as well as physiological measures of brain health. The treatment group in the latter study also showed an increase in beneficial bacteria in their guts.

Why is this notable? Studies have found that microbiomes of Alzheimer's patients differ from those of healthy seniors. For one, Alzheimer's patients have lower levels of *Akkermansia muciniphila,* a bacterial strain that produces the short-chain fatty acid propionate from dietary fiber.

Propionate helps regulate appetite as well as brain inflammation and amyloid buildup. In one study, propionate was found to reduce brain inflammation and amyloid in mice

with the rodent version of Alzheimer's disease. So perhaps a probiotic cocktail or more fiber in the diet could slow progression, much like antiamyloid treatments.

Another potential antidote: lithium salts. A study published last week in the journal Nature found that amyloid can trap lithium, resulting in a deficiency of the mineral. Lithium protects neurons. Mice given a lithium-deficient diet had more

amyloid, damaged neurons and impaired learning and memory. A low dose of lithium orotate reversed cognitive problems and restored memory.

How the microbiome and lithium affect Alzheimer's is the sort of basic scientific research that deserves more government attention and funding. Ditto the effects of viruses and vaccines. Take herpes viruses, which cause chickenpox, shingles and cold sores. Most seniors have been infected by at least one type of herpes virus. After an initial infection, the virus lies dormant in cells, including in the brain. Reactivation of the virus has been linked to increased amyloid buildup, brain inflammation and risk of dementia.

Vaccines and antivirals may be able to help prevent Alzheimer's. A quasirandomized control trial earlier this year found that people vaccinated for shingles were 20% less likely to develop dementia. Recent research has also found that head injuries increase amyloid and brain inflammation by reactivating herpes viruses. So perhaps administering herpes antivirals after concussions could help protect the brain.

Alzheimer's tends to run in families, and the APOE4 variant is the biggest genetic risk factor. Women with one copy, inherited from mom or dad, are at four times as much risk. Those with two, one from each parent, have 10 times the risk. Men with one variant show no increased risk, and those with two copies are at fourfold increased risk.

You can't change your genes, but an experimental cholesterol drug was recently found to reduce Alzheimer's hallmarks in APOE4 carriers in a late-stage trial. Perhaps that's because APOE4 can cause cholesterol to build up in the brain. All these studies underline the potential to stop Alzheimer's dead in its tracks— as long as the Food and Drug Administration doesn't get in the way.

The Health and Human Services Department on Saturday announced that Vinay Prasad was returning as the FDA head of biologics and gene therapies. Dr. Prasad stepped down late last month after a public backlash over his scuttling of a gene therapy for Duchenne muscular dystrophy. He's shown similar hostility to Alzheimer's treatments.

In a tweet last summer referencing Biogen-Eisai's antiamyloid treatment, he wrote that paying "someone to come to an Alzheimer's patients house and help with the dishes" would do more good than "funding these garbage drugs." Tell that to the poor souls afflicted by Alzheimer's and their families who have years more of quality life together.

By Allysia Finley