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Vaccine trial for Alzheimer's clears key hurdle

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A vaccine which revives a promising but long-abandoned path to thwart Alzheimer's disease has cleared a key safety hurdle in human trials, researchers say.

In a small-scale test, the formula was found to be safe and primed the body's frontline defences against protein deposits in the brain that are associated with the catastrophic disease.

Swedish doctors report the results in Wednesday's issue of the journal *Lancet Neurology*, saying that the way is now open for wider trials.

The prototype vaccine, called CAD106, is a new exploration of traditional vaccine engineering.

In this approach, the pathogen that causes a disease is used to teach the immune system to identify an intruder and attack it.

In Alzheimer's, one of the enemies is a toxic protein called amyloid beta peptide, which accumulates in plaques in the brain, although exactly how it works remains unclear.

A decade ago, doctors launched a first attempt at an amyloid beta vaccine, called AN1792.

But they were forced to abandon it at the second of the three-phase trial process after six percent of the volunteers fell ill with

meningoencephalitis, an inflammation of the brain.

The suspected reason was that AN1792 activated white blood cells called T cells that attacked the brain tissue.

The new vaccine uses a smaller fragment of the protein and combines it with a booster, called an adjuvant, intended to prevent T-cell activation.

After lengthy trials in the lab, a team led by Bengt Winblad of the Karolinska Institutet's Alzheimer's Disease Research Centre, tested the vaccine on 46 volunteers aged 50 to 80, diagnosed with mild to moderate Alzheimer's.

A "control" group of 12 patients received a harmless formula, called a placebo, as a comparison.

The group was studied over 52 weeks and given a follow-up examination two years later.

Eighty-two percent of the patients who received CAD106 developed antibodies, a sign that the immune defences had responded to the dangerous protein.

Overall, nine patients had episodes of ill health during the trial, but investigations showed these were unrelated to the drug, and none entailed meningoencephalitis.

The next step after this Phase 1 safety trial should be a larger test, possibly with modifications of the dose, to see if the vaccine works, says the study.

Around 26 million people around the world have Alzheimer's, which remains an incurable and progressive disease characterised by memory

loss and dementia.

The toll by 2050 is likely to be 115 million, according to figures cited in the journal.

More information: "Safety, tolerability, and antibody response of active Aβimmunotherapy with CAD106 in patients with Alzheimer's disease: randomised, double-blind, placebo-controlled, first-in-human study", Bengt Winblad, Niels Andreasen, Lennart Minthon, Annette Floesser, Georges Imbert, Thomas Dumortier, R Paul Maguire, Kaj Blennow, Joens Lundmark, Matthias Staufenbiel, Jean-Marc Orgogozo & Ana Graf, *Lancet Neurology*, online first 6 June 2012, doi:10.1016/S1474-4422(12)70140-0