Alzheimer's treatments: What's on the horizon?

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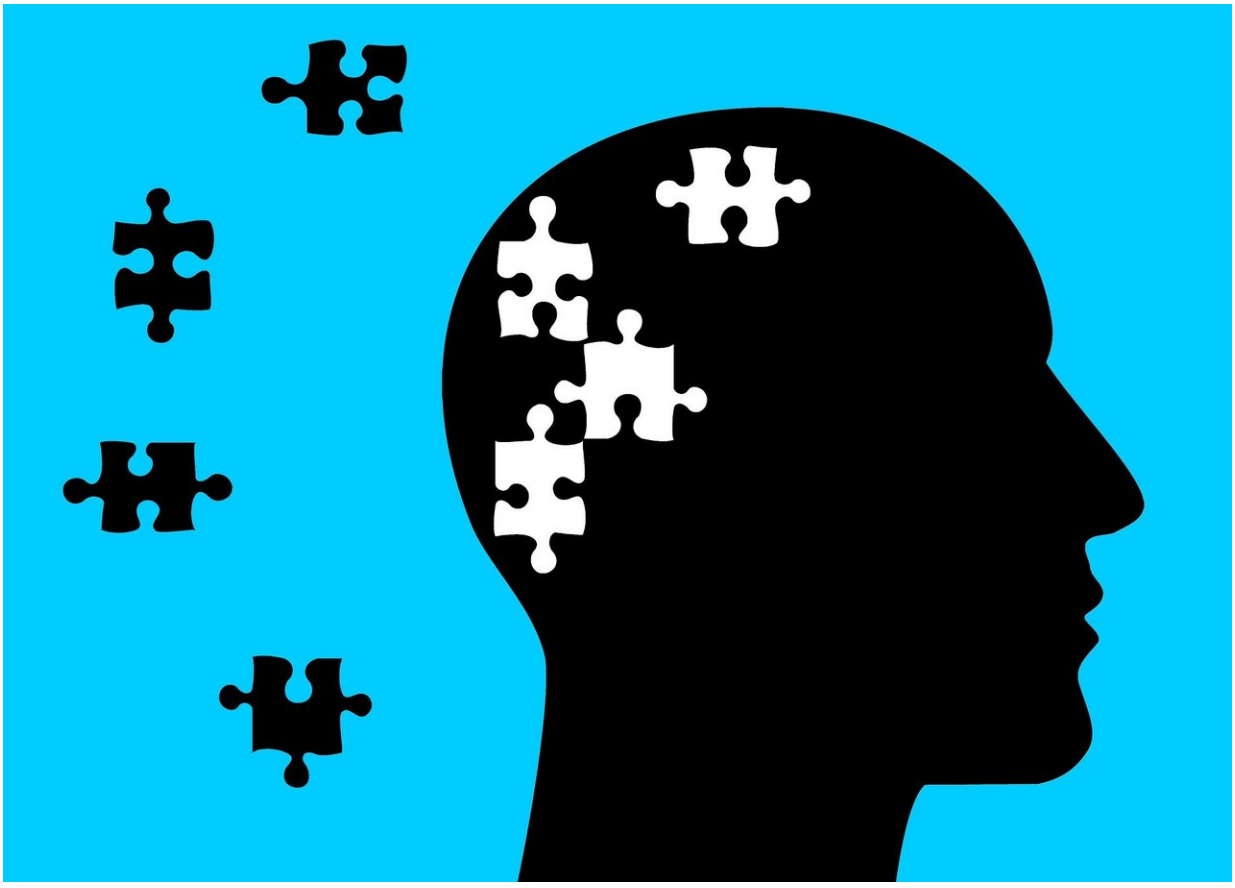

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Current Alzheimer's treatments temporarily improve symptoms of memory loss and problems with thinking and reasoning.

These Alzheimer's treatments boost performance of chemicals in the brain that carry information from one brain cell to another. However, these treatments don't stop the underlying decline and death of brain cells. As more cells die, Alzheimer's disease continues to progress.

Experts are cautiously hopeful about developing Alzheimer's treatments that can stop or significantly delay the progression of Alzheimer's. A growing understanding of how the disease disrupts the brain has led to potential Alzheimer's treatments that short-circuit basic disease processes.

Future Alzheimer's treatments may include a combination of medications, similar to how treatments for many cancers or HIV/AIDS include more than a single drug.

The following treatment options are among the strategies currently being studied.

Taking Aim At Plaques

Some of the new Alzheimer's treatments in development target microscopic clumps of the protein beta-amyloid (plaques). Plaques are a characteristic sign of Alzheimer's disease.

Strategies aimed at beta-amyloid include:

- Recruiting the immune system. Several drugs—known as monoclonal antibodies—may prevent beta-amyloid from clumping into plaques or remove beta-amyloid plaques that have formed and help the body clear the beta-amyloid from the brain. Monoclonal antibodies mimic the antibodies your body naturally produces as part of your immune system's response to foreign invaders or vaccines.

The monoclonal antibody solanezumab did not demonstrate any benefit for individuals with mild or moderate Alzheimer's disease. It's possible that solanezumab may be more effective when given earlier in the course of the disease. The drug seemed safe in recent studies, and solanezumab continues to be evaluated in the preclinical stage of the disease.

Aducanumab is another drug that has shown promise in preliminary studies. Study participants taking aducanumab had reduced amyloid plaque levels and a suggestion of possible delayed cognitive decline. More studies are underway for this treatment.

- Preventing destruction. Several years ago, researchers learned that beta-amyloid interacts with another protein called Fyn. When combined with beta-amyloid, Fyn is over-activated, which triggers a destruction of connections between nerve cells (synapses) in the brain. Studies are currently in progress for drugs that inhibit the Fyn protein. A drug initially developed as a possible cancer treatment—saracatinib—is now being tested in Alzheimer's disease. In mice, the drug turned off Fyn, which allowed synapses to start working again, and the animals experienced a reversal of some memory loss. Human trials for saracatinib as a possible Alzheimer's disease treatment are now underway.

- Production blockers. These therapies may reduce the amount of beta-amyloid formed in the brain. Research has shown that beta-amyloid is produced from a "parent protein" in two steps performed by different enzymes. Several experimental drugs aim to block the activity of these enzymes. They're known as beta- and gamma-secretase inhibitors. Recent studies showed that the beta-secretase inhibitor verubecestat did not slow down cognitive decline and was associated with several side effects in those with mild or moderate Alzheimer's.

Keeping Tau From Tangling

A vital brain cell transport system collapses when a protein called tau twists into microscopic fibers called tangles, which are another common brain abnormality of Alzheimer's. Researchers are looking at a way to prevent tau from forming tangles.

Tau aggregation inhibitors and tau vaccines are currently being studied in clinical trials.

Reducing Inflammation

Alzheimer's causes chronic, low-level brain cell inflammation. Researchers are studying ways to treat inflammatory processes at work in Alzheimer's disease. The drug sargramostim (Leukine) is currently in research. It's thought that the drug may stimulate the immune system to protect the brain from harmful proteins.

Researchers studied the diabetes drug pioglitazone (Actos) because it may lessen beta-amyloid and inflammation in the brain, but this trial was negative.

Researching insulin resistance

Researchers are studying the effects of insulin on the brain and brain cell function, and insulin changes in the brain that may be related to Alzheimer's. A trial testing an insulin nasal spray to determine whether it slows the progression of Alzheimer's was recently reported as negative.

Studying the heart-head connection

Growing evidence suggests that brain health is closely linked to heart and blood vessel health. The risk of developing Alzheimer's appears to increase as a result of many conditions that damage the heart or arteries.

These include high blood pressure, heart disease, stroke, diabetes and high cholesterol.

A number of studies are exploring how best to build on this connection. Strategies under investigation include:

- Current drugs for heart disease risk factors. Researchers are investigating whether drugs such as blood pressure medications now used to treat vascular disease may also help people with Alzheimer's or reduce the risk of developing the disease.

- Drugs aimed at new targets. Additional projects are looking more closely at how the connection between heart disease and Alzheimer's works at the molecular level to find new drug targets.

- Lifestyle choices. Research suggests that lifestyle choices with known heart benefits, such as exercising on most days and eating a heart-healthy diet, may help prevent Alzheimer's disease or delay its onset.

Hormones

In one study, taking estrogen-based hormone therapy for at least a year during perimenopause or early menopause appeared to protect thinking and memory in women with a higher risk of Alzheimer's disease.

But further research has been conflicting, with some studies indicating that estrogen didn't offer any benefit. More research and a better understanding of the relationship between estrogen and cognitive function are needed before any recommendations can be made.

Speeding Treatment Development

Developing new medications is a slow and painstaking process. The pace can be especially frustrating for people with Alzheimer's and their families who are waiting for new treatment options.

To help accelerate discovery, the Coalition Against Major Diseases (CAMD), an alliance of pharmaceutical companies, nonprofit foundations and government advisers, has forged a first-of-its-kind partnership to share data from Alzheimer's clinical trials.

The CAMD has also collaborated with the Clinical Data Interchange Standards Consortium (CDISC) to create data standards. Researchers anticipate that these data standards and the sharing of data from more than 6,500 study participants will speed development of more-effective therapies.