

New Ideas in Dementia

We don't have all the answers when it comes to dementia. However a lot of interesting and useful data does exist which gives clues to both prevention and treatment. The brain is peculiarly susceptible to inflammation and most of the risk factors are linked with brain inflammation. These include the following:

1) **Insulin resistance** (sometimes called metabolic syndrome). This is also caused by a diet high in sugars and refined carbohydrates (white flour, baked potatoes, white rice, baked products). Sugar reacts with proteins in the brain (this is called glycation) which denatures them. In particular it oxidises and denatures LDL which transports cholesterol, a key brain food, to the neurons. Sugar also reduced levels of neurotransmitters. We can measure glycation by a test called HbA1C (usually use to measure diabetic control). Elevated levels have been associated with brain shrinkage (atrophy) and mental decline. This is why having diabetes doubles the risk of dementia. But sugars are brain-damaging for all of us.

2) **Exercise.** There's a lot of data on exercise and mental function in both people and animals. Basically exercise makes you cleverer. The 10% who do least exercise have two to three times the risk of dementia compared with the 10% that do the most. Steady exercise, enough to make you sweat is better than stretching. Exercise reduces inflammation.

3) Exposure to toxic substance, especially heavy metals.

Important sources of toxicity are heavy metals including mercury, aluminium and copper –all three have been positively linked with Alzheimer's. Aluminium can be found leaching from aluminium pans, antiperspirants and some antacid tablets (though not usually in antacid solutions). The risk of Alzheimer's increases as the aluminium concentration in drinking water increases. Experiments have shown an aluminium coffee pot can leach 1600mcg of aluminium into a litre of water. Mercury can come from amalgam fillings and from eating certain predatory fish like tuna, halibut and swordfish which can be high in mercury. Some shellfish can have high amounts. Pesticides are also a known brain toxin.

The brain protects itself against heavy metals with an antioxidant called glutathione. However this antioxidant is regenerated by a process called methylation and this depends on B vitamins and our genes (especially one called MTHFR). Keeping a good supply of glutathione on board and making sure methylation is adequate is central to protecting against Alzheimer's disease. Nutrients that assist in this process are B vitamins, Alpha Lipoic acid, N Acetyl Cysteine, zinc and selenium.

4) Exposure to drugs.

Some commonly used drugs are associated with dementia. These include **PPI drugs** used for reflux (such as omeprazole and lansoprazole). A study of 74,000 people above the age of 75 years on these drugs found a 44% increased incidence of dementia (these drugs lower levels of B12, B6 magnesium and other nutrients).

Another study of 40,770 people found that **anticholinergic drugs** increased the risk of dementia. The drugs with the largest effect were anticholinergic drugs used for Parkinson's disease (45% increase in dementia). However these are not often used today. Next were bladder drugs such as oxybutynin and tolterodine (23% increase) and lastly antidepressants (especially amitriptyline, desulepin and paroxetine (13% increase).

Several studies have shown benzodiazepines such as diazepam and sleeping tablets increase the risk of dementia, but mainly with heavy use. However not all studies have shown this effect and sleep loss itself is a risk factor for dementia.

Cholesterol drugs (see below).

5) Exposure to Artificial Sweeteners

Artificial sweeteners are found in diet drinks, juices and processed foods. A study that followed 2000 adults over the age of 60 years for 10 years was published in 2017 in Stroke. **It found that artificial sweeteners increased the risk of dementia and stroke by nearly 300%.** Aspartame is a particular concern as it is known to be neurotoxic being converted into formaldehyde in the body.

6) **Low cholesterol.** The brain needs a lot of cholesterol and LDL (sometimes known as bad cholesterol) is crucial to deliver cholesterol to the neurones. A report from Boston University in 2005 found a whole range of brain functions (verbal fluency,

concentration, attention, abstract reasoning) correlated with cholesterol levels. **They found that the higher the cholesterol the greater the better the brain worked.** Some drugs that lower cholesterol, such as statins, are known to impair memory. Sadly they are sometimes prescribed in vascular dementia, despite a review in 2009 of two major studies of over 26,000 individuals at risk of Alzheimer's. The study found statins give no protection against dementia and there were numerous case reports of memory being adversely affected

- 7) **ApoE4 gene** – at the moment this cannot be tested on the NHS but it increases the risk of dementia between 30-50% depending whether you have one or two copies of the gene. The gene encodes for transporting cholesterol and other fats through the body. (Most of us - 80% - have the Apo E3 gene). However even those with this gene can lower their risk. By having a diet lower in sugars and refined carbohydrates, avoiding smoking, having a plant-based diet, taking exercise and eating plenty of anti-oxidants (from fruit, vegetable, herbs and spices).
- 8) **Elevated homocysteine.** (see below)
- 9) **High Cortisol** (from chronic stress)
- 10) **Sleep deprivation**
- 11) **Lack of mental stimulation.** (Note: mental stimulation is not as effective as exercise in protecting the brain.)

What will Help:

Over 200 drugs have been tested and failed to produce benefits in the last decade. Only 4 are licensed and none of these prevent the decline typical of Alzheimer's disease (in fact a recent study found they could accelerate decline). However the first trial ever to show a reversal of cognitive decline in Alzheimer's disease was published in Aging in 2014. Dr Dale Bresden's trial showed a reversal in 9 out of 10 patients. A further trial of 100 patients found 90% had reversal of their mental decline. Since then he has treated over 1000 patients successfully. However this involves treating 36 different risk factors (called the Breseden protocol). He also discovered there are 3 different types of Alzheimer's and the best way to prevent these subtypes will be somewhat different.

This is a complex treatment matched to each individual and it means it is unlikely that a single drug will be found to cure Alzheimer's in

the future. The disease is too complex. Unfortunately this protocol is not available on the NHS. (See separate Alzheimer's leaflet on this protocol).

The Right Diet

One of the factors treated in the Breseden protocol is diet. It involves a ketogenic diet (low in sugar and carbohydrates but high in fat & protein). It involves stopping eating for at least 12 hours (between evening meal and breakfast). The enzyme that breaks down amyloid and other harmful brain toxins also breaks down insulin. This means if the body has too much sugar to deal and hence too much insulin then the enzyme gets used up and can't help with breaking down toxins in the brain.

More on Ketosis

When we stop carbohydrates we develop ketosis. When we fast for over 12 hours (for instance if we leave over 12 hours between the last food in the evening and the first in the morning) we will have burned up all the carbohydrates in our body and will be "running on fats". In other words we will be burning ketones, especially one called betahydroxybutyrate.

A study from the University of Kansas looked at 14 patients with mild Alzheimer's who were put on a ketogenic diet plus medium chain triglycerides (MCT) which helps trigger ketosis. All 9 kept on the diet improved. However they deteriorated after stopping the diet for 1 month confirming it was the ketosis that was causing the improvement. In a further study of 152 patients with mild to moderate Alzheimer's, those given betahydroxybutyrate, which produces mild ketosis, improved.

The bottom line here is that leaving a big gap between the last food in the day and the first in the morning protects against Alzheimer's. Periodic fasting is another good strategy as it also produces ketosis.

Avoid Anything that Harms the Brain

This includes artificial sweeteners, suspect drugs (such as PPIs, anticholinergics and statins) and heavy metals.

B Vitamins

A groundbreaking study from Oxford University published in Proceeding of the National Academy of Sciences found that in patient with cognitive decline, taking three B vitamins slowed brain shrinkage by 90% and the area where brain shrinkage was reduced most was the area normally affected by Alzheimer's disease. Their mental function also improved. These B vitamins were vitamin B12 500mcg daily, folic acid 800mcg daily and Vitamin B6 20mg daily.

Researchers at the University of California gave mice, with the rodent form of Alzheimer's disease, large amount of Vitamin B3 – the human equivalent of 2000-3000mg of niacin daily. The authors said that mentally they were cured. Of course animal studies don't always translate into human benefits but it was an fascinating piece of research.

We already know that niacinamide (vitamin B3) prevents demyelination of nerve cells in the animal equivalent of multiple sclerosis. In a study of over 6000 Chicago residents over 65, those with the lowest niacin intake (another form of B3) had the greatest risk of Alzheimer's disease. The group with the highest intake had 70% less Alzheimer's. We also know that vitamin B3 along with Vitamin B12 and folic acid will reduce homocysteine, a substance which damages nerves (and the heart). A review of 33 studies found there was a consistent association between dementia and cognitive decline on the one hand and homocysteine or B vitamins (inverse relationship) on the other.

Vitamin B3 can be taken as niacinamide (high doses can cause nausea), niacin (can cause flushing at high doses) or as inositol hexanicotinate (which causes no flushing).

The Breseden protocol involves testing homocysteine but this is not always available on the NHS. Homocysteine goes up as Vitamins B12 and folic acid goes down. Dutch researchers gave adults over 50, who had raised homocysteine, folic acid. Those given this vitamin had highly significant improvement in memory and information processing.

In the USA people with mild to moderate Alzheimer's were given folic acid (5mg daily), vitamin B12 (1mg daily) and vitamin B6 25mg daily for 18 months. Those with milder Alzheimer's had virtually no decline over 15 months –an astonishing result. Those using placebo all declined.

In Hong Kong volunteers with mild to moderate Alzheimer's dementia and vascular dementia were given folic acid (5mg daily) and Vitamin B12 (1mg daily) for 2 years. The group given supplements had significantly less mental decline than those on placebo as measured on a dementia rating scale.

There is a consistent pattern here. B vitamins have an important role to play in preventing dementia.

Other Nutrients

Lithium is an essential nutrient and higher levels in the water are associated with reduced mortality. There has been a lot of interest in its role in dementia. Lithium causes the formation of new brain cells and protects the brain against toxins. Three different studies, including one published in the Lancet, showed it increased grey matter. A ten year Danish study on those at high risk of dementia given lithium found they had no more dementia than the general population whereas a similar high-risk group not given lithium developed significantly more dementia. The normal dose is lithium orotate 5-20mg daily.

There are also studies on other vitamins. A study in Utah of nearly 5000 residents over 65 found that those given both Vitamin C and Vitamin E had a 64% reduction in Alzheimer's disease. This was most marked in those taking at least 1000mg of both. There was no benefit for those taking Vitamin E alone.

Dennis Crouse has described how he reversed his mother's Alzheimer's disease by removing sources of aluminium and using silica water.

Aluminium is removed from the body by a naturally occurring substance called **orthosilicic acid (OSA)** sometimes called silica water. The major source of this is vegetables and certain types of water. Silica supplement have poor bioavailability so don't resolve the problem.

Many vegetables and herbs contain OSA and to a lesser extent they can be found in fruits. Typically the skin and husks contain more OSA. Good sources are oats, wholegrains, beans and basil. Beer often contains OSA but beware as much beer comes in aluminium cans.

Water is an important source of OSA. Some waters are naturally high in OSA: these include Fiji and Volvic water. However bottled water is bulky and environmentally unfriendly. Another solution is to make your

own which can be done cheaply (see Dennis Crouse on you tube: Silica Water: How to make it at home).

Saunas, including infrared saunas can also help remove aluminium and other heavy metals.

Giving the supplement **N Acetyl Cysteine** for 6 months was found to have a beneficial effect in Alzheimer's disease. This increases the level of glutathione, an important nutrient in detoxification.

Researchers in Chicago followed 815 people over 65 and found a low intake of fish or low intake of Omega 3 fatty acids was strongly linked with the risk of Alzheimer's. The higher the intake of **docosahexaenoic acid (DHA)**, an omega 3 fat found in oily fish, the lower the risk of Alzheimer's. There was no benefit at doses below 100mg daily.

In the Framlingham study 899 men and women, free of dementia, were followed for nine years and those with the highest levels of DHA had a 50% lower risk of developing dementia. In another study, people with cognitive decline given DHA and EPA supplements (both Omega 3 fats) had improvement in recall and brain processing. Omega 3 fats also lower levels of a toxic compound called Tau which builds up in Alzheimer's. (Note fish contain beneficial Omega 3 fats but can also contain harmful mercury so the type of fish can be important). Omega 3 fats are highest in herrings, sardines and mackerel, pilchards and anchovies and wild, but not farmed, salmon (farmed salmon have lower levels of Omega 3 fats and **very high toxicity** and it is food best avoided). The suggested dose of combined EPA/DHA is 3 grams daily.

A number of studies have found the Mediterranean diet reduces the risk of dementia. A study in 2002 found those who ate the highest amount of anti-oxidants had a 70% reduction in dementia. The most important anti-oxidants come from fruit and vegetables; ideally with a range of colours (different anti-oxidants are often associated with different colours).

The **Lions Mane Mushroom** contains substances (hericenones and DLPE) known to stimulate nerve growth factor (NGF) which is necessary for brain function and healing. We know lack of NGF causes amyloid formation and an Alzheimers-like condition in mice. Studies in humans have shown this mushroom improves cognitive function significantly. In a rat study lion's mane was superior to the drug donepezil and reversed the effect of dementia. It also improves well-being. It is early days but this looks like a promising compound for dementia.

Other

Some types of mental stimulation such as learning a language, a new skill, puzzles and specific programs like Brain HQ have been shown to protect against dementia.

Summary

I think there is an emerging pattern developing giving us new ideas about how to prevent Alzheimer's disease based on research evidence.

Our main protection against these is as below.

- 1) Having an optimal diet, **low in sugar and refined carbohydrates** and high in anti-oxidants (fruit, vegetables, spices) and essential fats (oily fish, seeds and nuts).
- 2) **Regularly having a 12 hour period without food.** Also consider fasting.
- 3) Taking exercise.
- 4) Avoiding harmful drugs
- 5) Reducing exposure to toxic chemicals, especially heavy metals and pesticides, as these are stored in fatty tissues such as the brain.
- 6) **Numerous studies now show the protective effects of supplements, notably B vitamins.** Keeping up protective levels of nutrients and protecting the efficiency of our methylation pathways. B vitamins can help prevent and even treat dementia. This is well worth knowing as pharmaceutical treatment has proved disappointing with no new drugs in sight.
- 7) Consider types of brain stimulation
- 8) For those at high risk it is worth looking at the Breseden protocol or ReCODE which covers other factors (see book The End of Alzheimer's by Dale Breseden).