

INFLAMM-AGEING

THE BIGGEST THREAT TO YOUR HEALTH



FIVE SIMPLE
STEPS THAT WILL
PROTECT YOU

DR. PAUL CLAYTON & COLIN ROSE BSC

Inflamm-Ageing

**“Inflammation is an underlying contributor to
virtually every chronic disease...
rheumatoid arthritis, Crohn’s disease, diabetes
and depression, along with major killers
such as heart disease and stroke.”**

Scientific American (2009)

© Paul Clayton and Colin Rose

First published 2013

by Accelerated Learning Systems Ltd
Aylesbury, Bucks, UK

This edition 2014

All rights reserved

ISBN 0 905553 76 4



Dr Paul Clayton graduated summa cum laude in Medical Pharmacology from Edinburgh University, prior to obtaining his PhD.

He is a former Senior Scientific Advisor to the UK government's Committee on the Safety of Medicines and a past President of the Forum on Food and Health at the Royal Society of Medicine.

Dr Clayton frequently presents at and chairs international conferences on nutrition and health. He is a Fellow of the Institute of Food, Brain & Behaviour, Oxford, and a visiting professor of Pharmaco-Nutrition at Pecs University, Hungary.



Colin Rose BSc is a writer and publisher. His company, Accelerated Learning Systems, published Dr Clayton's first book *Health Defence*, which became a best-seller.

He is also an educational consultant and principal contributor to the EU funded programme *EduScience*, designed to improve the teaching of science in schools.

A founder member of the UK Campaign for Learning, he is also a member of the Royal Society of Medicine and a Fellow of The Royal Society of Arts.

Why we wrote *Inflamm-ageing*

The pharmaceutical *magic bullet* model dominates healthcare. When the symptoms of a non-communicable degenerative disease emerge, doctors generally reach for a drug or drugs.

But this strategy is fundamentally too little, too late. Most drugs treat the symptoms rather than the root causes of disease and by the time symptoms emerge, the disease has already progressed a long way. The major 'age related' diseases – cancer, arthritis, heart disease, diabetes and Alzheimer's – develop silently for years before they finally emerge and start to cause pain or disability.

However, science has developed to a stage where earlier and curative intervention is possible – without drugs. We now know that **most of these diseases are driven by chronic inflammation**. We know too that chronic inflammation is due largely to nutritional and lifestyle choices that can be changed quite easily.

This report will not take you long to read, because the message is simple: if you take action against the silent killer called chronic inflammation, you take a major step towards living longer and living more healthily. The actions you can take are simple too. Positive changes will begin to take effect, and can be measured, within weeks.

Your first step is to read this report.

CHAPTER 1

CHRONIC INFLAMMATION IS THE MAIN CAUSE OF DEGENERATIVE DISEASE

*'Inflammatory factors predict virtually all
bad outcomes in humans... having heart attacks
having heart failure, becoming diabetic...
becoming fragile in old age...
cognitive function decline,
even cancer to a certain extent.'*

**Russell Tracy, Professor of Pathology and Biochemistry,
University of Vermont, College of Medicine**

Don't confuse ageing with the passing of time. We can't change the speed at which the world turns, but the rate at which we age, known as *biological* ageing, is well within our control. Taking control of your biological age means you will not only look and feel younger but you will also cut your risk of developing degenerative diseases, and increase your prospects of a healthy middle and old age.

Ageing used to be seen as the steady accumulation of damage to the body's cells and tissues. This was an uncritical 'wear and tear' model that went hand in hand with the concept of 'age-related diseases'; and it led to a terrible medical fatalism. After all, if your symptoms are due to 'wear and tear', medics can't expect to do more than try to manage your symptoms.

Current research, however, reveals that almost all the age-related diseases – from declining mental powers to coronary artery disease, cancer, hypertension, arthritis, diabetes and stroke – have little to do with ageing per se. Instead, they are largely driven by chronic, sub-clinical inflammation, a condition that is not inevitable at all. In fact, it is surprisingly easy to prevent.

Chronic and sub-clinical means continuous and unnoticed – until the chronic inflammation has caused so much tissue damage that symptoms of disease finally emerge. There is a growing consensus that chronic inflammation should be minimised or avoided altogether. Yet, thanks to the way we live today, it occurs in almost every adult over the age of about 30 – and in increasing numbers of teenagers and those in their twenties.

Some people are at even higher risk. Are you:

- Over 50?
- Overweight?
- A frequent dieter?
- A smoker or city-dweller inevitably exposed to polluted air?
- A heavy consumer of baked goods, confectionery, deep-fried or fast-food products?
- Or have you been diagnosed with any long-term illness ending in 'itis' (which means inflammation)?

If you answered yes to any of the above, then you almost certainly have a level of chronic inflammation in your body that should be reduced now to protect your long-term health.

Acute inflammation is usually a positive and healing reaction

Not all inflammation is bad. **Acute** inflammation is usually positive: think of how the skin reddens and warms following a cut or an insect bite. Acute inflammation is a short term, protective immune response that is switched on to counteract harmful external threats. It's generally a productive response and the symptoms are short-lived. Once the acute inflammatory response has neutralized the threat, powerful *anti-inflammatory* compounds are released to allow healing processes to take over.

But sometimes the acute inflammatory response is insufficient to clear the threat. If the threat that initially triggered the inflammation remains, or is constantly drip-fed into the body as occurs with poor food choice, exposure to environmental particulates or a tobacco habit, this can result in continuous, low level inflammation: a.k.a. **chronic** inflammation.

Chronic inflammation destroys tissue

Chronic sub-clinical inflammation is a silent threat that simmers undetected in the body, progressively damaging tissues in the body wherever it occurs: in the heart, brain, joints, bowel, colon, prostate, lungs and skin – in fact, in potentially *any* organ.

Harvey Jay Cohen, of the Center for the Study of Aging at Duke University in the USA, likens inflammation to *'little waves lapping on the shore. It's a relatively low level of activity that, sustained over time, wears away at the beach and stimulates other bad events.'*

This insidious and gradual process of tissue destruction is why chronic inflammation is now seen as a main cause of almost all the age-related illnesses. And why chronic inflammation is associated with faster ageing; or *inflamm-ageing*, as some scientists now call it.

Although 'a main cause' does not mean the *only* cause, it has become clear that taking action to reduce chronic inflammation should be a priority if you want to cut the risk of

degenerative disease, and maximise your chances of long-term health. Fortunately you can reduce your levels of inflammation quickly and effectively.

But first a little more background.

Chronic inflammation is a recent problem

Heart disease and cancer are major causes of disease and death in our society, but it was not always so. The mid-Victorians, for example, were relatively free of these diseases (Clayton & Rowbotham 2009). The records show that the Victorians' chances of a healthy old age were better than ours, even without the modern drugs, surgery and diagnostics that we have come to rely on!

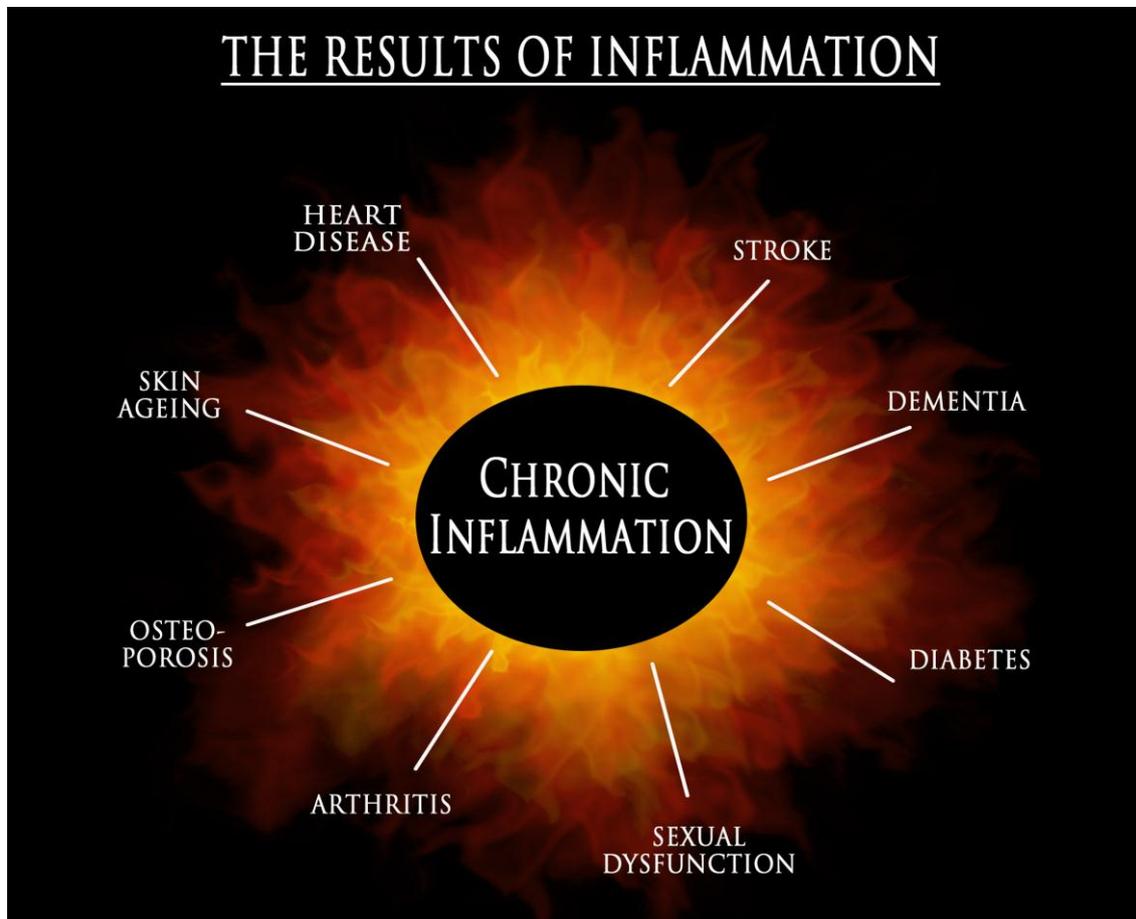
The first few years after birth were hazardous, but those who reached their fifth birthday had a life expectancy similar to our own. They did not die of degenerative diseases in the main, but in childbirth, in fires, of trauma and of infections spread by crowded, insanitary living conditions and polluted water supplies.

A few Victorians did develop heart disease and cancer, but most of the population enjoyed relative freedom from degenerative disease. The reason? A diet rich in natural anti-inflammatory compounds (of which more in Chapter 4), that provided extensive protection against chronic inflammation.

Chronic inflammation has never before been seen on the scale that we see it in the developed nations today. This is because we not only consume far lower levels of natural anti-inflammatory compounds in our diets than did our ancestors, but also we are exposed to far higher levels of pro-inflammatory compounds, thanks to modern food processing and cooking methods, and, for some, the prevalence of tobacco and environmental toxins.

As so many of us suffer from chronic, sub-clinical inflammation, it is no wonder that the steady accumulation of tissue damage eventually surfaces as a major degenerative disease – and why the degenerative diseases increase in frequency as we get older.

It is little to do with ageing as such, for if we ate a profoundly anti-inflammatory diet we would not become more prone to disease as we aged.



CHAPTER 2

WHAT CAUSES CHRONIC INFLAMMATION?

'Low-grade inflammation is associated with everything from heart disease and diabetes to Alzheimer's and arthritis ...'

University of California Berkeley, School of Public Health (2010)

There are five main and three secondary causes of the modern epidemic of chronic inflammation.

1. Too much Omega 6, not enough Omega 3

The main hormones that control the inflammatory response are called eicosanoids. The body uses fatty acids from the food we eat to make these eicosanoids.

Omega 6 fatty acids, found in polyunsaturated plant oils like safflower, sunflower and corn oil, produce eicosanoids that promote inflammation.

Omega 3 fatty acids (from oily fish) have the opposite effect, producing eicosanoids that reduce inflammation.

For most of human history, we ate a diet with a ratio of Omega 6 to Omega 3 of between 1 to 1 and 2 to 1, which is a healthy ratio. The balance today has become profoundly unhealthy. We consume foods far too high in Omega 6 and far too low in Omega 3. In fact, our current ratio is anywhere between 10 to 1 and 40 to 1, and in some cases may be as high as 100 to 1!

The body is therefore forced to use too many Omega 6 fatty acids to build cells, tissues and hormones – and the balance in the body becomes pro-inflammatory.

The prevalence of Omega 6 over Omega 3 in today's diet is because our intake of oily fish, the only significant source of the Omega 3s we need, has fallen, while our intake of plant oils, which provide Omega 6s, has risen dramatically.

Plant oils such as soya, palm and corn oil are widely used in cooking and in processed foods because they are cheap and palatable (food manufacturers have no legal requirement to produce healthy food).

To make matters worse, most animals raised for human consumption are also fed with foods that are high in Omega 6. Grass-fed animals have healthier levels of Omega 3 but

today only sheep are consistently raised this way. Most cows and pigs are cereal-fed and have a much higher 6 to 3 ratio as a result.

You find the same results in chickens and eggs. Battery and barn chickens are fed grains high in Omega 6 and their meat and eggs have a high Omega 6 to Omega 3 ratio as a result. Free-range chickens consume more Omega 3 fatty acids and produce meat and eggs with a better Omega 6 to 3 balance.

Do please note that the Omega 6 fatty acids are essential for life. It's just that we eat far too many of them. However, with sound food choices, and an Omega 3 supplement, you can tip the balance back towards a lower 6 to 3 ratio that is anti-inflammatory and therefore considerably healthier.

2. Not enough fruits and vegetables

Fruits and vegetables are important because they contain, amongst other compounds, **flavonoids**. These exert powerful anti-inflammatory effects in the body.

Flavonoids block the key enzymes that drive inflammation. These include COX-1 and COX-2, the same enzymes that are targeted by many anti-inflammatory drugs. They also block a second pair of pro-inflammatory enzymes called LIPOX-5 and LIPOX-8. Perhaps even more critically, they block a third group of pro-inflammatory and highly destructive enzymes called the matrix metallo-proteases (MMPs).

This three-way blocking action exerts a more fundamentally protective effect than any pharmaceutical drug because MMPs are directly responsible for the tissue damage that turns chronic inflammation into overt disease.

Unfortunately, we do not eat enough fruits and vegetables. The American Cancer Institute now recommends nine portions a day – but we manage an average of only 3. Without enough fruits and vegetables, the critically important enzyme-blocking flavonoids are not present in our bodies in adequate amounts. Together with the excess Omega 6 to 3 ratio, this creates the conditions for the perfect inflammatory storm.

In contrast, when the diet contains enough flavonoids to block the pro-inflammatory enzymes and enough Omega 3 to help create anti-inflammatory hormones, then chronic inflammation is minimised or stopped and natural healing processes in the body can once again predominate.

3. Pro-inflammatory cooking methods

When foods containing proteins are cooked at high temperatures, the protein binds with glucose or other sugars in the food to produce compounds called Advanced Glycation End products, or AGEs.

Many foods brown at high temperatures and this discolouration is a sign of AGE production. AGE compounds are very pro-inflammatory – and very ageing.

The best-known AGE compound is acrylamide, which forms when starchy foods are cooked at high temperatures. Acrylamide has been found in crisps, French fries, toast and other foods. Worryingly, acrylamide has been classified as carcinogenic in humans.

AGEs can also be formed within the body when levels of glucose are too high for too long, as happens in diabetes.

In a non-diabetic state, enzymes bind glucose molecules to proteins, forming glycoproteins that are essential to normal body functioning. But when blood sugar levels are too high, glucose can bind to proteins in the body through non-enzymatic action. This drives the formation of AGEs and thus leads to inflammation – which explains why diabetics suffer from excessive inflammation, increased risk of serious disease and accelerated ageing.

AGEs stimulate inflammation, but this is not the only way they accelerate the ageing process. The binding of glucose to proteins causes cross-linking between proteins, linking them together in a random and dysfunctional manner. This shows up externally as skin ageing, wrinkling and reduced elasticity. Internally, it drives diseases such as cataracts, hypertension, blood clotting and kidney damage.

Dr Levi of the American Journal of Kidney Diseases says: *'AGE reactions ... gradually accumulate over the lifetime of the protein. The goal must be to prevent AGEs forming in the first place'*.

It is not just AGEs we have to guard against. When fats and oils are heated to high temperatures, ALEs (Advanced Lipoxidation End products) are created. These might sound friendlier but they are just as harmful and are highly pro-inflammatory.

Foods containing high levels of both AGEs and ALEs include:

- high-temperature fried and grilled meat and poultry
- deep-fried and shallow-fried fish
- coffee and colas
- soy sauces and balsamic products
- smoked and cured foods

In short, fast food staples – and even the heat-dried milk used in infant formula.

Higher levels of these pro-inflammatory compounds in the blood are linked to higher rates of many degenerative diseases, including a large number of cancers.

But let us not all become Puritans. The aim is **balance**.

Humans (and other omnivores) like high-fat, high-sugar foods, and life without the occasional dessert, cake, chip or snack would be, well, rather less enjoyable. If you consciously balance those foods with anti-inflammatory foods and nutrients, you can indulge occasionally without harm.

4. Getting older

Levels of the sex hormones oestrogen, progesterone and testosterone fall as we age, and lower hormone levels are implicated in age-related inflammation. Symptoms of chronic inflammation often become more apparent during and after menopause in women and in men as testosterone levels reduce.

Chronic inflammation has been cited as one cause of sarcopenia, the muscle loss that occurs with ageing. For both sexes, therefore, the tendency to increased inflammation typically accelerates after about 45-50.

To make matters worse, there is evidence that our immune systems may become less efficient at controlling inflammation as we get older.

You can't stop the years rolling by but there is overwhelming evidence that you can slow ageing by reducing or preventing the damage caused by chronic inflammation. And although in our view it makes sense to start doing something about it from early adulthood, you can see why the time to take *serious* preventative action is around age 45-50.

5. Being overweight or obese

Overweight and obesity are major causes of chronic inflammation today. This is because excess adipose (fat) tissue secretes pro-inflammatory compounds. It used to be thought that apple-shaped obesity (fat around the belly) was more dangerous than the pear-shaped kind (fat around the hips) – but that is now discredited. Fat around the hips, thighs and bottom also secretes proteins that lead to inflammation and insulin resistance.

In a society where almost 30% of people are obese and 62% are officially overweight, the pro-inflammatory role of fat has become an important cause of ill health and accelerated ageing. Our expanding waistlines are linked to high intakes of pro-inflammatory, processed foods high in sugars and Omega 6 fats, and to our generally low level of physical activity, which itself is pro-inflammatory.

Since excess fat is pro-inflammatory, and chronic inflammation is a factor in heart disease, stroke, diabetes, Alzheimer's and a range of cancers, it is hardly surprising that being overweight is a risk factor for all these diseases.

The good news is that the anti-inflammatory food regime in Chapter 4 can also be a weight loss regime.

6. Smoking and pollution

Exposure to air pollutants can trigger oxidative damage and chronic inflammation. Smoking is a leading cause of illness, accelerated ageing and death, and city dwellers exposed to high levels of diesel exhaust particulates are also at risk. Exposure to certain pesticides may also trigger inflammation.

6. Excess free radicals

Most people have heard that *free radicals* can damage your health. In fact, it is only an **excess** of free radicals that is damaging. Some level of free radical action is normal and a necessary part of the immune response to pathogens such as bacteria and viruses.

However, excess free radical action can indeed cause cell and tissue damage and, eventually, major health problems.

Free radicals are minute particles formed during the billions of chemical processes that take place in the human body, and make life possible. We are made of molecules that are in turn made up of atoms, and both molecules and atoms have electrons surrounding them.

Electrons are generally paired, but during certain reactions one electron may become detached. The remaining atom (or molecule) now becomes an unstable 'free radical', with one unpaired electron. To become stable again, the free radical must grab an electron from another molecule, but now that other molecule becomes a free radical! This chain reaction of molecules stripping electrons from each other continues, sometimes reaching thousands of events long and wreaking destruction until the sequence ends.

The process of free radical formation is also called *oxidative damage*, as oxygen molecules are often involved. The rusting of iron, fats turning rancid or a cut apple turning brown are familiar examples of oxidative/free radical damage.

Excessive free radical/oxidative damage to the tissues contributes to age-related diseases from heart disease to cancer. There are a number of well-known factors that increase the levels of free radicals in our bodies, which include smoking, exposure to radiation (eg ultra-violet, X-rays and all things radioactive) – and inflammation.

When cells are damaged by inflammation they produce toxic compounds that trigger the release of excess free radicals. The resulting *oxidative stress* further damages those cells, and this process releases a second wave of inflammatory compounds.

This vicious circle drives both disease and the ageing process itself – *unless* sufficient anti-inflammatory *and* anti-oxidant defences are in place.

Some years ago, the Centre for Environmental and Health Science in Australia stated that: *'Evidence is accumulating that most of the degenerative diseases that afflict humanity have their origin in deleterious free radical reactions. These diseases include atherosclerosis, cancer, inflammatory joint disease, asthma, diabetes, senile dementia and degenerative eye disease. The process of biological ageing might also have a free radical basis.'*

Their more recent position is that ageing and age-related diseases are driven by the vicious circle of chronic inflammation creating free radicals creating further inflammation.

CHRONIC ►► EXCESS FREE ►► MORE
INFLAMMATION RADICALS INFLAMMATION

This is why there is a fast growing consensus among scientists and clinicians that for a lifestyle to be comprehensively disease-preventative and health-protective, it should include foods and supplements with high anti-inflammatory and high anti-oxidant capacity.

This is less complicated than it sounds, as anti-inflammatory and anti-oxidant foods are often the same foods – and we're going to look at those in detail later.

8. Genetic influences

We don't want to give the impression that all illness and age-related diseases are exclusively caused by lifestyle and dietary factors.

Genetic inheritance can be a contributing factor, and a determining factor in single locus diseases such as Huntington's Disease or Sickle Cell Anaemia. Strong genetic risk factors have also been implicated in about 5-8% of cases of heart disease, cancer, Alzheimer's and the other major diseases.

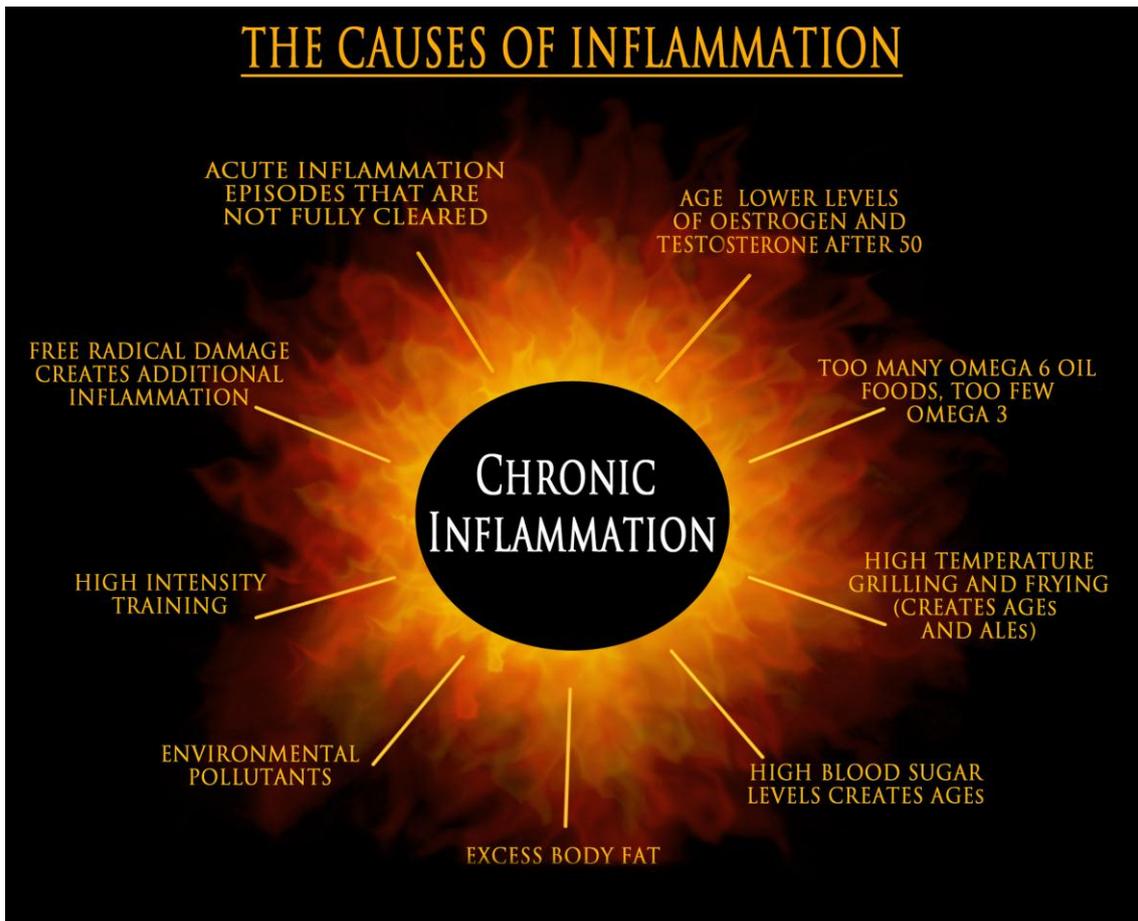
But for most of us, our destiny is not written in our genetic code. Our genetic inheritance may make us more or less susceptible to lifestyle and dietary influences – but we can control those.

For example, researcher Federico Licastro and others from the University of Bologna state that: *'Alzheimer's disease, atherosclerosis, diabetes and even sarcopenia (loss of muscle mass) and cancer, just to mention a few, have an important inflammatory component, though disease progression seems also dependent on the genetic background of individuals.'*

In other words, certain gene types are more susceptible to age-related disease. But the same researchers conclude that: *'controlling inflammatory status may allow a better chance of successful ageing.'*

So whatever your genes, establishing an anti-inflammatory lifestyle is a priority if you wish to improve your health prospects.

It's time for a comprehensive anti-inflammatory and anti-oxidant solution!



CHAPTER 3

HOW INFLAMMATION WORKS IN SPECIFIC DISEASES

'The connection between inflammation and cancer has now moved to center stage in the research arena.'

Massachusetts Institute of Technology's Whitehead Institute
for Biomedical Research (2009)

HEART DISEASE

Heart disease is sometimes described as a 'plumbing' problem – plaque builds up in the walls of blood vessels, clogs and blocks them. But blood vessels are not like pipes; they are composed of living, reactive tissue, and are sensitive to damage and injury.

For example, they are highly sensitive to pro-inflammatory compounds such as AGEs and ALEs the toxic compounds formed when different types of foods are cooked at high temperatures which we talked about before.

These compounds can also be formed in the body; diabetics produce their own AGEs due to their high blood sugar levels and smokers produce ALEs internally because of the high oxidative stress in their bodies caused by smoking.

Whether eaten or formed in the body, these toxic compounds attack the linings of the blood vessels, causing inflammation and damage. Immune cells then target the damaged site, and migrate into the vessel wall where they attempt to resolve the damage.

If the toxins are present in excessive amounts, the immune cells die. This causes further inflammation, further immune cell infiltration and more cell death. The cell remains gradually build up as *atheroma*, a toxic sludge rich in oxidised cholesterol compounds that came *not* from circulating cholesterol but primarily from the dead immune cells.

If there are too many pro-inflammatory compounds and not enough anti-inflammatory and anti-oxidant compounds in your diet, the rate at which atheroma is formed outstrips the body's ability to remove it.

Consequently, the atheroma builds up over time, forming plaques inside the artery walls which can eventually restrict blood flow. If this happens in an artery supplying the heart, it can cause angina; if it supplies the brain, it can cause confusion or dizziness. If the plaques rupture, as they often do, this can cause a heart attack or a stroke.

The problem is made worse by the fact that the same inflammation that drives the formation of atheroma in the artery walls also causes them to constrict, so that there is a gradual rise in blood pressure. This forces the heart to work harder and it makes the arteries less elastic, creating a combination of effects that increases stresses and shock waves within the arterial system.

Statins are not very effective because they attack the wrong target – cholesterol levels in the blood. In fact, blood cholesterol is a very inaccurate biomarker, as fully half of all heart attacks occur in people with normal cholesterol levels.

There is a growing suspicion that the relatively minor protective effects of statins (and we will not talk about their adverse effects here) are due to the fact that some of them have a mild anti-inflammatory effect as well as a cholesterol-lowering action.

The role of undetected, chronic inflammation in heart disease may explain why 50% of heart attacks occur in patients with normal cholesterol levels. Elevated levels of inflammatory C-reactive protein (CRP) and an amino acid called homocysteine have been suggested as more important predictors of heart attacks.

ALZHEIMER'S DISEASE

Inflammation is a significant factor in Alzheimer's. It was long ago known that the risk of Alzheimer's was reduced in people who, because they had an inflammatory condition such as arthritis, took certain anti-inflammatory drugs. These drugs are, however, too toxic for long-term preventive use.

An extended piece of research called the Honolulu-Asia Aging Study found that men with the highest levels of inflammation, as measured by CRP, were three times more likely to develop dementia than those with the lowest levels.

How dementia develops is the focus of intense study, and is undoubtedly a very complex process. But we do know that chronic inflammation is involved, and that this attacks and kills brain cells.

We also know that the brain relies on a continuous supply of fatty acids, and particularly Omega 3 fatty acids, to build and renew the walls of its brain cells. One study in *Neurology* suggests that an Omega 3 rich diet could reduce damage by between 20-30% and could '*play an important role in preventing or delaying the onset of Alzheimer's disease*'.

Omega 3s are not the only neuro-protective nutrients. Flavonoids derived from fruits and vegetables reduce inflammation both directly and also indirectly, by binding free iron (which is pro-inflammatory) and by reducing the production of excess free radicals that would otherwise cause collateral damage.

More evidence on the importance of combining a range of nutrients comes from scientists at the University of California, published in the *Journal of Alzheimer's Disease*. They tested a combination of curcumin and vitamin D3 to enhance the activity of two types of immune

cell acting in the brain. They state: *'Our findings demonstrate that active forms of vitamin D3 and curcumin may be an important regulator of immune activities of macrophages in helping to clear amyloid plaques'*.

DIABETES

Harvard Medical School researchers have noted a connection between chronic inflammation and Type 2 diabetes. We have seen that fat cells release pro-inflammatory chemicals. These inhibit the body's ability to regulate blood sugar.

The hormone insulin works by ensuring that muscle cells take up blood sugar after a meal, thereby lowering blood sugar levels. A combination of excess body fat, a carbohydrate-rich diet and insufficiently exercised muscle hinders this process, leading to chronically elevated blood sugar levels.

Elevated blood sugar in turn creates AGE products and cross-linking damage to tissues, leading over time to accumulated damage in many sites including the blood vessels, eyes, kidneys and brain.

The diet and nutritional supplement regime we recommend here is anti-inflammatory *and* has a low Glycaemic Load (GL) – in other words it only raises blood sugar levels moderately. This makes it a particularly suitable defence against diabetes, especially when coupled with exercise and, where appropriate, weight loss.

CANCER

Cancers have many causes, but chronic inflammation is increasingly considered as an important causative factor. Patients with colon cancer, for example, have consistently raised levels of biomarkers for inflammation; and chronic inflammation is looking more and more as if it may be an essential link in the chain of events that leads to the disease.

Here's what *Scientific American* said in a key article in 2008. *'Cancer begins with a series of genetic changes that prompt a group of cells to over-replicate and then invade surrounding tissue, the point at which true malignancy begins. Eventually some tumour cells may break off and establish new growths (metastases) at distant sites.'*

What appears to cause that progression from DNA damage to cancer is chronic inflammation, which then encourages free radical damage. As the magazine then puts it: *'Genetic damage is the match that lights the fire, and inflammation is the fuel that feeds it'*.

CHAPTER 4

FIGHTING INFLAMM-AGEING

'Chronic inflammation – the enemy inside you – a slow, silent disturbance that never shuts off. You can't feel it. You can't be tested for it. Yet it has become a medical hot topic. It's an underlying cause for many, many diseases.'

Women's Health December 2012

It is clear that for long term health, chronic inflammation and excess free radical action must be kept in check. There are five actions you can take that match the main causes of inflammation and they are surprisingly easy to carry out.

ANTI-INFLAMMATORY ACTION 1: Get your diet right

You'll inevitably get one year older every 365 days or so. However, given that biological ageing is largely driven by chronic inflammation with a degree of free radical damage, it follows that increasing the level of anti-inflammatory and anti-oxidant nutrients in your diet will slow the rate at which you age biologically.

The key anti-inflammatory foods include fruits, vegetables and Omega 3-rich oily fish.

Fish high in Omega 3 include:

- **wild salmon** (not farmed, as this is fed on high-Omega 6 grains) ● **mackerel**
- **herring** ● **tuna** ● **sardines** ● **pilchards**

Fruits with high anti-inflammatory and anti-oxidant scores include:

- **blueberries** ● **raspberries** ● **blackberries** ● **strawberries** ● **cherries**
- **blackcurrants**

High-scoring vegetables include:

- **broccoli** ● **asparagus** ● **beetroot** ● **chard** ● **spinach** ● **cabbage**
- **mushrooms** (which are actually fungi but they usually live in the vegetable section)

These fruits and vegetables are all good sources of flavonoids, carotenoids and other phyto-nutrients with anti-inflammatory and anti-oxidant properties. Eating a rainbow is sound advice. Generally the more (natural) colours there are on your plate, the higher the anti-oxidant and anti-inflammatory content of your diet.

Use Table 1 to increase anti-inflammatory foods in your diet and reduce pro-inflammatory foods. Although not a weight-loss diet in itself, many people find it easier to maintain a healthy weight on this type of food regime and most lose weight.

Note that the table is headed **MORE** and **LESS**, because it is all about **balance**. There is no one food that is all good, or all bad. Bananas, for example, raise blood sugar levels – but are a source of potassium and fibre.

Balance! Or, as Colin’s father used to say: “Moderation in all things – including virtue!”

Table 1 Anti and pro-inflammatory foods

	EAT MORE	EAT LESS
Fruits	Red/black/purple fruits, all berries inc strawberries, raspberries, blackberries, blueberries, elderberries, blackcurrants, citrus, plums, cherries, grapes	There are no fruits we should eat less of
Veg	Broccoli, chard, spinach, cabbage, collards, kale, onions, carrots, sweet potatoes, garlic, peppers, mushrooms, courgettes (zucchini), celery, asparagus	Potatoes or potato products, corn or corn products, unless you are very active physically
Legumes Legume products	Lentils, beans, peas Tofu (from soybeans), dhal (from lentils), hummus (from chickpeas)	
Herbs and Spices	Turmeric, garlic, ginger, cayenne, chilli, curry powder, basil, thyme, black pepper, cinnamon, oregano, rosemary, nutmeg	Salt
Fats and oils	Olive or rapeseed (canola) oil	Other vegetable and palm oils inc sunflower. Hard margarines.
Fish	Salmon (if wild), herring, tuna, mackerel, sardines, pilchards, trout, oysters	Deep-fried fish, fish fingers
Meat	Game, grass-fed beef, mutton & lamb, free range chicken	Intensively farmed beef, pork or poultry. Sausages, burgers, bacon, cured meats such as hot dogs, salami
Dairy products	Real cheeses especially green & blue, plain yoghurt, particularly “live”	Sweetened yoghurt, ice cream
Breads	Wholemeal & rye in moderation, although physically active people can eat more	White (refined) flour products
Cereals	Bran cereals, no added sugar muesli, porridge oats	Cornflakes, all sugared cereals
Biscuits and snacks		Crisps, chips, pretzels, biscuits, cookies and pies
Pasta and grains	Wholemeal pasta, brown rice, quinoa	White rice, white pasta, gnocchi
Nuts and seeds	Eat in moderation – they are full of omega 6 fatty acids	Salted and roasted nuts
Sweeteners	Prefer intense natural sweeteners such as stevia if needed.	Sugar, honey, syrup, molasses
Desserts and sweets	Dark chocolate	Most sweets and desserts, ice cream, baked pastries
Drinks	Fruit and vegetable juices, tea, coffee, milk, moderate red wine	Sugar-sweetened soft drinks, colas, spirits

Some cooking tips

- Use fewer Omega 6 polyunsaturated plant oils; switch to (mono-unsaturated) olive oil or rapeseed oil.
- Reduce foods cooked at high temperatures (grilled, fried, barbecued, roasted). Instead, stew, slow-cook, stir-fry or sauté quickly.
- Steam or microwave vegetables.
- Rub joints for roasting with thyme and/or oregano which helps counteract the formation of AGE products. Never use honey to coat or glaze meat as this encourages AGEs.

ANTI-INFLAMMATORY ACTION 2: Take an anti-inflammatory supplement

A conventional daily A-Z vitamin and mineral tablet provides a baseline of those micro-nutrients for which there are Recommended Daily Amounts (RDAs), but will do little or nothing to reduce chronic inflammation.

This is one reason why studies on simple vitamin and mineral supplements generally show no reduction in age-related disease.

The American Cancer Institute now recommends **nine** portions of fruit and vegetables a day. If this is too much for you, you can move the balance of your diet towards anti-inflammatory status by choosing a nutritional supplement that includes more than the conventional vitamins and minerals.

It should also include potent anti-inflammatory compounds such as Omega 3 fish oil, curcumin, green tea and grape-seed flavonoids.

Drawing on over 30 years of research, Paul has designed a supplement programme that combines anti-inflammatory nutrients with an A-Z range of vitamins and minerals – at levels and in forms that research indicates are optimal.

The formula is included as [Appendix 1](#). It has been tested under pharmaceutical laboratory conditions and the results showed that cell inflammation markers were essentially eliminated at the levels used in the supplement.

As you get older – typically over 45 to 50 – inflammation tends to increase, so it then makes sense to add additional anti-inflammatories and other nutrients that research indicates can help protect eyes, brain, heart and cellular health.

These would certainly include **lycopene**, **lutein**, and **beta carotene**, all *carotenoids* which, amongst other benefits, help maintain normal ‘cell signalling’ function. Cells need to communicate with each other to function properly and errors in cell signalling can lead to cancer. *Pub Med*, the on-line publishing arm of the American National Institutes of Health, confirms that carotenoids ‘*can be useful in the prevention of cancer and other degenerative diseases.*’

It would also include **co-enzyme Q10** which participates in the production of energy in the mitochondria – the tiny energy factories within each cell. Q10 has research support for cardio health and is available as a medicine in some European countries. Its role appears to be inhibited by statins.

It would also include **soy isoflavones**. The Journal of the National Cancer Institute in 2003 concluded that higher intake of soy foods like miso soup and tofu in the Japanese diet was linked to lower levels of breast cancer. Other epidemiological studies show a relationship between high soy consumption and less incidence of prostate cancer.

Finally it would certainly include **betaine**, which helps lower a blood protein called homocysteine. Elevated levels of homocysteine are associated with a higher risk of heart disease.

These additions create an even more anti-inflammatory 'cocktail' and all-round preventative healthcare. See [Appendix 2](#).

The supplements listed at Appendices 1 and 2 are designed to combine the most protective elements from the healthiest diets as identified by laboratory and epidemiological (population based) research. Since some of the nutrients listed are less familiar, or have multiple benefits, here is a little more background.

Omega 3

We learned about the importance of Omega 3 fatty acids earlier, but Omega 3 has other anti-inflammatory benefits.

A 2012 study carried out at Ohio State University and published in *Brain, Behaviour and Immunity* found that as little as four months' supplementation with Omega 3 was associated with an increase in the length of telomeres in immune system cells.

What are telomeres and why does their length matter? Telomeres are sequences of DNA at the end of chromosomes, sometimes likened to the tags at the end of a shoelace. Without the tags the lace would unravel and without telomeres, cells cannot divide.

Telomeres get shorter and shorter as cells replicate and die. Indeed some researchers measure ageing by the shortening of telomeres. Once the telomere is totally consumed, the cell dies. Any nutrient that can reduce the rate at which telomeres shorten (or even reverse the process) is therefore potentially exciting longevity news.

The lead researcher at Ohio State commented: *'Our findings strongly suggest that inflammation is what is driving the changes in the telomeres'*.

Other anti-inflammatory compounds also play a role. The nutrients lycopene, lutein, vitamin E and the flavonoids and isoflavones are important here, as are the minerals zinc, manganese, copper and selenium, the essential co-factors for the anti-oxidant enzymes. So include them in any anti-ageing programme.

Beyond a possible role in longevity, the research on Omega 3 is extensive and shows that it is a highly important nutrient for heart, joint and brain health.

Curcumin

Derived from turmeric, the yellow spice which is used in curry, and a member of the ginger family, it has potent anti-inflammatory and anti-oxidant properties. In animal studies it has been shown to inhibit the development of cancer and dementia.

Intriguingly, those areas in India with the highest intakes of curcumin appear to have the lowest rates of age-adjusted dementia. As a result of these and other findings human trials are under way, and starting to produce encouraging results.

Curcumin is best absorbed in the presence of oil, so taking it with a fish oil capsule is logical. As it protects the Omega 3 fatty acids from oxidation in the body, the combination makes good sense.

Vitamin D3

Vitamin D3 is a good example of how the *form* of a vitamin matters. Some forms of some vitamins are more effective than others. Vitamin D3 is preferred to D2 on those grounds.

Vitamin D is really a *hormone* rather than a vitamin, and is vital for the normal functioning of every system in the body, including the immune system.

People with insufficient D appear to be more prone to inflammation; conversely, people with adequate levels of D in their bodies have a lower risk of cancer, arthritis, heart disease, dementia, auto-immune disease, depression and osteoporosis. There is even evidence suggesting that a healthy D status may help maintain a healthy weight.

D research also provides a good example of the critical difference between **deficient** and **insufficient** – or depleted.

Data from the US National Health and Nutrition Examination Survey found that 9% of children across the USA were vitamin D deficient, (ie. did not reach the RDA level). However, a staggering 61% (50.8 million children!) were vitamin D insufficient or depleted (ie. had levels that were insufficient to afford protection).

'We expected the prevalence of vitamin D insufficiency would be high, but the magnitude of the problem nationwide was shocking,' says lead author Juhi Kumar, a fellow in paediatrics at the Albert Einstein College of Medicine.

There is no reason to suppose that the situation is any better in Western Europe.

Dr Clayton has been making the point for many years that in a sedentary population with low energy requirements, and where 2000 to 2500 calories per day is considered normal, it is no longer possible to get everything needed for long term health from even a well-balanced diet.

The 'well-balanced diet' will generally prevent outright deficiency, but it will not prevent micro-nutrient and phyto-nutrient depletion, and thus cannot protect against chronic inflammation, or degenerative disease.

Vitamin K2

Vitamin K is well known as an essential blood-clotting agent but it is also critical in the control of calcium in the body. Insufficient K damages the body's ability to build calcium into the bones, or to keep calcium from depositing in our arteries and soft tissues.

There are several forms of this vitamin. Vitamin K1 occurs in leafy green plants such as spinach, chard, kale, salad greens, parsley, mustard greens and broccoli. Absorption of K1 from these sources is poor, at only about 20%; and it does not stay long in the blood, which makes it relatively ineffective at building bones and protecting arteries.

K2 is derived from cheeses such as quark and the blue and green cheeses, and occurs in high levels in the fermented soy dish called natto – a Japanese delicacy few Westerners have experienced (or enjoyed – it is a very acquired taste!). K2 is very well absorbed and remains in the bloodstream for hours at a time making it a much more effective bone and cardiovascular protector. K2 is more expensive than K1, which is why it is rarely found in mass-market supplements.

ANTI-INFLAMMATORY ACTION 3: Speed up to slow down ageing

Moderate exercise increases your health prospects, in part because it has anti-inflammatory effects. The standard advice is to take 30 minutes of exercise, five times a week, at a level that raises your heart rate.

People who exercise at around this level have lower rates of heart disease, cancer, diabetes and dementia.

However, you can over-dose. Intense exercise can trigger inflammation and excessive free radicals, so take anti-inflammatory supplements to counter negative effects.

ANTI-INFLAMMATORY ACTION 4: Lose weight if you need to

If you carry excess weight, slim down in a gradual and sustainable way. There is evidence that yo-yo dieting is intrinsically pro-inflammatory, so avoid crash diets.

Support any weight-loss regime with a supplement that includes a full range of anti-inflammatory nutrients and phyto-nutrients, as these all tend to be low in calorie-restricted diets.

ANTI-INFLAMMATORY ACTION 5: Make sure the acute inflammation response fully clears infection

If a harmful microorganism invades the body and the acute inflammatory response is insufficient to clear that threat, the infectious agent may linger on. The body will then switch over to a chronic inflammatory response that, as you know by now, will eventually lead to serious diseases. This is why, for example, poor oral hygiene and subsequent chronic gingival (gum) inflammation are linked to heart disease.

It is therefore important to ensure that your acute immune response is efficient in fully clearing infections. The most effective (and natural) way to boost your immunity is to take 1-3, 1-6 beta glucans. These are polysaccharides, derived from bakers' yeast, that have been proven to increase the effectiveness of your front-line immune system defence against bacteria and viruses.

The 1-3, 1-6 beta glucans (not to be confused with the 1-3, 1-4 beta glucans in oats and other cereals) have been tested against a wide range of pathogens from E.coli to flu viruses and even the deadly anthrax bacillus, and shown to be highly protective against all of them.

When the Canadian Department of Defence was searching for an immune enhancer that could help counteract radiation, they tested over 100 products – and one beta glucan extract came out on top. This was a patented ingredient called Wellmune, and it is the main ingredient in the immune enhancer supplement called ImmunoShield www.immunoshield.com.

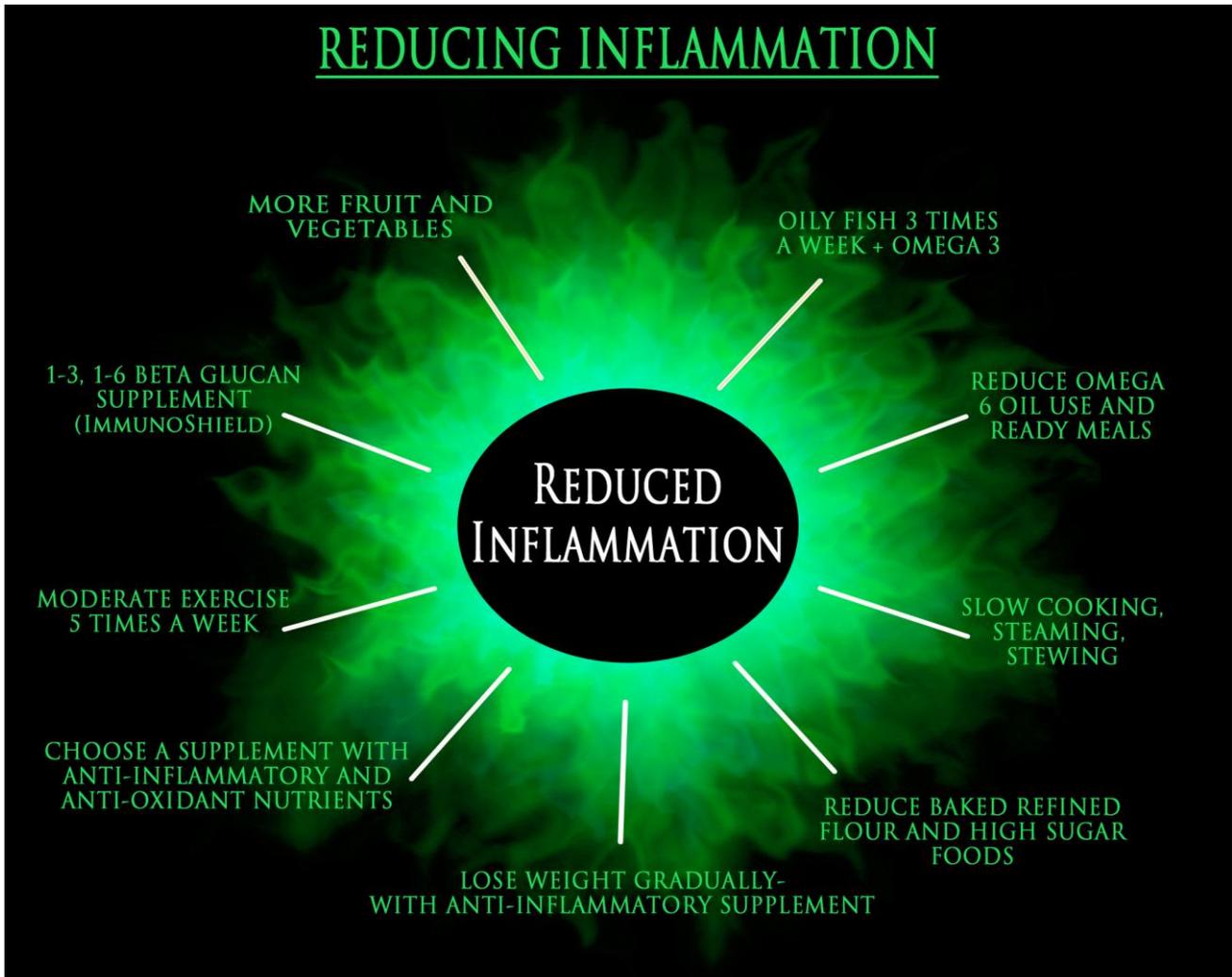
A comprehensive anti-inflammatory supplement will help reduce *long-term chronic* inflammation and a 1-3, 1-6 beta glucan supplement is designed to enhance the immune system's *short-term acute* response. The combination has exciting potential.

And finally ...

Stop smoking (but you already knew that!) and minimise exposure to air pollution where possible. If you live in a city where air quality is an issue, you should seriously consider an anti-inflammatory supplement.

It really works ...

A study in a 2004 issue of *Metabolism* magazine showed that a diet rich in anti-inflammatory fruits, vegetables and whole grains and reduced in refined flours, sugars and saturated fats, led to a 45% average reduction in inflammation levels as measured by CRP in just two weeks. Moreover, the supplements detailed on the next two pages effectively eliminated inflammation in cell tests.



APPENDIX 1

Dr Clayton's recommended supplement formula for ages 30 to 50 is **NUTRISHIELD ESSENTIALS**

www.nutrishield.com

Nutrient	Level	Function
Omega 3	650 mg	Anti-inflammatory, heart health
Green tea extract	150 mg	Anti-inflammatory & anti-oxidant
Curcumin	250 mg	Anti-inflammatory & anti-oxidant
Grapeseed extract	100 mg	Anti-inflammatory & anti-oxidant
Vitamin C	500 mg	Anti-inflammatory & anti-oxidant
Natural Vitamin E	55mg/83IU	Anti-inflammatory & anti-oxidant
Vitamin K1 Vitamin K2	50 mcg 25 mcg	Anti-inflammatory at high doses. K2 is the most potent form
Vitamin D3	20 mcg	Important immune system support
Selenium	150 mcg	Anti-inflammatory & immune support
Chromium	120 mcg	Supports the action of insulin
Zinc	10mg	Essential to build anti-oxidant enzymes
Magnesium	114mg	Essential in many metabolic reactions
Iodine	100mcg	Essential to produce thyroid hormones
Copper	1mg	A co-factor for anti-oxidant enzymes
Calcium	177mg	Important in bone formation
Manganese	2mg	A co-factor for anti-oxidant enzymes
Molybdenum	40mcg	A co-factor for several vital enzymes
Vitamin A	800mcg	Important in immune function
Vitamin B1	7.5mg	Helps convert food into energy
Vitamin B2	7.5 mg	Essential to metabolise food for energy
Vitamin B3	15mg	Helps boost protective HDL cholesterol
Vitamin B5	11.25mg	Helps convert food into energy
Vitamin B6	7.5 mg	Essential to metabolise food for energy
Biotin (B7)	150mcg	Helps convert food into energy
Folic Acid (B9)	200mcg	Provides vital methyl groups
Vitamin B 12	6.75 mcg	Anti-inflammatory

APPENDIX 2

People over about 50 – or with a particularly stressful lifestyle – should consider **NUTRISHIELD PREMIUM**, which ADDS the following nutrients to those in Essentials.

www.nutrishield.com

Nutrient	Level	Function
Co Enzyme Q10	30 mg	Anti-oxidant – mitochondrial health
Soy Isoflavones	40 mg	Anti-inflammatory – may also help normalise damaged cells
Betaine	450 mg	Provides vital methyl groups; lowers dangerous homocysteine levels
Beta carotene	7 mg	Anti-oxidant, anti-inflammatory
Lutein	6 mg	Anti-oxidant. Eye health
Glucosamine	415 mg	Works to help build connective tissue, working together with vitamins K and D
Zeaxanthin	42 mcg	Anti-oxidant, eye health
Cryptoxanthin	49 mcg	Anti-oxidant
Lycopene	5 mg	Anti-oxidant. May protect prostate, brain and gastro-intestinal tract

Note that men, and women after the menopause, generally do not require supplemental iron, as excess iron in the body is pro-inflammatory. Women before their menopause do need iron in their supplement.

APPENDIX 3

LABORATORY TESTS

Test results on NutriShield can be seen at

<http://uni-vite.com/Nutrishield/documents/VivacellSummaryWeb.pdf>

The independent laboratory “Vivacell” in Germany used the industry standard inflammatory biomarkers Interleukin 1 beta (IL1beta), Tumor Necrosis Factor (TNF alpha), Interleukin 6 (IL6), Interleukin 8 (IL8), Prostaglandin E2 (PGE2) and Isoprostane 8-(Iso-PGF2-alpha Isoprostan).

The report supports the conviction that only a combination of nutrients that mimics an ideal diet can be truly effective.

The report concluded:

“Our data clearly provide evidence that NutriShield® creates potent anti-inflammatory and anti-oxidant effects.

“NutriShield® is therefore a bioactive nutraceutical to be used to help prevent inflammatory disease of any kind.

“Our data find a synergistic effect of the several ingredients of NutriShield® since the combination was more effective than the summary of the single ingredients.”

WHAT NEXT?

You can visit the NutriShield website at www.nutrishield.com

Dr Paul Clayton has written a very well-reviewed and highly recommended bestseller called *Health Defence*, which you can buy from www.healthdefence.com.

About *Health Defence*

“Dr Paul Clayton has developed a multitude of creative and innovative solutions for the promotion of human health and wellbeing.”

David Richardson

**Visiting Professor, Food and Nutrition Science
University of Newcastle on Tyne**

“This book is a must for everyone –
it will educate and inspire.”

What Medicine? Magazine

He also has a website at www.drpaulclayton.com

A Personal Note from Colin Rose

“My parents died too young and I have always been interested in the impact of diet and lifestyle on health. When I met Dr Paul Clayton 10 years ago I recognised someone who was more knowledgeable about nutrition and health than anyone I had ever met or read. He was clearly passionate about improving the nation’s health.

“I suggested he write a book capturing his knowledge and advice. It was eventually published as *Health Defence*, and it contained a well-documented rationale for supplementation which was extended in a series of papers he co-authored in the *Journal of the Royal Society of Medicine*.

“But no existing supplement came close to meeting his specifications, so I decided to found a company to develop one (called NutriShield) to fill that gap.

“The logic and book came first, and the supplement followed. We assumed the supplement would be for people of 50 years and over. But a mountain of research, and increasing rates of degenerative disease in younger age groups, has now led to the realisation that the need for an anti-inflammatory programme starts much earlier than that, particularly for vulnerable individuals.

“Consequently we believe there is a requirement for two ‘levels’ of anti-inflammatory and anti-oxidant support; one for the younger person living fairly healthily, and a second for older subjects, and those younger folk who don’t have the time or inclination to live as well as they should.

“Dr Paul Clayton stills consults for the company that I founded in order to produce NutriShield, but he has no financial interest in that company or its products. He remains an independent health researcher.”

END NOTE

The science is still under construction, but most scientists now believe that chronic inflammation is at the core of almost all of the degenerative diseases. As a result, chronic inflammation is being targeted by the pharmaceutical industry, and industrial teams are trying to develop new synthetic anti-inflammatory drugs.

Our view is that this is a dead end. Drugs have an overwhelming tendency to produce adverse effects, and more of these emerge the longer the drugs are used. Very few drugs are safe enough to be used for long-term prevention.

In any case, why wait for the next crop of artificial drugs when you could be eating a natural harvest of fruits, vegetables and oily fish? The diet and supplement combination detailed here is inherently safe, and likely to be far more effective.

Evidence for this comes not only from the tests and extensive research behind this book, but from the mid-Victorians. They ate a diet containing levels of anti-inflammatory compounds roughly ten times higher than we do. As a result, they were almost immune to degenerative disease. Heart attacks and cancer were known but they were rare, occurring at less than 10% of the levels we think of as normal today, and most mid-Victorians had a healthy old age.

Living in the way that we do today almost guarantees that our old age is increasingly compromised by disability and disease.

Many of us might like the idea of living for longer, but not at any cost. The prospect of extending our healthy lives seems much more attractive – quality of life not just length of life.

The chances of achieving this are greatly enhanced by preventing chronic inflammation.

Chronic inflammation is like a series of slow, smouldering fires that gradually burn away healthy tissue and drive us towards illness, disability and premature death.

CRP and the other tests are fire alarms. The right diet, supplements and lifestyle provide you with a set of fire extinguishers.

Now it's up to you.



REFERENCES

- Clayton P, Rowbotham J.** How the mid-Victorians worked, ate and died. *Int J Environ Res Public Health*. 2009 Mar; 6(3):1235-53.
- Cutolo M, Seriola B, Villaggio B, Pizzorni C, Craviotto C, Sulli A.** Androgens and estrogens modulate the immune and inflammatory responses in rheumatoid arthritis. *Ann N Y Acad Sci*. 2002 Jun; 966:131-42.
- Duntas LH et al.** Selenium and Inflammation. *Hormone and Metabolic Research* June 2009
- Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F, Giugliano G, D'Armiento M, D'Andrea F, Giugliano D.** Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA*. 2004 Sep 22;292(12):1440-6.
- García JJ, Bote E, Hinchado MD, Ortega E.** A single session of intense exercise improves the inflammatory response in healthy sedentary women. *J Physiol Biochem*. 2011 Mar; 67(1):87-94.
- Geleijnse, J.M.** et al 2004: Dietary intake of menquinone (Vitamin K2) is associated with a reduced risk of coronary heart disease: The Rotterdam Study. *Am Soc Nutr Science*. May 2004. *Nutritional Epidemiology*
- Joseph JA, Shukitt-Hale B, Denisova NA, Prior RL, Cao G, Martin A, Taghialatela G, Bickford PC:** Long-term dietary strawberry, spinach, or vitamin E supplementation retards the onset of age-related neuronal signal-transduction and cognitive behavioral deficits. *J Neurosci*. 1998 Oct 1; 18(19): 8047-55.
- Kelavkar UP, Hutzley J, McHugh K, Allen KG, Parwani A.** Prostate tumor growth can be modulated by dietarily targeting the 15-lipoxygenase-1 and cyclooxygenase-2 enzymes. *Neoplasia*. 2009 Jul; 11(7): 692-9.
- Knoops KT, de Groot LC, Kromhout D, Perrin AE, Moreiras-Varela O, Menotti A, van Staveren WA.** Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. *JAMA* 2004 Sep 22; 292(12):1433-9.
- Kournikakis B, Mandeville R, Brousseau P, Ostroff G.** Anthrax-protective effects of yeast beta 1,3 glucans. *MedGenMed*. 2003 Mar 21;5(1):1.
- de Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N.** Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation*. 1999 Feb 16; 99(6):779-85.
- Louisiana State University:** Vitamin C Acts as Anti-Inflammatory Agent in Men.
- Mori T.** Omega 3 Fatty Acids and inflammation.
- Rautiainen S, Levitan EB, Orsini N, Akesson A, Morgenstern R, Mittelman MA, Wolk A.** Total Anti-oxidant Capacity from Diet and Risk of Myocardial Infarction: A Prospective Cohort of Women. *Am J Med* 201; 125(10);974-980.
- Rasouli N, Kern PA.** Adipocytokines and the Metabolic Complications of Obesity. *J Clin Endocrinol Metab*. 2008 November; 93(11 Suppl 1): S64–S73.
- Scarmeas N, Luchsinger JA, Mayeux R, Stern Y.** Mediterranean diet and Alzheimer disease mortality. *Neurology*. 2007 Sep 11; 69(11):1084-93.
- Simopoulos AP.** The importance of the omega-6/omega-3 fatty acid ratio in cardiovascular disease and other chronic diseases. *Exp Biol Med (Maywood)*. 2008 Jun; 233(6):674-88. Review.
- Singh U et al.** Vitamin E, Oxidative Stress, and Inflammation. *Annual Review of Nutrition* July 2005
- Stavitsky K, Brickman AM, Scarmeas N, Torgan RL, Tang MX, Albert M, Brandt J, Blacker D, Stern Y.** The progression of cognition, psychiatric symptoms, and functional abilities in dementia with Lewy bodies and Alzheimer disease. *Arch Neurol*. 2006 Oct; 63(10):1450-6.
- Teixeira de Lemos E, Oliveira J, Páscoa Pinheiro J, Reis F.** Regular physical exercise as a strategy to improve anti-oxidant and anti-inflammatory status: benefits in type 2 diabetes mellitus. *Oxid Med Cell Longev*. 2012; 2012:741545.