DR PAUL CLAYTON'S Health Newsletter

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Inflammation:
Beta Glucans
Flavonoids
Omega 3

Salt

Inflammation – the Good, the Bad and the Ugly

Inflammation is a fascinating process. It is a critically important part of the body's defence against invading pathogens and its response to injury; but if an acute inflammatory response is insufficient to clear all the pathogens, or repair the damaged tissues, the acute inflammatory response will eventually be replaced by a chronic inflammatory response.

And chronic inflammation, as we now know, plays a critical role in driving degenerative diseases such as coronary artery disease, hypertension, Alzheimer's, osteoporosis, the arthritides, cancer, obstructive lung disease – the list is a long one.

Because inflammation exerts both positive and negative effects, it is vitally important to keep the right balance of anti- and pro-inflammatory elements. Unfortunately, most of us are not in balance. The on-going pandemics of degenerative disease reveal that we are far too prone to excessive chronic inflammation.

It was not always thus. As regular readers of this newsletter are aware, the degenerative diseases were relatively rare as recently as the 19th century (Clayton & Rowbotham '09); and the tendency to chronic inflammation, and degenerative disease, is a relatively modern phenomenon. It is also easy to remedy.

What made us more prone to chronic inflammation, and more vulnerable to degenerative disease, was the progressive removal of immuno-modulating and anti-inflammatory compounds from the diet. The first step to better health involves putting these compounds back in the food we eat.

Among these, the most important are the **1-3, 1-6 beta glucans**, the **flavonoids**, and the **omega-3** poly-unsaturated fatty acids. These all have different but mutually reinforcing mechanisms of action.

1-3, 1-6 Beta Glucans improve the acute inflammatory response

Yeast-derived 1-3, 1-6 beta glucans increase the effectiveness of the acute inflammatory response. The resulting improvement in the body's ability to deal with pathogens (ie Kournikakis et al '03) and repair tissue damage (Berdal et al '07, Lehtovaara & Gu '11) means that there is less likelihood of a progression to chronic inflammation.

Our intake of 1-3, 1-6 beta glucans has been very significantly reduced, for a range of reasons which include the introduction of the synthetic fungicides circa 1950, micro-filtration in brewing in the 1960s, and our declining consumption of bread.

The uncontrollable increase in asthma and allergy since 1950 (Haahtela et al '01, Mannino et al '02) is indirect but clear evidence of inadequate intakes of the 1-3, 1-6 beta glucans and widespread beta glucan depletion (Kirmaz et al '05).

There is an overwhelming public health case to fortify all of our flour-based foods with these immune-modulating compounds, but until our idiot governments start to take public health seriously you would be well advised to add them to your own diet in supplement form.

Flavonoids block inflammatory enzymes

The flavonoids, pluri-potent compounds that occur in many plant foods, are also powerful anti-inflammatory agents.

They work by blocking some of the most important inflammatory enzymes, inhibiting COX-1 and COX-2 (the same enzymes blocked by common analgesic drugs such as aspirin and ibuprofen), LIPOX-5 and LIPOX-8, and, unlike the analgesics, the crucial matrix metallo-proteases (MMPs).

This wide spectrum of anti-inflammatory activity makes them far better at protecting tissues such as cartilage from inflammatory breakdown, although here I cannot quote you chapter and verse as the requisite clinical trials have not been done. I am forced to rely on a plethora of clinical reports, and my own personal experience.

Our intake of flavonoids has also declined; although this decline started rather earlier than the decline in 1-3, 1-6 beta glucans and can be traced back as far as the 19th century (Clayton & Rowbotham '09).

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Complementary anti-inflammatory action of Omega-3

The Omega-3 fatty acids have a different but complementary anti-inflammatory mode of action.

The fatty acids in cell membranes are substrates for the enzymes listed above. When these enzymes break down saturated or Omega-6 fatty acids in our cell membranes they generate inflammatory metabolites such as IL-1 beta, IL-2, IL-6 and TNF-alpha; when they break down Omega-3 fatty acids they form anti-inflammatory metabolites (Colin et al '03, Simopolous et al '08).

If Omega-3 fatty acids predominate in cell membranes we tend not to suffer from chronic inflammation, and are protected against degenerative disease. If Omega-3 fatty acids are in the minority, and our cell membranes are dominated by saturated and Omega-6 fatty acids, we are more likely to suffer from chronic inflammation and degenerative disease. This is particularly true in individuals with specific genetic vulnerabilities, such as those with variants of delta-6-desaturase and delta-5-desaturase (Schaeffer et al '06).

The relative amounts of the different fatty acids in our cell membranes are determined by the relative amounts of the different fatty acids in our diet, and this has changed dramatically over the last century or so (Clayton & Rowbotham '09, Blasbalg et al '11).

More Omega-6, less Omega-3 now in our diets

For example, the estimated per capita consumption of soybean oil increased more than 1000-fold from 1909 to 1999, whereas consumption of oily fish declined. Accordingly, intakes of the Omega-6 fatty acid linoleic acid (LA) increased from 2.79% to 7.21% of energy, and intakes of the plant-derived Omega-3 precursor alpha-linolenic acid (ALA) increased from 0.39% to 0.72% of energy. But there were substantial declines in intakes (as a percentage of energy) of the essential Omega-3 poly-unsaturated fatty acids (PUFAs) eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA).

In the typical Western diet the ratio of Omega-6 to Omega-3 essential fatty acids in the diet (and therefore in the cell membranes) is now as high as 15 or even **17 to 1**. This excessive Omega-6/Omega-3 ratio drives the pathogenesis of many diseases, including cardiovascular disease, cancer, depression, and inflammatory and autoimmune diseases (Simopolous '08, Sublette et al '06, Colin et al '03).

Conversely, a lower ratio improves tissue function and controls many disease states. For instance, whereas a ratio of 10:1 or higher exacerbates asthma, a lower ratio of 5:1 has a beneficial effect on patients with asthma and a ratio of 2-3:1 suppresses inflammation in patients with rheumatoid arthritis (Simopoulos '02).

To optimise immune and inflammatory function, and thereby dramatically reduce the burden of disease, we should all increase our intakes of beta glucans, flavonoids and Omega-3 fatty acids.

Alternative Omega-3 sources

But while producing (and eating) more beta glucans and flavonoids is relatively easy, there is a limit to the amount of Omega-3 fatty acids we can haul out of the seas. In fact, if you do the math, there is not enough fish in the sea to feed every human even the minimum 250 mg intake that many countries are recommending, and not nearly enough to provide the 5 grams or more that science now indicates is needed for optimal health. In order to provide enough EPA and DHA to support the human population, we will

need to find alternative sources. One such source has been identified. This is the flowering plant Echium plantagineum, aka **Purple Viper Bugloss** or **Blueweed**.

Ecchia vulgare is a weed native to most of Europe, and western and central Asia. It is also common in North America. It grows wild and free, but in the very near future you will be seeing this plant being grown intensively in fields near you – because it is an excellent source of an Omega-3 fatty acid called **stearidonic acid (SDA)**.

Stearidonic acid is a minor Omega-3 fatty acid in fish, making up only about 0.5-2% of total fatty acids (Simopolous '08), but it occurs in echium seed as 12.5% of total fatty acids (Chilton et al '08). And now we have to look (briefly!) at some biochemistry.

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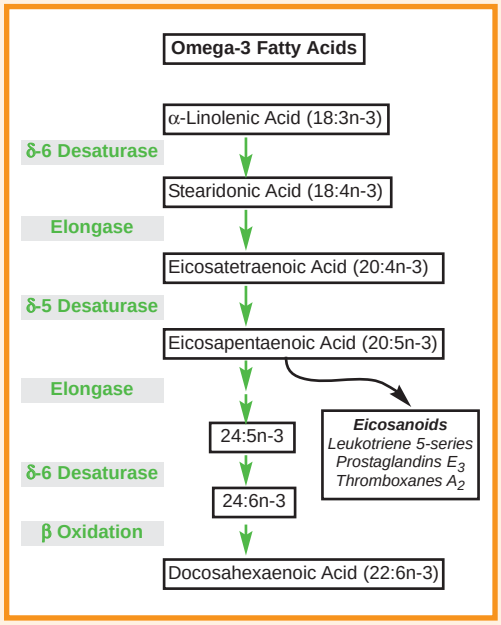
Biochemistry of Omega-3

In the body, the most basic plant-derived Omega-3 fatty acid alpha-linolenic acid (ALA) can be metabolised to the essential Omega-3 fatty acids EPA and DHA, but it is a complex and inefficient 3-step process.

Alpha-linolenic acid (ALA), is not a good source of the essential Omega-3s EPA and DHA. This is because the conversion of ALA to EPA requires a chain of three different enzyme-catalysed reactions (right), and is very inefficient; only **5%** of ALA is converted in the body to EPA.

And this is because the rate-limiting first step in the reaction chain – the enzyme delta-6-desaturase, which converts ALA to the intermediate fatty acid SDA – is very ineffective. This is why so-called 'health foods' such as flaxseed or evening primrose oil, which are chock-full of ALA, are not worth bothering with. They offer no protection whatsoever against heart disease (Ramsden et al '11, Vedtofte et al '11), and are highly unlikely to have any other benefits at all.



The next two steps in the reaction chain involving the enzymes elongase and delta-5-desaturase are much more efficient. The body converts about 30% of dietary SDA to EPA (James et al '04), making SDA 6 times more effective as a source of the essential Omega-3s than ALA.

The high efficiency of conversion means it should be possible to consume stearidonic acid as a good substitute for fish oils (if fish oils become too expensive or disappear altogether), to optimise our cell membranes and thereby protect us from excessive inflammation.

Human studies confirm this. Stearidonic acid can be used as a precursor to increase the EPA content of human lipids and cell membranes; and is up to 5 times more effective at doing this than alpha-linolenic acid (Miles et al '04, Horia et al '05, James et al '03).

SDA not only offers us an inexpensive, natural and land-based way to achieve better health (Harris et al '08), but is also clean-tasting, and eminently suitable for vegetarians and vegans.

What is more, there is evidence that SDA has anti-inflammatory (Kockmann et al '89, Guichardant et al '93, Horia et al '05), cardio-protective (Chilton et al '08, Whelan et al '09) and cancer-protective (Petrick et al 2000, Kelavkar et al '09) benefits of its own, ie outside its ability to act as a precursor for the essential Omega-3 fatty acids.

The case for Omega-3 supplementation

I will end on a political note. The Omega-3 story has been building for many years, thanks to the work of such eminent scientists as Professors Michael Crawford, John Stein, Joe Hibbeln and Helga Refsum; but even though the science to support wide-spread supplementation of the Western diet with Omega-3s is overwhelmingly strong, the politicians who profess an interest in public health have ignored it. They don't care that our unbalanced diet is not only harming us physically, but also making a huge contribution to our burden – individually and socially – of depressive illness and suicide. One of the most common disorders of our times – **depression** – is unequivocally related to a diet depleted in Omega-3 fatty acids (Tanskanen et al '01a, '01b, De Vriese et al '04, Huan et al '04, Sublette et al '06, Hibbeln at al '09), and responds well to Omega-3 supplementation.

But now the military are involved. Suicide rates among US military personnel on active duty are at record numbers, doubling since Operations *Enduring Freedom* (Afghanistan) and *Iraq Freedom* (Iraq). The Pentagon is concerned that the recent escalation of US military suicide deaths to record numbers is not only seriously bad PR but is also impairing the effectiveness of their foreign policy adventures, and has accelerated the search for reversible risk factors.

In a recent study they found, firstly, that their boys and girls had VERY low levels of Omega-3 fatty acids in their blood; in other words, the serving personnel were eating the usual junk provided by the cheapskates and profiteers who run the army catering corps. And secondly, they found that those with the lowest levels of Omega-3s in their blood were the most at risk of committing suicide (Lewis et al '11).

Extrapolating from this military study, it seems very likely that the current pandemic of depressive illness and self-harm up to and including suicide is exacerbated by the huge quantities of soybean and other vegetable oils we consume, and the diminishing amount of fish oils. And this, in turn, emphasises the potential importance of stearidonic acid.

I first understood what stearidonic acid could do back in the mid-80s, and made enquiries with a UK-based company that was starting to grow Bugloss to extract the SDA-containing oil. I wanted to use this oil in supplements and in functional foods because I knew a number of depressive patients who were vegetarian and would not eat fish or fish oil. The regulators, however, would not allow it. Bugloss was not a food plant, they said, the oil was experimental and could not be fed to humans. I told them the oil was pure, had been fully characterised, that SDA was a natural part of human fatty acid metabolism. In vain. Idiot bureaucracy won the day, and has contributed to too much depression, too many deaths, and too much antisocial behaviour since then.

The St Louis-based agri-biotech company Monsanto has now developed an even richer source of SDA, from genetically modified soy beans. This new soy oil, called Soymega SDA, has already been shown to increase levels of EPA and DHA when consumed by humans (Harris et al '08, Lemke et al '10). Alternatively it can be used to improve the nutritional profile of foods we eat, as it also boosts EPA and DHA levels when fed to fish (Bharadwaj et al '10, Codabaccus et al '11), chickens (Rymer et al '11) and cows (Bernal-Santos et al '10), to produce Omega-3 enriched milk.

There are not enough fish in the sea. To provide enough EPA and DHA to support the human population, we need alternative sources. **Purple Viper Bugloss**, **GMO plants** and **Soymega SDA** will all be needed to meet this growing demand.

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Shock horror! New study finds salt reduces heart disease!?

I have written before about the insidious dangers of consuming too much salt, and now to undo all the good work, here comes a study, reported in a very good journal, that says the opposite (Stolarz-Skrzypek et al '11). The new findings showed that higher salt intakes protected against heart attacks and stroke!

This study made the headlines, and many of you wrote in to ask if the salt shaker should be put back on the table.

The short answer is – **NO**.

To begin with, the study's findings fly in the face of a multitude of other studies conducted over the past 25 years that show a clear and direct relationship between high salt intakes, high blood pressure, and cardiovascular disease risk (ie WCRF '07, He & MacGregor '09). And the authors' claim that previous estimates of the hundreds of thousands of lives that could be saved by reducing salt intake (ie Strazullo et al '09, Brown et al '09) were wrong, should itself be taken with a shovel-full of salt.

Leading scientists have torn the Stolarz-Skrzypek study apart. It was far too small to support the authors' conclusions, and was based on only a few per cent of the numbers that first proved the salt / heart disease link in the famous North Karelian trials (Karpannen et al '05, Karpannen & Mervaala '06). Sodium intakes were estimated from a single measurement at the start of the study, an approach which is both incomplete and misleading. And critically, other important diet and lifestyle variables were not allowed for.

In short, the European researchers were trying to ask questions that their data could not have answered, and were way out of their depth.

Salt, or more specifically **excessive sodium**, is still a major contributor to unnecessary heart and stroke deaths. In fact, a much larger and better controlled new study published in parallel with the Stolarz-Skrzypek paper found that people who eat high sodium, low potassium diets have a higher risk of dying from a heart attack or indeed from any cause (Yang et al '11).

Potassium and magnesium form healthy salts. They are the key salts in fruits and vegetables and the constituents of PanSalt, the salt substitute that has done so much to reduce unnecessary cardiac deaths in Finland.

Sodium and potassium, in particular, have opposite effects on heart health. High salt (sodium) intakes increase blood pressure, contributing to heart disease; high potassium intakes help relax blood vessels and decrease blood pressure. Our bodies need far more potassium than sodium to stay healthy, but the modern (processed) diet provides the opposite ie. more sodium than potassium.

The Yang study, which was based on participants in the National Health and Nutrition Examination Survey, followed over 12,000 men and women for an average of 15 years. Sodium intakes averaged about 4,300 milligrams per day in men and 2,900 milligrams a day in women. Potassium intakes were lower (3,400 mg for men and 2,400 mg for women), and substantially lower than the 4,700 milligrams per day that is generally recommended.

People with the highest ratio of sodium to potassium in their diets had double the risk of dying of a heart attack than people with the lowest ratio, and they had a 50% higher risk of death from any cause.

Given that processed foods are responsible for much of people's sodium intake in the developed nations, health agencies have started working with food manufacturers to lower sodium levels. The salt industry, however, continues to argue that salt has little influence on blood pressure (IoM '10), and spends surprising amounts of money on lobbying our honest and incorruptible politicians.

You will be a long time waiting for anything sensible to come out of Westminster or Brussels, so I would advise you to take matters into your own hands and change your diet yourself – if you have not already done so.

When advising on dietary change, the media places a good deal of emphasis on 'eating the colours', in articles written by health journalists who have little understanding of their subject matter.

The rationale for this advice is that many of the carotenoids and flavonoids linked to better health are coloured, and are used by plants as sun-screens and signalling compounds. But while eating berries is certainly a good thing, and does provide the phytonutrients cited above, they are not necessarily the best sources of potassium and magnesium.

Better are the bulkier, and less glamorous, **apples and pears**. According to a study just published in Stroke: Journal of the American Heart Association (Oude Griep et al '11), higher intakes of **white fruits and vegetables** protect against stroke; while green, yellow/orange and blue/purple fruits and veg do not.

This study, carried out by an excellent team at the University of Wageningen (one of my favourite campuses), included 20,069 men and women aged 20 to 65 years who were free of cardiovascular diseases at baseline, and followed them for ten years. Each 25-grams/day increase in white fruit and vegetable consumption was associated with a 9% lower risk of stroke. Apples and pears were the most commonly consumed white fruit and vegetables (55%), and simple maths indicates that a 100g apple (or pear) a day can reduce the risk of stroke by a whopping 36%.

I have long been fascinated by Dutch names, many of which were originally chosen as jokes and in response to the French arrogance during the 18th century when Holland was occupied by the French. This is the nation that gave us footballers with names that translate as Rice-Hills, Sour-Beer, Leg-Breaker and Mountain-Camp. I will sign off by observing fondly that the authors of this excellent paper include Messrs. Ancient-Flu, Crooked-Wood and Freshly-Scrubbed. *Groetjes!*

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