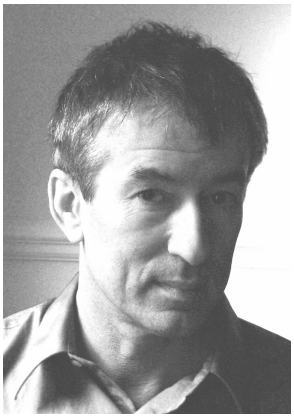

Dr Paul Clayton's Health Newsletter

The Way to Health—a Road Map

Our society is very sick and very fat, and it is getting sicker and fatter.

An authoritative and depressing study recently predicted, on the basis of current trends, another 76 million obese adults by 2030 with an additional 6 to 8.5 million cases of diabetes, 6 to 7 million cases of cardiovascular disease and 492,000 to 669,000 cases of cancer in the UK and USA alone (Wang et al '11). This huge burden of disease will cause dramatic and unaffordable increases in health care costs, already out of control at a fifth of GNP. Things do not get any better after 2030; leaders in these fields forecast that by 2050 the incidence of diabetes will double (Boyle at al '10), while Alzheimer's Disease (Alzheimer's Assocn '12) and cancer (Bray & Moller '06) will triple. In technical terms, we are going to hell in a handcart.

Given the growing mis-match between our spiralling healthcare costs and the wider economic environment, we will soon arrive (many would say we have already arrived) at an inflection point. We cannot blindly continue, as we have been doing for the last century, to medicalise and medicate our lives. Developing new drugs to treat the symptoms of these rising tides of disease is like applying new coats of paint to crumbling plaster while the foundations of the house disintegrate and rot.

We must return to basics and rebuild the foundations—which means re-designing our lifestyles and diets. The science we need to do this is already in place, and it is only political hurdles that are preventing the emergence of a far more effective and cost-effective system of healthcare than the one we now suffer under.

There is an emerging consensus that almost all the major diseases have, at their core, a common cause: **chronic inflammation**. Depending on your diet, lifestyle and to some extent your genes, continuous low-grade **inflammation** damages and destroys:-

►the linings of the arteries, leading to **hypertension**, **stroke**, **coronary artery disease**
►brain cells→**dementia** ►bone→**osteoporosis**
►cartilage → osteo- and rheumatoid **arthritis**
►the linings of the airways → **asthma**
►cells→**cancer**, **auto-immune disease** etc

This new Grand Unified Theory of Disease is transforming modern medicine just as the Grand Unified Theory of Forces transformed modern physics – and its implications are staggering. It shows that the tides of chronic illness we see today are unnecessary. It also shows that our apparently unavoidable and increasing risk of acquiring a so-called 'disease of ageing' as we get older is entirely artificial, something that could be neutralised if we could find a way of suppressing the chronic inflammation that sickens and kills so many of us.

"Recognition of chronic inflammation as a common cause for almost all the major diseases represents a new Grand Unified Theory of Disease."

Big Pharma makes a very good living from chronic inflammation. In 2010, global sales of drugs against overtly inflammatory diseases (asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease etc.) amounted to over $35 **b**illion.

Now consider the vast numbers of people (between a quarter and a third of the population!) who suffer from intermittent or chronic pain (IoM '11). The primarily anti-inflammatory NSAID painkillers take the drugs bill up above $100 billion. Most of the rest of the drugs on offer do little more than suppress the diseases caused by chronic inflammation; and now we have a total global drug economy (Fig.1 over) worth in excess of **$720 billion**.

And as with *petrodollars* and *cocabucks*, *pharmadollar*s can be extremely destructive. Over 100,000 deaths a year are caused by adverse drug effects in the US alone (Lazarou et al '98) and another 100,000 die as a result of medical errors and other causes due to the medical treatment of avoidable diseases (Starfield '00).

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The Paul Clayton Health Newsletter

- Easy to read
- All references on the back page
- Up-to-date news and design
- Pioneering and insightful approach
- Inimitable no-holds-barred style

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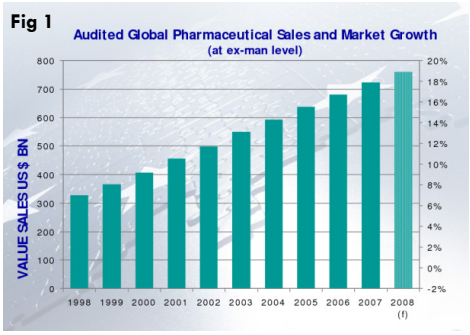
Pharmadollars are also deeply implicated in the systemic corruption of regulatory and educational systems. For example, regulators such as EFSA and the FDA arbitrarily restrict manufacturers of food and supplements from

"A Mediterranean Diet with its high levels of anti-inflammatory nutrients reduces the risk of many diseases by around 50%."

Fig 1



giving out information to the public that people could use to materially improve their health; if I was on the Uni-Vite payroll I would not have been allowed to write this newsletter.

As the playing field is so sharply tilted to favour Big Pharma, and as public health has suffered so much as a result, the obvious answer is to take matters into your own hands. Beating chronic inflammation via nutrition is cheap, easy, safe and considerably more effective than relying on the tender mercies of the current healthcare model.

Numerous pre-clinical studies show that when animals are fed diets containing higher levels of the key anti-inflammatory nutrients, their risk of developing the signs and symptoms of the degenerative diseases linked with ageing diminishes dramatically (Willis et al '09, Latour et al '13).

"Over 100,000 deaths are caused by adverse drug effects every year in the USA alone, and another 100,000 die as a result of medical errors and other causes due to the medical treatment of avoidable disease."

There is little doubt that humans react in the same way; similar findings have emerged in a range of multi-national epidemiological studies. A Mediterranean Diet, for example, which contains higher levels of anti-inflammatory compounds than occur in our depleted Western diet, reduces the risk of many diseases by around 50% (ie de Lorgeril et al '99, Knoops et al '04, Varraso, Fung, Barr et al '07, Gu et al '10).

The take-home message is obvious. Increase your intake of the key anti-inflammatory nutrients – either in food or in supplements – and reduce your exposure to pro-inflammatory factors.

That means stopping smoking; taking moderate exercise; cutting back on sugary and starchy foods; switching from deep fried, grilled and barbecued to steamed, stewed foods.

Then enjoy good health!

Ask Dr Clayton — Should we ta

As recently as the turn of the century, there was no medical consensus on the thorny subject of aspirin and cancer. A few scientists were suggesting that aspirin might be chemo-protective but the majority of medics were sceptical or downright hostile. How could aspirin, an old-fashioned, out-of-patent (hence unprofitable) medicine protect against one of the most feared and most common of diseases?

In fact, the first hints that aspirin might reduce cancer risk emerged from trials designed to measure its cardio-protective effects, which found – to the surprise of the researchers – that myocardial and cancer deaths were both reduced by aspirin (Peto et al '88, MRC '98).

But the fact that aspirin was rapidly becoming an important weapon in the fight against heart attacks initially cut little ice in cancer circles. If anything it made the cancer claims seem even more outlandish. The current medical model is very specific, and purportedly relies on precisely machined magic bullets to hit very specific targets. The fact that this strategy kills huge numbers of patients (Starfield 2000 see p.1) is embarrassing but irrelevant; the current medical paradigm rules out the very concept of a panacea.

Aspirin not a drug but a phytonutrient?

Aspirin, however, is no ordinary drug. In fact, it can be argued that aspirin is not a drug at all but a phytonutrient.

Many people know that salicylic acid was first identified in **willow bark**, a traditional treatment for arthritis, but there are many other plant sources. Salicylates are found in abundance in most spices, many types of fruit and some vegetables, and – like other phyto-nutrients – are actually plant defence compounds.

Salicylic acid is involved in defending against dehydration, for example, and closes leaf stomata so that water loss is reduced during dry spells. [This is why adding aspirin to the water in a vase delays wilt in cut flowers.]

Salicylates are also part of the plant's defence against harmful microbes; when a plant is attacked it produces salicylates which in turn trigger the production of anti-pathogen proteins. Some salicylates pass through the plant, transferring resistance from the infection site throughout the rest of the plant's leaves and roots. Others, such as the volatile compound methyl salicylate, trigger defence

...ke aspirin to protect against CANCER as well as HEART DISEASE?

activity in neighbouring plants before the infection can even reach them.

Salicylates—and the modified salicylate aspirin—are very like vitamins

Aspirin is a slightly chemically modified version of salicylic acid. Adding an acetyl group makes it slightly less prone to causing gastric irritation, but not completely safe; indeed aspirin and related NSAIDs are the most common cause of adverse drug reactions requiring hospitalisation, due to gastrointestinal bleeding.

But that is beside the point. The main fact is that salicylate, and by implication aspirin, is very like a vitamin. The definition of a vitamin is something that we need to maintain health, and cannot make in our own bodies but must obtain, in trace amounts, from our diet. Salicylate fits this description. We cannot make it ourselves but must obtain it in small amounts from our diet, and, judging by our experience with aspirin, it extends our healthy life expectancy by reducing the risk of some very major chronic degenerative diseases.

If we consider aspirin as a phytonutrient rather than a drug, the idea that it can confer such generalised protection is not so outlandish after all. And given our new understanding of the role of chronic inflammation in causing degenerative disease, aspirin may be protecting us via an anti-inflammatory mechanism, such as the inhibition of the pro-inflammatory and cancer-promoting enzyme COX-2 (Sheehan et al '99). COX-2 is also involved in angiogenesis, a key process in cancer growth and spread (metastasis); so here is another way in which aspirin and other COX-2 blockers might slow or prevent cancer growth.

But how relevant is this to clinical practice?

Clinical trials on aspirin in cancer

There have been many clinical trials of aspirin in cancer during the last decade, and lately the pace is picking up. In the spring of last year, no fewer than three studies were published in The Lancet journals by an eminent Oxford University group, which, together with their earlier work, formed a rather convincing case for the drug/phytonutrient in cancer prevention (prophylaxis) and management.

Preventing cancer and its spread

One paper looked at the effect of aspirin in preventing cancer. It was a meta-analysis of 51 trials, involving more than 77,000 patients, comparing people who took aspirin every day with people who took no aspirin. This showed that taking daily low-dose aspirin (less than 300mg) for 3 years or more cut the risk of developing any type of cancer by roughly 25% (Rothwell et al '12a).

The second and third papers looked at the effect of aspirin on cancer spread. These found that during an average 6½ years of taking aspirin (75mg+ a day), the risk of metastatic (spreading) cancer was cut by up to 46%. Aspirin also lowered the risk of non-metastatic cancer progressing to metastatic cancer, especially in patients with colon cancer; and there was significantly lower risk of cancer and metastasis in colon, throat, gastric, biliary and breast cancer (Algra & Rothwell '12, Rothwell et al '12b).

These studies provided important evidence that long-term daily low-dose aspirin lowered the risk of developing cancer, but this does not mean that everyone should start taking aspirin. As with cardio-protection, we need to be a little more specific. Some individuals are particularly prone to gastric bleeds with aspirin, and they should be very cautious about aspirin prophylaxis. And as aspirin has an anti-clotting effect, it should not be used by anyone with uncontrolled hypertension or a history of haemorrhagic stroke.

Aspirin for certain specific cancer therapies

Cancer research is moving in a parallel direction, ie it is also becoming more specific. Aspirin appears to be particularly effective at reducing the risk and spread of colorectal cancer, but new research shows that this does not mean that every colorectal cancer patient should take aspirin. A follow-up paper from the Oxford group shows that aspirin prophylaxis is only effective in patients with the genetic marker mutated PIK3CA (Langley & Rothwell '13), a marker which otherwise denotes poor prognosis. And although preliminary evidence suggested that aspirin might have a role in breast cancer, a recent large prospective observational study found no relationship between aspirin use and breast cancer incidence in post-menopausal women (Zhang et al '12).

In many cancers, however, aspirin and similar anti-inflammatory drugs are already being used, generally in conjunction with other therapies. Aspirin plus radiotherapy seems to be a useful combination (Kim et al '03), as does aspirin plus anti-cancer monoclonal antibodies (Pennarun et al '13).

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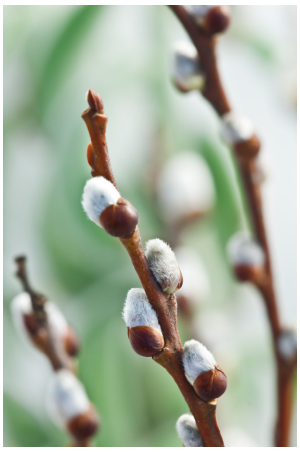
Low-dose aspirin contains about 80 mg of aspirin, roughly a quarter of the full-strength version.



Aspirin was developed from salicylic acid, found in willow bark

"If we consider aspirin as a phytonutrient rather than a drug, the idea that it can confer such generalised protection is not so outlandish after all."

continued from p3

The Dr Paul Clayton Health Newsletter describes developments in the new field of pharmaco-nutrition, where nature and science are combined to offer non-drug solutions to degenerative disease.

The newsletters are intended to increase knowledge and awareness of health issues and are for information only. No health claims for specific products are made or intended and the information should not be used as a substitute for medical advice.

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For **healthy individuals**, any reduction of cancer risk must be offset against the increased risk of haemorrhage, typically in the gut or less frequently the brain. This risk is real, as was shown in a prospective cohort study of 200,000 subjects in Italy where low dose aspirin use was associated with a 50% increase in bleeds (de Berardis et al '12). This means that about 1 in 769 people treated with low-dose aspirin suffer significant bleeding. But because cancer is so common in our unhealthy age, medics are increasingly recommending that new guidelines be issued to recommend the wider use of low-dose aspirin in healthy adults.

So where do we go from here?

Improve aspirin pills?

Well, aspirin pills could be improved, because not all aspirin is the same. There are different isomers of aspirin, specifically there are ortho-, meta- and para- versions of the acetyl salicylic acid molecule; and these have rather different biochemical effects. Of these three forms, only the ortho-isomer generates a permanent inhibition of COX-2 (Kodela et al '13). This strongly suggests that a more refined form of aspirin, consisting only of the ortho-variant, would pack a more powerful anti-cancer punch. This would allow the use of lower doses, and might reduce the risk of gastric and other bleeds.

Or look at other therapeutic phytonutrients

Or we could be more ambitious, and look at other phytonutrients with even better therapeutic profiles. It is well known that diets rich in fruits and vegetables reduce the risk of almost all cancers, and while such diets contain above-average levels of salicylates, they also contain above-average levels of many other chemo-protective compounds such as the **polyphenols**.

Salicylic acid is a phenolic compound, distantly related to polyphenols such as the flavonoids (for instance, curcuminoids), which have a range of similar but better properties. Like salicylic acid, the polyphenols are anti-inflammatory agents, and like salicylic acid, they protect against heart disease and cancer, and Alzheimer's, and many other disease besides. And far from causing bleeding and ulceration, they actively protect against it (ie Mahattanadul et al '09).

In short, I am pretty sure that modern medicine has barked up the wrong willow tree. The focus on aspirin, due to its medicalisation by Bayer back in the 1890s, has been a missed opportunity; the related polyphenols were discovered 40 years later, by which time the pharmaceutical business had already begun to dominate medical training and practice, and hence these critically important natural products were mostly ignored.

In any case, I do not share my colleagues' new-found enthusiasm for aspirin. **I believe that non-medicinal prevention should be prioritised**. Smoking cessation, the avoidance of distilled spirits, regular exercise, maintaining a healthy weight and a healthy diet, including food supplements, should be the first steps in any cancer prevention programme.

If that diet is designed to reduce levels of the pro-inflammatory compounds formed in fast foods, and to provide high levels of polyphenols and the other chemo-protective phytonutrients, the evidence suggests that we could reduce the cancer burden by up to 90% (Clayton & Rowbotham '09).

REFERENCES

P1-2 Way to Health

Alzheimer's Association. 2012 **Alzheimer's disease facts and figures.** Alzheimers Dement. 2012;8(2):131-68.

Boyle JP et al. **Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence.** Population Health Metrics 2010;8:29.

Bray F, Møller B. **Predicting the future burden of cancer**. Nature Reviews Cancer 2006;6:63–74.

Gu Y, Luchsinger JA, Stern Y, Scarmeas N. **Mediterranean diet, inflammatory and metabolic biomarkers, and risk of Alzheimer's disease.** J Alzheimers Dis. 2010;22(2):483-92.

IoM 2011. Inst of Medicine of Nat Academies Report. **Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research.** Washington DC: The National Academies Press.

Knoops KT et al. **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.

Latour A et al.**Omega-3 fatty acids deficiency aggravates glutamatergic synapse and astroglial aging in the rathippocampal CA1**. Aging Cell. 2013 Feb;12(1):76-84.

Lazarou J, Pomeranz BH, Corey PN **Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies.** *JAMA* (April 1998);**279** (15): 1200-1205

de Lorgeril M et al. **Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report Lyon Diet Heart Study.** Circulation. 1999 Feb 16;99(6):779-85.

Starfield B. **Is US health really the best in the world?** JAMA Jul2000;**284**(4):483-5.

Varraso R, Fung TT, Barr RG, Hu FB, Willett W, Camargo CA Jr. **Prospective study of dietary patterns and chronic obstructive pulmonary disease among US women.** Am J Clin Nutr. 2007 Aug;86(2):488-95

Wang YC, McPherson K, Marsh T, Gortmaker SL, Brown M. **Health and economic burden of the projected obesity trends in the USA and the UK.** Lancet 2011;378:815–25.

Willis LM, Shukitt-Hale B, Joseph JA. **Recent advances in berry supplementation and age-related cognitive decline.** Curr Opin Clin Nutr Metab Care. 2009 Jan;12(1):91-4. Review.

P2-4 Aspirin and cancer

Algra AM, **Rothwell** PM. **Effects of regular aspirin on long-term cancer incidence and metastasis: a systematic comparison of evidence from observational studies versus randomised trials.** Lancet Oncol. 2012 May;13(5):518-27. Review.

De Berardis G et al. **Association of Aspirin Use With Major Bleeding in Patients With and Without Diabetes.** *JAMA*. 2012;307(21):2286-2294.

Clayton P, Rowbotham J. **How the mid-Victorians worked, ate and died.** Int J Environ Res Public Health. 2009 Mar;6(3):1235-53

Kim KY, Seol JY, Jeon GA, Nam MJ. **The combined treatment of aspirin and radiation induces apoptosis by the regulation of bcl-2 and caspase-3 in human cervical cancer cell.** Cancer Lett. 2003 Jan 28;189(2):157-66.

Kodela R et al. **Positional isomers of aspirin are equally potent in inhibiting colon cancer cell growth: differences in mode of cyclooxygenase inhibition.** J Pharmacol Exp Ther. 2013 Apr;345(1):85-94.

Langley RE, Rothwell PM. **Potential biomarker for aspirin use in colorectal cancer therapy.** Nat Rev Clin Oncol. 2013 Jan;10(1):8-10.

Mahattanadul S et al. **Comparative antiulcer effect of bisdemethoxycurcumin and curcumin in a gastric ulcer model system.** Phytomedicine. 2009 Apr;16(4):342-51

MRC General Practice Research Framework. **Thrombosis prevention trial: randomised trial of low-intensity oral anticoagulation with warfarin and low-dose aspirin in the primary prevention of ischaemic heart disease in men at increased risk**. Lancet. 1998;351:233–241.

Pennarun B et al. **Targeting FLIP and Mcl-1 using a combination of aspirin and sorafenib sensitizes colon cancer cells to TRAIL.** J Pathol. 2013 Feb;229(3):410-21

Peto R et al. **Randomised trial of prophylactic daily aspirin in British male doctors.** Br Med J (Clin Res Ed) 1988;296:313–316.

Rothwell PM et al. **Short term effects of daily aspirin on cancer incidence, mortality, and non-vascular death: analysis of the time course of risks and benefits in 51 randomised controlled trials.** Lancet. 2012a Apr 28;379(9826):1602-12.Review.

Rothwell PM, Wilson M, Price JF, Belch JF, Meade TW, Mehta Z. **Effect of daily aspirin on risk of cancer metastasis: a study of incident cancers during randomised controlled trials.** Lancet. 2012c Apr 28;379(9826):1591-601.

Sheehan KM, Sheahan K, O'Donoghue DP, MacSweeney F, Conroy RM, Fitzgerald DJ, Murray FE. **The relationship between cyclooxygenase-2 expression and colorectal cancer.** JAMA. 1999 Oct 6;282(13):1254-7.

Zhang X et al. **Use of aspirin, other non-steroidal anti-inflammatory drugs and acetaminophen and post-menopausal breast cancer incidence.** J Clin Oncol. 2012 Oct 1;30(28):3468-77.