



DR PAUL CLAYTON'S

Health Newsletter

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Big Pharma
Stupid? Ignorant?
Criminal?

End of the Age of
Antibiotics?

Big Pharma - Stupid, Ignorant or Criminal?

I spend a lot of time researching the pharmacological effects and therapeutic applications of food derivatives, but every now and then I look over my shoulder at the pharmaceutical industry to see what it is getting up to. I try to keep up with the latest developments and scandals, and this newsletter presents my latest analysis.

The pharma model isn't working: we're getting sicker

Today's "baby boomers", the generation currently in their 60s, 70s and 80s, make up the first generation since 1900 to be less healthy than the generation before them. They are fatter, weaker and sicker than their parents. Those currently in this age group are more susceptible to debilitating diseases than were previous generations of elders, with problems stemming primarily from poor diet and lack of proper exercise.

The combination of disease and unfitness is creating enormous socio-economic problems, by dramatically increasing the numbers unable to perform normal daily activities. Ten years ago, 12% of over-60s required assistance to carry out routine daily activities such as walking a quarter mile, climbing a small flight of stairs, or even getting out of a chair. Today, that figure has risen to an alarming 20% (Seeman et al '10).

Technological advancements have played a significant role. As Americans and Brits have increasingly been weaned off physical labour and instead placed in front of computer screens, the level of physical activity among the population has dropped significantly. People's calorific needs have declined, and this, too often combined with poor food choices, means that their nutritional standards have declined. Type B malnutrition is now rife.

Ironically, the technological advancements that benefited the Baby Boomers when they were younger are proving to be their downfall in later life.

And if anything, things are getting worse. Due to increasing use of the internet and games consoles, and more obesity, children's fitness levels are falling – and nowhere more rapidly than in Britain. Levels have been falling by around four per cent per decade on average worldwide, but in the UK they have plummeted by eight per cent (Sandercock et al '10).

"Children don't climb trees or use their bikes any more",

said the researchers. "They are inactive." Guidelines recommend children undertake at least 60 minutes of moderate to vigorous exercise a day, including taking part in sports, brisk walking and running – but children today are managing less than a quarter of that.

These findings indicate that as this new generation of children age, they will be fatter, weaker and sicker even



than the baby boomers; a deterioration in public health similar to the one that occurred towards the end of the 19th century (Clayton & Rowbotham '08) that will have equally devastating consequences for social well-being and health care costs as we stagger towards the 2050s.

The only way to prevent the slide into national decay is to promote increased levels of physical activity and better eating habits. Drugs will not and cannot solve these severe individual and public health problems.

The pharma model is dangerous

The adverse effects of drugs harm and kill substantial numbers of people. For example, one in every five patients readmitted to the hospital within a year of an inpatient treatment ends up there because of an adverse drug reaction (ADR), according to a study conducted by researchers from the Royal Liverpool and Broadgreen University Hospitals NHS Trust (Davies '09).

When ADRs occurring in hospital are included, the dangers of adverse reactions are even more substantial. One of the best papers of its kind is a

huge meta-analysis of no fewer than 39 prospective studies in American hospitals (Lazarou et al '98). This paper found an overall incidence of serious ADRs occurring in 6.7% of patients, and fatal ADRs in 0.32%. These are large numbers: they equate to around 2,216,000 serious ADRs and 106,000 deaths per year, and make ADRs one of the top 6 causes of death.

The authors said, rather coyly, "These data suggest that ADRs represent an important clinical issue."

Big Pharma - Inefficient and Corrupt?

The drugs industry justifies the costs of its products by telling us how much they must spend on research, but according to a recent study (Gagnon & Lexchin '08), Big Pharma spends almost twice as much on promotion as they spend on research and development. In 2004 the industry spent \$57.5 billion on marketing and promotion; compared to \$31.5 billion spent on research. The industry also spends lavishly on lobbying governments and regulators, and when these outgoings are added to their total costs the percentage spent on research works out even less.



How do they spend their vast promotional and lobbying budgets? Well, apart from orthodox advertising, they ruthlessly target and manipulate health care professionals. They expend huge amounts of money and resources on buying the affection and time of doctors (Fugh-Berman and Ahari '07). According to the authors of this paper:

"Drug reps are trained to assess physicians' personalities, practice

styles, and preferences, and to relay this information back to the company. Reps ask for and remember details about a physician's family life, professional interests, and recreational pursuits. A photo on a desk presents an opportunity to inquire about family members and memorize whatever tidbits are offered (including names, birthdays, and interests); these are usually typed into a database after the encounter. Reps scour a doctor's office for objects — a tennis racquet, Russian novels, seventies rock music, fashion magazines, travel mementoes, or cultural or religious symbols — that they can use to establish a personal connection.

"A friendly physician makes the rep's job easy, because the rep can use the 'friendship' to request favours in the form of prescriptions. Physicians who view the relationship as a straightforward goods-for-prescriptions exchange are dealt with in a businesslike manner. Skeptical doctors who favour evidence over charm are approached respectfully, supplied with reprints from the medical literature, and wooed as teachers.

"Physicians who refuse to see reps are detailed by proxy; their staff is dined and flattered in hopes that they will act as emissaries for a rep's messages." Nurses, and especially prescribing nurses, are increasingly seen as an alternative and softer target (Jutel & Menkes '08).

SUMMARY: Our sickening society, and the equally sickening drugs industry that caters to it, is on a road to ruin. The evidence cited above demonstrates the need for redirecting our health priorities, re-structuring Big Pharma towards more research and less marketing, and quashing the greed and corruption that run so rampant within it.

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Don't forget fruit juice

A highly regarded group of scientists at the Tufts University Human Nutrition Centre have just published an important new paper, in collaboration with the University of Cincinnati Academic Health Centre (Krikorian et al '10). The team, led by Prof Jim Joseph, found that daily consumption of black grape juice for 12 weeks enhanced memory in older people with mild impairment in brain function. (nb. This is not dementia but Age-Related Cognitive Decline, a condition generally regarded as pre-clinical dementia).

This small but well-designed trial showed that verbal learning, verbal recall and spatial recall all improved over the three months. These positive results were very much in line with previous findings, from the same researchers, that grape juice reversed the course of neuronal and behavioural aging in rats (Shukitt-Hale et al '06); and that other foods rich in flavonoids such as walnuts and blueberries were similarly protective (Joseph et al '09). They also fit the epidemiological data; several studies have found that a higher consumption of fruit juice is linked to a lower incidence of dementia (ie Dai et al '06).

So should we all be drinking more fruit juice, and in

particular grape juice? Well, yes and no. The Alzheimer's Society, mindful of its financial relationships with the drug industry and unwilling to promote any particular natural product or supplement, concedes that lifestyle factors are important. They acknowledge that there is a relationship between diet and the risk of dementia, and recommend a diet rich in fruit and vegetables.

So do I, but we must be realistic. Substantial numbers of people in the UK manage only one portion per day (Billson et al '99), and there is little reason to expect much improvement here (Cox et al '98). For those who do not like fruit and veg, and for those who for whatever reason cannot manage to eat the minimum of 5-a-day, a micro- and phyto-nutrient support programme that includes the flavonoids is a suitable alternative.



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End of the Age of Antibiotics?

Scientists speculate that the age of antibiotics may be coming to an end. There has been a relentless increase in antibiotic resistance across all classes of drug; recent articles on antibiotic resistance in China paint an alarming picture of a near-future where antibiotics will have little therapeutic value (Heddini et al 2009).

Sadly, the use of antibiotics inevitably leads to the selection of resistance traits; the overuse and misuse of antibiotics in medical and other situations makes it increasingly unlikely that we will be able to stay ahead in the war against infection. Important work in such areas as quorum-sensing blockade may produce important new drugs, but these will not be available soon.

Various alternatives have been proposed from the natural world, and this article reviews some of the more prominent candidates including **colloidal silver**, yeast-derived **1-3, 1-6 beta glucans**, and the **lactoperoxidase** system.

Colloidal silver

Silver is used as an antiseptic and disinfectant in medicine and in industry. Silver-impregnated bandages are routinely used in the treatment of burns (Atiyeh et al '07), and silver-coated filters and fabrics are widely accepted in water-processing and in the clothing industry.

The use of colloidal silver as an antibiotic is controversial, however, as the evidence for this application is patchy; so much so that the US National Center for Complementary and Alternative Medicine recently described colloidal silver's marketing claims as 'scientifically unsupported'.

They added that colloidal silver can cause serious adverse effects including argyria, neurologic problems and kidney damage (NCCAM '06). The FDA and the Australian TGA

issued similar statements (FDA '99, TGA '05).

Silver, then, is effectively bactericidal in vitro but does not have a sufficiently wide therapeutic index or levels of evidence to be recommended for clinical systemic use. It falls at the same hurdle as so many promising drug candidates; the fact that it is a natural compound is immaterial.



Silver bandage

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1-3, 1-6 beta glucans

The innate immune system recognises molecules called 1-3, 1-6 beta glucans, found in the cell walls of moulds and yeasts; and responds to their presence by increasing its level of activity (Kernodle '98, Wakshull '99, Mansell '75, Robertsen '94).



Before fungicides were developed, almost everything we ate was contaminated with yeasts and moulds, and this was a critical factor keeping our

innate immune systems at peak capacity. Very late in evolutionary terms, modern technology effectively sterilised our food chain. Levels of yeast and moulds fell, leaving the innate immune system compromised. Replacing 1-3, 1-6 beta glucans in the diet normalises and restores the innate immune system, greatly enhancing resistance to bacterial and viral infection (Rasmussen, Seljelid et al (several), Kernodle '98, Williams & Deluzio '78 '79 '80, Deluzio & Williams '83, Tzianabos & Cisneros '96, Jung '04, de Felipe '93, Babineau & Hackford '94, Babineau & Marcello '94, Dellinger '99).

BiotheraPharma's highly effective beta glucan, Wellmune, has been shown to protect individuals from stress-related infections such as upper respiratory tract infections (Harger-Domitrovich '08, Talbott & Talbott '09 '10).

Wellmune is a uniquely valuable prophylactic, but in cases of established infection is better regarded as an adjunct.

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Lactoperoxidase (LPO)

The enzyme LPO is one of the body's major first-line defences against infection (Pruitt '87, Ratner & Prince '00, Gerson '00, Wijkstrom-Frei et al '03).

LPO produces ions such as HOSCN, which have a broad spectrum of activity against gram-positive and gram-negative bacteria, HIV-1 and other viruses, moulds, yeasts, mycoplasma and protozoa (Pruitt & Reiter '85, de Wit & van Hooijdonk '96, Wang et al '00, van Hooijdonk et al '00, Seifu et al '05, Fweja et al '08).

LPO is critical for the control of pathogens in milk from lactating animals (Reiter et al '86) including humans (Shin et al '00). It also plays a key role in defending the respiratory and gastro-intestinal tracts (Wijkstrom-Frei et al '03).

LPO utilises dietary thiocyanate as one substrate, producing hypothiocyanite (HOSCN) ions. These ions kill pathogenic bacteria via three separate mechanisms: (1) they inhibit bacterial glycolysis; (2) they inhibit bacterial nicotinamide adenine dinucleotide (NADH)/nicotinamide adenine dinucleotide phosphate (NADPH)-dependent reactions (Reiter & Perraudin '91); and (3) they oxidise bacterial sulphhydryl groups (Slungaard & Mahoney '91, Thomas & Aune '78).

LPO also utilises iodine, forming hypohalide ions. These have an additional spectrum of anti-bacterial activity.

Uniquely, HOSCN ions also have potent anti-viral activity. Many viruses have sulphhydryl groups on their coat (ie Mangold & Streeck '93); when these are oxidised (ie by thiocyanate) the viral coat structure is damaged or destroyed (Almeida et al '79).

HOSCN ions are not toxic to human cells at the levels produced by LPO, and have little if any effect on probiotic species, making them a near-perfect antibiotic system. Furthermore, it is very difficult for microorganisms to acquire resistance to LPO; if it was easy for pathogens to become LPO-resistant, a key element in our immune system would have been disabled and we would not have survived as a species.

Today, however, the LPO system is frequently compromised. Lacto-peroxidase is a ferroprotein, and iron depletion / deficiency is one of the most common forms of dysnutrition.

There are also growing problems with two of LPO's substrates: thiocyanate and iodine. Thiocyanates are derived from dietary glucosinolates (in brassica), or from cyanogenic glycosides (in beans, sweet potato and millet).

Since 1950, UK consumption of fresh vegetables has fallen by 24% (Hinton '08). Iodine depletion is becoming more prevalent, due inter alia to reductions in salt intake and the use of (non-iodinated) sea salt (Li et al '06, Nawoor et al '06). The net effect of depletion in iron, iodine and cyanogens on LPO activity is likely to be very significant in reducing our ability to ward off infections.



Due to its chemistry, LPO is not a suitable therapeutic tool; if the milk-derived enzyme were to be consumed it would, like other milk proteins, be digested and rapidly rendered ineffective.



However, the bactericidal effects of LPO can be mimicked and amplified by delivering HOSCN ions directly. This technology was initially developed in France for food plant sterilisation, and subsequently to sterilise salad leaves. It is used as an antiseptic in Belgium, and has been adapted by the WHO for bulk milk sterilisation in China and Korea (FAO/WHO '05).



It has been suggested that the extensive use of HOSCN might encourage the development of microbial resistance strategies, but I believe that this is unlikely. Only a small number of intrinsically LPO-resistant microorganisms are known (ie Oram & Reiter '66). While resistance may be acquired in certain specific circumstances (ie Leyer & Johnson '93), the evolutionary historical evidence indicates that this is clinically insignificant. Moreover, most mammals utilize LPO/HOSCN on a daily basis and it remains an effective element in the innate immune system.

With regard to safety, it should be pointed out that the level of hypothiocyanous ions in available supplements is well below the safe and tolerable levels of thiocyanate ions produced within the body (Borgers & Junge '79, Weuffen '82, WHO '95).

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