dr paul clayton's Health Newsletter

Spring 2008

Public health, diet and government

This Spring newsletter tackles the inter-twined themes of public health, the importance of diet, and governmental responsibility – or more realistically, the lack of it.

Our first subject is **HEART DISEASE**, a perennial British favourite which is always either one or two in the causes of death league tables. In the UK, the official approach to risk reduction is statins.

GPs must prescribe statins

GPs are obliged to prescribe these drugs whenever they come across a patient with raised cholesterol levels, regardless of the fact that raised cholesterol levels are not a good predictor of risk; and regardless of the fact that the statins are not very effective drugs.

High cholesterol is <u>not</u> a risk factor for the elderly

To begin with, high cholesterol is not a risk factor for old people (Ravnskov '03), a critical finding as the greatest numbers of cases of heart disease and stroke occur in the elderly. You would not expect statins to be helpful in this group, and indeed in the recent PROSPER trial (Shepherd et al '02), the only statin trial that included old people exclusively, and the results of which were used as an argument for including old people for statin treatment, total mortality was unchanged. This was because 22 fewer deaths from heart disease and stroke were outweighed by 24 more cancer deaths.

Statins don't seem to help women

Then again, statins do not seem to help if you are a woman. A recent and very respectable review of cholesterol-lowering drug treatment concluded that "for women without cardiovascular disease, lipid lowering does not affect total or CHD mortality" and for women with known cardiovascular disease "treatment of hyperlipidemia ….does not affect total mortality" (Walshe & Pignon '04). The absence of overall benefit was because any decrease of heart mortality was balanced by an increased mortality from other causes, including cancers.

Very small benefits

Even in the highest male risk groups for heart disease, statin treatment resulted in only 0.5% fewer deaths per year, and this small benefit was only found in the most positive of all trials. Other major statin trials eg. ALLHAT showed no benefit at all, a fact that has been conveniently buried.

The usual propaganda tells us that statin treatment can reduce heart mortality by between 20% and 50%, but this is one of those damn statistical lies. For instance, in the ASCOT trial fatal and nonfatal stroke was reported as being reduced by 27% (Sever et al '03). But the truth is that these fatal and non-fatal strokes were only seen in a very small number of patients, ie. in about 1.7% of the statin-treated and in about 2.4% of the non-treated patients. The reported 27% reduction in risk was an absolute difference of only 0.7%, which means that up to 350 people would need to take statins for up to 3 years to save a single life.

Statins in combination new drugs - any better?

The latest Big Pharma brainwave is Vytorin, a combination of simvastatin and ezetimibe, an expensive new drug which acts by reducing cholesterol absorption in the small intestine. The ENHANCE trial, just reported, showed that the combination significantly lowered blood cholesterol levels (whoopee!), but had no effect on atheroma progression whatsoever (No authors '08). To make matters worse, the Pharmaceutical Business Review reported that the drug companies behind Vytorin (Merck and Schering Plough) attempted to suppress findings of liver toxicity, despite prior warnings from an FDA reviewer (PharmBus '08).

Considerable side-effects

The results of the statin trials are pretty pathetic, especially when you consider the cost of these drugs (they are not cheap), and their toxicity. Their side-effects include muscle and nerve damage (Ahn '08), memory loss (Wagstaff et al '03), and a whole host of psychiatric disturbances (Tatley & Savage '07).

So why statins?

So why are the statins so widely used? Simple. It is still widely believed by many medics – who are not scientists – that high cholesterol is the main cause of heart disease, and this myth is aggressively sold to them by the drug companies that market statins. It is even more insidious than that, because so many drug company representatives are on the advisory committees which keep lowering the threshold at which cholesterol levels should be 'treated' with statins.

This must just seem like a typical anti-medicine rant, but I am a great believer in medical science. What I dislike is the combination of Big Pharma's data falsification and dishonest marketing, and our politicians' naivety, a combination that has created a situation where increasing numbers of British people are effectively being force-fed statins and given little alternative. This makes enormous amount of money for industry, but the benefits for British health are dubious indeed.

Dietary alternative to statins in Finland

There is an alternative to statins, however – and that alternative is Finland.

North Karelia, an area in Finland, is famous in medical epidemiology circles because for many years it had the highest rates of heart disease and stroke in the world; so much so that in 1972, the North Karelia project was launched to try to do something to protect the Finns' health. Unlike the American model, in which health matters are primarily regarded as a profit centre (see, for example, Michael Moore's recent film 'Sicko'), the Finns see health as a public matter. Instead of rushing down the Gadarene slope and into Big Pharma's arms, they implemented a series of changes to the Finnish diet, and these simple changes have had almost miraculous effects.

Significant blood pressure reductions

During the last 30 years the Finns, much like us, have become less physically active and as a result have grown heavier. Men are smoking slightly less than in 1972, women slightly more. But where the Finns differ from Brits and Americans is that their blood pressure and cholesterol levels have fallen.

Across Finland, average systolic blood pressure has fallen by 15 mm Hg, and diastolic blood pressure has fallen by 12 mm Hg. This is more than double the effect you would expect if you were to put every man, woman and child on anti-hypertensive drugs, but no such drugs were used. Average cholesterol levels fell by 1.1 mmol/l. This about 100 times more effective than the effects of statins, at the population level, but no statins were used either.

Fewer deaths from heart attack and stroke

More importantly (because blood pressure and cholesterol are just biomarkers), Finnish rates of cardiovascular disease have fallen as well, and dramatically rapidly. Death rates from heart attacks have fallen by 75%, and death rates from stroke have fallen by the same amount (Puska '99, Karpannen et al '05). Because the numbers of drug prescriptions have fallen, so has the incidence of drug-related toxicity. And all of this has been achieved by minor dietary modifications.

More vegetables, less saturated fat

One factor has been an increase in the intake of vegetables over the last 30 years, and a reduced intake of saturated fat. The other has been the introduction of PanSalt, a salt substitute developed by Heikki Karppanen, Professor of Pharmacology in the Institute of Biomedicine at the University of Helsinki.

Widespread replacement of table salt by PanSalt

There are several salt substitutes around, but PanSalt is unique. It combines low sodium with high potassium and magnesium, and adds an amino acid (lysine), to get the right taste blend. It lowers our blood pressure because we currently eat too much sodium, and too little potassium and magnesium. Whereas an excess of sodium over potassium and magnesium causes smooth muscle constriction (thus raising blood pressure), an excess of potassium and magnesium over sodium leads to smooth muscle relaxation, and hence a lowering of blood pressure.

Government co-ordination of food suppliers

The widespread replacement of table salt by PanSalt in Finland has reduced the average intake of sodium by around a third; while approximately doubling potassium intake. These changes in sodium and potassium intakes are very much in line with current health recommendations, and are enough to explain the remarkable falls in blood pressure, heart disease and strokes.

Because in Finland public health is seen as a public concern, the Finnish Government has coordinated the food manufacturers and suppliers to use PanSalt instead of table salt in most Finnish foods. Even mighty Macdonalds, the harbinger of so much bad health, has had to bow the knee. If you go to a Helsinki Macdonald's, the burger buns are made with PanSalt. This is in marked contrast to the products they sell in London and New York, which are made with table salt.

I have lectured on this topic to British GPs and cardiologists, and it is a sad reflection on their pharmaceutical and national prejudices that the vast majority of them are unfamiliar with the Finnish experiment, and a significant number are actively hostile. It is only when they take the trouble to study the literature, and – in some cases, to visit Finland – that they see the light. More depressingly, our own government refuses to acknowledge the North Karelia Project, and continues to deny the British public the health benefits that we too could enjoy. Messrs Brown and Co. are clearly more aligned to the USA model of health as business opportunity, than the Finnish model of health as a public good.

Alarming predictions for the new flu pandemic

I have written about bird flu before, but recent alarming developments suggest that the flu pandemic, when it arrives, may be even worse than was initially believed. A pandemic is reliably predicted, because we know that one comes around every 30 years or so, in a cycle that has repeated through at least the last three centuries. The periodicity is partly to do with the rates at which the flu viruses mutate, and partly due to changes in host immunity. 30 years is, more or less, a human generation.

Three flu pandemics in the 20th century - the next is overdue

There were three pandemics in the 20th century, and all spread worldwide within a year of being detected. The **'Spanish' flu** in 1918-19 killed up to 50 million people. In the 50s the **Asian flu** pandemic killed a mere million, and in '68 **Hong Kong flu** killed another million or so.

That was 40 years ago – so we're due for the next one. The current strain of bird flu H5N1 has already shown a few cases of probable human-to-human transmission, but is probably not a major threat. However, the wait for the pandemic strain will not be a long one; and there is a real concern that this one could be very serious indeed.

Klaus Stohr of the WHO Global Influenza Programme recently stated, 'There will be another pandemic. In the best case we expect billions to fall ill, with 2 to 7 million deaths – but it could be far worse'. In the UK, for example, the Department of Health predicts a worst case of as many as 750,000 deaths. But the reality could be far worse than that; partly because we do not have the right medical tools to deal with this problem, and partly because we have allowed our immune defences to drop.

Medical tools - Antibiotics and Vaccines?

With regards to the medical tools, antibiotics are no use in treating viral infections, and the right vaccines to protect us against the new strain of flu won't be ready until at least 4

months after the epidemic has started. This, of course, will be too late for many.

Medical tools - Anti-viral drugs?

Then there are the anti-viral drugs. Various EU member state governments have decided to purchase anti-viral drugs such as Tamiflu for, in some cases, as many as 1 in 4 of the population. Those decisions were based on two assumptions: firstly, that the emergency could be managed, and secondly that the anti-viral drugs will be reasonably effective. Both of these assumptions are questionable. Our ability to deal with the fall-out of a contagious and highly lethal viral epidemic is, realistically, inadequate; and to make matters worse, Tamiflu and other drugs are probably only helpful if given very early in the infection.

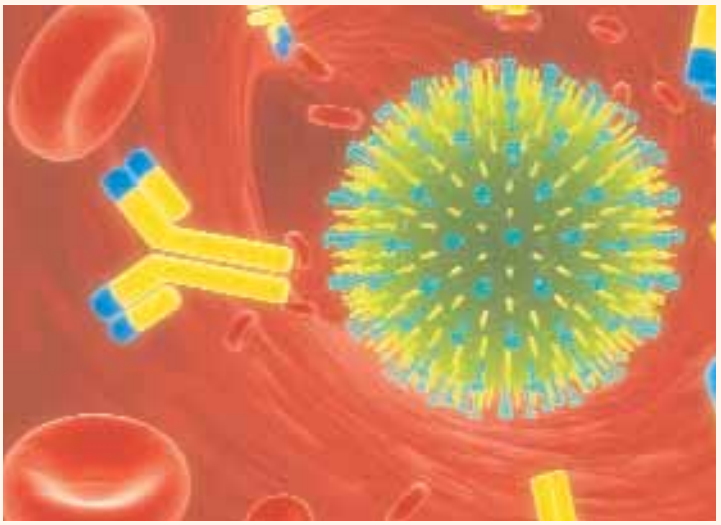
The first signs of flu are remarkably non-specific; a cough, sneeze, headache or the first half-degree rise in temperature could all be significant. This means that when the pandemic arrives parents will be screaming for antiviral drugs for their children, for their partners, for themselves. Our fragile social fabric is unlikely to survive for long, and the current government plans (which involve rationing, priority allocation, buddy schemes, emergency morgues and, reportedly, armed guards at all pharmacies) will rapidly descend into farce and tragedy.

Medical tools - Cytokine blockers?

The drug industry is actually doing some very interesting work on such topics as cytokine OX-40 blockers, which are

demonstrating good effects in mouse models of flu, but these will be expensive, experimental, and probably not ready in time.

So what can we expect, and what can we do to protect our own when the government has already shown, in so many ways, that it is unable to comprehend or face up to these new challenges?



Antibodies attacking a flu virus

turn to back page

The new flu pandemic (continued)

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To begin with, I believe that the impact of the next flu pandemic could be far worse than the official projections, because our herd immunity is at an all-time low. I am not talking about the acquired immune system, which is the part of the immune system that has memory, but the innate immune system; and it is the innate immune system that is important in protecting us against the influenza virus.

Once a virulent flu virus has invaded our deep tissues, it tricks the acquired immune system into over-reacting; and this over-reaction is what kills us. It is known as Systemic Inflammatory Response Syndrome (SIRS), or a cytokine storm. If the innate immune system is working well, however, it will head the virus off at the pass, neutralising it before it can penetrate into the deeper tissues and trigger SIRS. And here's the rub … there is very persuasive evidence that our innate immune systems are at an all-time low.

The Hygiene Hypothesis

This is little to do with nutritional issues. It is, instead, an unexpected consequence of our mania for cleanliness, and falls within the remit of the so-called 'Hygiene Hypothesis'.

Humans evolved in a dirty environment. We have been on the planet for hundreds of thousands of years but soap, antiseptics, disinfectants, canned and frozen foods have only been with us for a few generations, and antibiotics arrived less than a century ago.

During most of our time on this planet, therefore, our environment was replete with bacterial and viral hazards, and our immune systems were constantly challenged. Indeed, recent studies have shown that the innate immune system adapts to facing constant challenges and responds to attack by up-regulating its state of readiness and effectiveness. The innate immune system learned in particular to recognise molecules called beta 1-3, 1-6 glucans, which are present in the cell walls of moulds and yeasts; and it responds to their presence by mounting a strong counter-attack. In an age before fungicides were routinely sprayed onto every food crop, almost everything we ate would have been contaminated with yeasts and moulds, and this was, paradoxically, one of the main factors keeping our innate immune systems at peak capacity.

The decline in innate immune ability is a critical factor underlying the staggering increases in asthma and allergy that have occurred over the last 40 years or so, and is almost certainly involved in the rising cancer figures also. More urgently, it means that we have become uniquely vulnerable to virulent flu viruses.

The 'Spanish' flu (really the Ardennes flu) killed 1.5% of the world's population, which equates to around 250 million today, and about 750,000 UK subjects. But back in 1918, levels of fungal contamination in the food chain were far higher than today; bread and beer contained far higher levels of yeast also, due to changes in food production. That means that our great-grandparents' innate immune systems were more effective than ours are today, a fact which is substantiated by their much lower levels of asthma and allergy. And if our innate immune systems are less effective (ie if our herd innate immunity is lower), then the flu will affect more of us, and kill a higher proportion of those infected. In the worst case we could be looking at 2-3% mortality, or 1.5 million deaths in the UK alone.

Put yeast extract back into the food chain?

There is a solution, which like PanSalt, is cheap, safe, and diet-derived; and that is to put yeast extract back into the food chain. These extracts have already been shown to protect mice (Mandeville '02) and pigs against the flu virus (Jung et al '04); and are so effective at improving resistance to infection that they have replaced antibiotics in fish food in aquaculture the world over.

So here we have a situation where we are willing to use these food extracts to protect our young salmon, but not our children or loved ones. This is scientific insanity, and the government's continuing failure to implement such a cost-effective measure is baffling. Either they are completely ignorant of this relatively new science, or they don't care. Either way it is gross public health malpractice, and our political representatives should hang their heads in shame. Unfortunately, their behaviour over the last decade or so suggests that most of them have become immune to this interesting and sometimes productive emotion.

References

Ahn SC. **Neuromuscular complications of statins**. Phys Med Rehabil Clin N Am. 2008 Feb;19(1):47-59.

Backes JM, Howard PA. **Association of HMG-CoA reductase inhibitors with neuropathy**. Pharmacother. 2003 Feb;37(2):274-8.

Jung K, Ha Y, Ha SK, Han DU, Kim DW, Moon WK, Chae C: **Antiviral effect of Saccharomyces cerevisiae beta-glucan to swine influenza virus by increased production of interferon-gamma and nitric oxide.** J Vet Med B Infect Dis Vet Public Health. 2004 Mar;51(2):72-6.

Karppanen H, Karppanen P, Mervaala E. **Why and how to implement sodium, potassium, calcium, and magnesium changes in food items and diets** Journal of Human Hypertension 2005; 19:S10-S19.

Mandeville R: Biophage Pharma Inc, personal communication

[No authors listed] In brief: Zetia and Vytorin: the ENHANCE study. Med Lett Drugs Ther. 2008 Jan 28;50(1278):5.

Pharmaceutical Business Review '08. www.pharmaceutical-business-review.com/article_feature.asp?guid=4B8B1699-777E-41DD-893E-F88AF410D1C5

Puska P. **The North Karelia Project: from community intervention to national activity in lowering cholesterol levels and CHD risk.** European Heart Journal 1999.

Ravnskov U. **High cholesterol may protect against infections and atherosclerosis.** Q J Med 2003;96:927-34.

Rosch PJ. **Statin Associated Peripheral Neuropathy**. Lancet 2004 Nov 6-12;364(9446):1663-4.

Sever PS, Dahlöf B, Poulter NR, Wedel H, Beevers G, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes GT, Mehlsen J, Nieminen M, O'Brien E, Ostergren J; ASCOT investigators. **Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial.** Lancet 2003;361:1149-58.

Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, Ford I, Gaw A, Hyland M, Jukema JW, Kamper AM, Macfarlane PW, Meinders AE, Norrie J, Packard CJ, Perry IJ, Stott DJ, Sweeney BJ, Twomey C, Westendorp RG; PROSPER study group. **PROspective Study of Pravastatin in the Elderly at Risk of vascular disease (PROSPER): a randomised controlled trial.** Lancet 2002;360:1623-1630.

Tatley M, Savage R. **Psychiatric adverse reactions with statins, fibrates and ezetimibe: implications for the use of lipid-lowering agents.** Drug Saf. 2007;30(3):195-201. Review.

Wagstaff LR, Mitton MW, Arvik BM, Doraiswamy PM. **Statin-associated memory loss: analysis of 60 case reports and review of the literature.** Pharmacotherapy. 2003 Jul;23(7):871-80.

Walsh JME, Pignone M. **Drug treatment of hyperlipidemia in women.** JAMA 2004;291:2243-2252.