Cholesterol: It's Not the Killer

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There is no doubt about the significance of cardiovascular disease (CVD) in Australia and other Western nations. In 2006, it was the largest contributor (34%) to all registered deaths [1]. However, it is only since the advent of cholesterol lowering drugs that cholesterol has become "public enemy number one" and has taken nearly all the blame for the increase in CVD. As a result, there is a growing belief that the lower your cholesterol, the healthier your body will be. The world has become fixated on lowering cholesterol through medication. Unfortunately this has led to a lot of misinformation and misdirection in treating the real illness of CVD and its causes.

The current ideology is far from the truth and can be dangerous—particularly since the overwhelming current evidence points to CVD as a result of poor lifestyle and dietary choices that lead to inflammation. In reality, CVD is no longer considered a disorder of lipid accumulation; instead, it is recognized as a disease process characterized by low-grade inflammation of the vascular lining and an inappropriate wound healing of blood vessels [2]. There is now extensive and growing evidence that inflammation is central to all stages of this disease, from the initial lesion to end-stage thrombotic complications [3,4,5,6]. CVD is not a disease of cholesterol or even cholesterol accumulation.

Cholesterol is carried in the blood in the form of lipoproteins, the type being determined by the apoprotein, a protein coating that acts as an emulsifier [7]. Accumulation of cholesterol arises when low-density lipoproteins (LDL)—often referred to as "bad cholesterol"—deliver more cholesterol than needed to the cells and too few high-density lipoproteins (HDL) are available to carry it away from degenerating cells. The relative balance between these lipoproteins is determined by various factors including genetics, diet and insulin resistance. Low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) carry cholesterol toward tissues [7,8]. There is a demonstrated relationship between the serum level of LDLs and the relative risk of coronary heart disease in high-risk patients [9]. In contrast, high-density lipoprotein (HDL) carries

cholesterol back to the liver and is associated with protection against cardiovascular disease. Cholesterol is associated with the risk of CVD but it is *not* the disease.

Cholesterol is a member of the large family of chemical compounds known as lipids (fats). However, cholesterol is a separate, specialised type of lipid that is chemically different from fat. Cholesterol is a part of the subgroup "sterols," whereas dietary and body fat are a part of the subgroup "glyceryl esters." There are two main categories of cholesterol. Dietary cholesterol comes from the animal-based food we consume and cannot be measured by the doctor. The other type of cholesterol is blood cholesterol, which is made in the liver. Although the two types are chemically identical, they are not representative of each other. The cholesterol levels measured at the doctor's office and in most studies are blood cholesterol levels and are representative of liver function [10].

Cholesterol is a symptom of an underlying health problem. It predicts less than 35% of cardiovascular disease. In fact, most heart attack and stroke events occur in individuals without elevated cholesterol and 20% occur in people without any traditional risk factors. Cholesterol is the messenger… telling us there is stress on the liver; it delivers the news but is not the killer it is made out to be. A significantly better predictor is the concentration of Omega 3 oils in the blood: the higher the concentrations the lower the risk, with Omega 3 concentrations predicting up to 95% of CVD, compared to 35% prediction rates from cholesterol readings. So why scare the public about cholesterol? The answer is simple: there is no money to be made in prescribing Omega 3 oils.

Another marker of inflammation in the body—and a major risk factor for heart disease—is C-reactive protein (CRP), a better predictor of CVD than cholesterol. However, it is just a marker and, like cholesterol, it is not the cause of CVD [11].

Along with other signaling molecules, insulin controls the production of fats such as cholesterol and triglycerides. It also controls the packaging of cholesterol and triglycerides into LDL (low-density lipoproteins), VLDL (very low-density lipoproteins), HDL (high-density lipoproteins) and other lipoproteins. Glucagon (a hormone secreted by the pancreas) inhibits the enzyme and insulin activates the enzyme. To control cholesterol production, you want to increase glucagon and decrease insulin. When we eat sugar or processed carbohydrates, we produce more insulin hormone, which stimulates more HMG-CoA reductase enzyme and, as a consequence, more cholesterol and triglycerides are produced. People with type 2 diabetes have elevated fasting insulin as well as elevated cholesterol is. In fact, elevated fasting insulin is a better predictor of cardiovascular disease than cholesterol. Glucagon, when present in the bloodstream, lowers insulin levels. Glucagon is released every time you eat lean protein.

There is also strong evidence that stress increases a person's inflammatory markers and cholesterol [12,13,14]. One possibility may be that stress encourages the body to produce more energy in the form of metabolic fuels—fatty acids and glucose. These substances require the liver to produce and secrete more LDL, which is the principal carrier of cholesterol in the blood [12]. Both adrenaline and cortisol trigger the production of cholesterol. Cortisol also has the effect of releasing sugar into the blood. To highlight the importance of this, we also know there is a strong association between stress and cardiovascular disease.

Not only is cholesterol *not* the enemy, but also it is essential to good health and wellbeing. Every cell in the body needs cholesterol in its membrane, where cholesterol plays a critical

role in cell communication. Without cholesterol, cell membranes are incomplete and, as a result, their functional role deteriorates. Cholesterol is also used in the mitochondria of the cell and plays a vital role in cell energy production—not to mention its essential role in the brain structure and function. Cholesterol is the starting material of many essential chemicals including vitamin D, steroid hormones and the bile acids necessary for digestion.
Cholesterol is metabolised into vital body steroids such as the steroid hormones, including: sex hormones; oestrogen, progesterone, testosterone and DHEA, as well as the adrenal hormones aldosterone and cortisol. None of these can be made without cholesterol and their production changes along with the levels of cholesterol in the blood [15]. Low levels of these hormones can have a significant impact on an individual's health and, in fact, low testosterone is associated with an elevated risk of all-cause mortality [16] as well as other chronic illnesses such as insulin resistance [17].

For major drug companies, convincing the public that lower cholesterol levels equal good health is a marketing scheme. The goal of these companies is not your good health; it's their profits. This "marketing messaging" has gone too far, especially considering that recent studies show that cholesterol may have protective properties against cancer [18]. An inverse relationship between low LDL cholesterol levels and cancer is shown when statins (lipid-lowering drugs) inhibit the normal levels of cholesterol production in the liver. A study in Hong Kong [19] found an LDL level of 107 to be associated with a 33% increased risk of cancer and death while an LDL level of 87 was associated with a 50% increase in risk. The risk of developing cancer is not only increased by statins that are inhibiting the production of cholesterol in the liver but also in cholesterol lowering drugs that inhibit the absorption of cholesterol across the digestive tract [20].

Cholesterol is the most abundant organic molecule in the brain 21 which contains almost a quarter of the unesterified cholesterol present in the entire body. In 2001, in groundbreaking research and with media fanfare, cholesterol was identified as the synaptogenic factor that is responsible for the development of synapses, the connections in the brain. The glial cells of the central nervous system that perform the housekeeping functions in the brain produce their own cholesterol for the specific purpose of providing nerve cells with the vital component required for synapse function [22,23,24]. Cholesterol is also required for the function of serotonin receptors in the brain. Serotonin is the chemical in our brain that makes us feel happy. Low cholesterol level has been associated with mortality due to suicides and accidental deaths [25,26,27]. Other studies have shown the inverse relationship between low cholesterol levels and physical aggression and impulsivity in both humans and primates [28,29]. The reasons proposed to account for this relationship between cholesterol levels and violence, aggression or suicide relate to cholesterol's role in central serotonergic activity [30].

The brain depends on a supply of cholesterol [31]. Unfortunately, the highly lipophilic statin drugs can easily pass through the blood-brain barrier and can therefore directly interfere with the synthesis of cholesterol by the glial cells [32]. No wonder a major side effect of the statin drugs is their impact on memory and thinking.

Cholesterol is a significant component of the cell membrane that influences its fluidity. Therefore, it indirectly affects neurotransmitters by interfering with their membrane bound receptors [33]. It also forms part of the myelin that surrounds our nerves, aiding in the fast transmission of nerve signals. Lower cholesterol levels in the blood are correlated with slower visuomotor speed [34].

Low cholesterol levels have been shown in studies to increase a person's susceptibility to infections [35]. This is due to cholesterol's functional role in preventing infections in the body. The lipoproteins, which carry cholesterol through the bloodstream, aid in protection against the harmful effects of bacterial endotoxins that are released during infection.

A thirty-year study published in 1987 provides evidence that elevated cholesterol in people over the age of 50 does not increase the risk of heart attack. Cholesterol levels of people free of coronary heart disease (CHD) and cancer were measured; the study found that there was no increase in death rate in those with high cholesterol [36]. Research on the effects of cholesterol levels and age shows that high cholesterol levels in people over the age of 75 are protective, not harmful. A separate study published in the *European Heart Journal* (1997) found that the risk of cardiac death was the same in groups of people with low or normal cholesterol levels as those with high cholesterol [37].

Maybe we need to rethink the billions of dollars we spend each year in Australia on drugs that lower cholesterol and spend the money on the real risk factors associated with cardiovascular disease: our lifestyles and choices, including nutritional and environmental factors that increase inflammation.

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1 Australian Bureau of Statistics 2006
2 Ridker et al. 2000
3 Dixon et al. 2009;
4 Loppnow et al. 2008;
5 Packard and Libby 2008;
6 Sukhanov et al. 2007
7 Brown et al. 2007
8 Tousoulis et al. 2007
9 Zafrir and Cohen 2006
10 Campbell 2006
11 Elliot et al. 2009
12 Steptoe and Brydon 2005;
13 Coleman et al. 1998;
14 Berger et al. 1980
15 Khaw et al. 1991
16 Khaw et al. 2007
17 Yeap et al. 2009
18 Goldstein et al. 2009
19 Xilin et al. 2008
20 Drazen et al. 2008.
21 Guyton 1996
22 Mauch et al. 2001;
23 Koudinov and Koudinova 2001;
24 Göritz et al. 2002

25 Jacobs et al. 1992;
26 Muldoon et al. 1993;
27 Lindberg et al. 1992;
28 Freedman et al. 1995;
29 Golomb et al. 2000
30 Roy et al. 1989
31 Graveline 2009
32 Takeshi et al. 2004
33 Heron et al. 1980
34 Zhang et al. 2004
35 Leardi et al. 2000
36 *Journal of the American Medical Association* 1987
37 Behar et al. 1997