

The Cholesterol Controversy

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Abstract

The General Practitioner has a great responsibility to implement lifestyle changes in his patient population to combat the hostile environment that modern society created for the maintenance of health. This is especially true in the case of coronary heart disease (CHD). Research evidence now lends strong support to the view that CHD is largely preventable by eliminating or modification of risk factors. Our intention is to shed some light on the cholesterol controversy

referring to two well-conducted studies by Dean Ornish and Michel de Lorgeril. They found that relatively simple lifestyle and dietary changes achieved greater reductions in risk of all-cause and CHD mortality in secondary prevention trials than any of the cholesterol lowering studies to date. The Family Physician is in the ideal position to motivate his/her patient to take control and to implement a multifactorial approach for lifestyle counselling and risk modification.

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Introduction

In no other area in medicine and medical nutrition has there been more confusion and controversy than in the field of cholesterol. The link between cholesterol and coronary heart disease is well established, specifically after 1952 when Ancel Keys initiated his landmark study, an international study called the Seven Countries Study that indicated a direct correlation between dietary fat and heart disease¹. Evidence relating plasma cholesterol levels to arteriosclerosis and CHD has become so strong as to leave little doubt of the etiological connection.

In Western industrialized countries, nearly 50% of the population is fated to die of cardiovascular disease. Since coronary heart disease continues to be a leading cause of morbidity and mortality among adults in the westernised world, research into this area intensified, and health professionals, the pharmaceutical industries, and the research funding and regulating agencies almost totally focused on lowering plasma cholesterol levels by drugs. It is heartening to see two recent well-conducted studies by Dean Ornish² and Michel de Lorgeril³ finding that relatively simple lifestyle and dietary changes

achieved greater reductions in risk of all-cause and coronary heart disease mortality in secondary prevention trials than any of the cholesterol-lowering studies to date.

This is quite a triumph for natural or preventive medicine. The great Greek physician Hippocrates was one of the firsts to recognize the value of prevention. Conventional physicians focus heavily on the use of specific medications and surgeries for specific problems, and do not always recognize the value of preventive medicine in the management of diseases of lifestyle.

Historical Perspective

Just after World War II, an unexplained epidemic of coronary heart disease affected middle-aged executives in America. At that time, no one was thinking about – let alone researching – a relationship between diet and heart disease. It was only when Ancel Keys announced that his research indicated a direct correlation between dietary fat and heart disease that scientists focused their attention on the effects of lipid modification on coronary heart disease (CHD) morbidity and mortality.

In fact, Keys¹ first recognized the health benefits of the Mediterranean diet some 40 years ago. This was before the announcement in 1994 of the Mediterranean Diet Pyramid (developed by the Oldways Preservation & Exchange Trust, WHO/FAO Collaborating Centre for Nutrition at Harvard School of Public Health and the World Health Organization Regional Office for Europe), and 40 years before the media began stressing the Mediterranean diet as a miracle diet.

The Seven Countries study initiated by Keys in 1952, looked at men in rural areas of Yugoslavia, Finland, Italy, the Netherlands, Greece, United States and Japan. This report demonstrated that the populations which ate the most saturated fat had the highest blood cholesterol and, not so coincidentally, the greatest incidence of heart attack. At first, scientists did not believe that fat in the diet can raise cholesterol in the blood, and that in turn can increase heart-disease risk. Mounting evidence

on the diet-heart disease risk could not be ignored. Examination of the diet on Crete – an area with exceedingly low risk of heart disease – revealed that it was very high in fat – in some areas, as high as 37 per cent of total calories. But the fat was almost all from olive oil, a mono-unsaturated fat. It became clear that it wasn't so much that a high fat diet mattered, but rather what *kind* of fat. It soon became clear that saturated fats are the major villains.

The longstanding Framingham Heart Study⁴, initially orchestrated by Ralph Paffenbarger, from the Stanford University School of Medicine in the USA, convincingly demonstrated that high blood pressure; cigarette smoking, inactivity and elevated blood cholesterol are major risk factors for developing coronary heart disease. It now became evident that lifestyle factors in the industrialized world; contributed significantly to the development of the epidemic of ischaemic heart disease (IHD), indicating convincingly that IHD is a multifactorial disease. The publication of the Lifestyle Heart Trial by Dean Ornish² demonstrated that intensive lifestyle changes might lead to regression of coronary arteriosclerosis after 1 year. More regression of coronary arteriosclerosis occurred after 5 years than after 1 year in the experimental group. In contrast, in the control group, coronary arteriosclerosis continued to progress and more than twice as many cardiac events occurred. The intensive lifestyle changes included a 10% fat whole foods vegetarian diet, aerobic exercise, stress management training, smoking cessation and group psychosocial support for 5 years.

According to this study, patients on the Ornish regimen had lower cholesterol levels and fewer angina episodes, and in many cases they were able to avoid bypass surgery and angioplasty. Ornish has long maintained that changes in diet and lifestyle can treat heart disease as effectively as drugs and surgery – perhaps even more so.

However, the same researcher indicated that only moderate changes in diet and lifestyle, as advocated by the Step II diet of the National Cholesterol Education Program and the American Heart Association (25% energy from fat, 3.5 times exercise per week), might not be sufficient to stop the progression of coronary arteriosclerosis unless combined with lipid lowering drugs⁵. Even Ornish acknowledges that his diet isn't for everyone. A third of the patients in his study dropped out.

The powerful pharmaceutical industry immediately responded by conducting well-designed studies on lowering of plasma cholesterol with drugs. The middle years of this decade revealed that lipid modification with some of the new HMG-CoA reductase inhibitors (statins) class of drugs was followed by significant improvements in CHD morbidity and mortality while non-cardiovascular morbidity and mortality were not affected adversely. Major studies that provide this information were the Scandinavian Simvastatin Survival Study (SSSS)⁶, West of Scotland Primary Prevention Study (WOSCOPS)⁷, Cholesterol and Recurrent Events (CARE)⁸, and Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID)⁹ study. In all four of these

studies, it was shown that in both primary and secondary prevention settings, lowering the concentrations of triglycerides, total cholesterol and low-density lipoprotein cholesterol (LDLC) resulted in a significant reduction in the risk of mortality and morbidity from CHD. They serve as landmark studies removing the doubts about cholesterol lowering, and they provide evidence for recommendations for clinical practice in allopathic medicine. In a drug-orientated society this might promote the prescription of cholesterol-lowering drugs for all perceived cholesterol related problems with the side effect of increasing healthcare costs and medicalisation of society.

Cholesterol lowering medication will always be considered in the more severe forms of hypercholesterolaemia such as Familial Hypercholesterolaemia (FH), or in severe hyperlipidaemic patients at high risk due to the presence of overt CHD. These patients may be resistant to dietary interventions only. The Scandinavian Simvastatin Survival Study (4S)⁶ produced a 32% relative reduction in the risk of major CHD risk, and the West of Scotland Coronary Prevention Study (WOSCOPS)⁷ led to a 30% relative reduction in risk of major CHD events.

Treatment of hypercholesterolaemia, however, will usually comprise intervention on several risk factors and, although the separate effects of different interventions (particularly lifestyle interventions) may be small, their synergistic effects can be substantial.

■ The emergence of an alternative approach to CHD management ■

Because there has been considerable morbidity and some mortality from drug and invasive management of CHD, other treatment options were explored. It is well known that most adverse effects of current treatments could be largely avoided by an effective dietary approach. With the

high cost of drugs and invasive procedures, which are the mainstay of management of CHD in the civilized world, promotion of a diet such as the much-published Mediterranean diet, could lead to very considerable savings in the cost of health care.

Of great importance then is the publication of the 46-month mean follow-up findings on the original report of the study on "Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease", the so-called Lyon Diet Heart Study³. This study was

undertaken because of the interest of the investigators in explaining the very much lower mortality from cardiovascular disease, mainly coronary heart disease, in countries bordering the Mediterranean compared with that in northern Europe. The benefits in the experimental group at that time was so favourable, that the study was terminated at 27 months mean follow-up time of what had been planned as a 5-year study. The initial report¹⁰ was published in *Lancet* in 1994. Despite the striking findings in this report of a 70% reduction in all-cause mortality due to a reduction in CHD mortality and comparable large reductions in non-fatal sequelae, many cardiologists are not aware of that study.

It is much to the credit of de Lorgeril and associates that they persisted in following the original enrollees despite the official termination of the study and publication of the initial findings so that they are now able to report their more extended observations. With the mean follow-up time of 46 months per patient, the initial remarkably beneficial

effects of the experimental dietary program persisted compared with the control group consuming the "prudent Western-type diet." An important finding was that the unprecedented reduction in risk of CHD was not associated with differences in total cholesterol between the control and experimental groups and that the survival curves showed a very early separation quite unlike what has been reported in the cholesterol reduction studies¹¹.

The continued high adherence of the experimental group to the program over the full 46 months of mean follow-up per patient is quite remarkable. This occurred even though all patients in the study were informed of the outcome and despite the publicity of the initial publication of the striking benefits of the trial, which seems to have influenced some in the control group to modify their diets toward that of the experimental group. The continued good adherence to the experimental diet indicates that it was readily tolerated. The 600 heart patients

prepared the recommended meals in their own homes – halve eating a Mediterranean diet, the other halve the American Heart Association (AHA) diet. Both were able to follow the diets after being given just one hour of instruction by a research dietician and a cardiologist. The Mediterranean diet was quite simple; more bread, more vegetables and legumes, more fish, less meat, not a day without fruit, no butter or cream. The only fats allowed were olive oil for cooking and a special high-monounsaturated-fat spread. Both groups were getting about 30% of their calories from fat. The main difference was the type of fat: blood analysis showed that the Mediterranean group had consumed more monounsaturated fatty acids while the AHA group had consumed higher levels of polyunsaturated fatty acids. The researchers suspect that the abundance of the plant and fish omega-3 fatty acids in the Mediterranean diet group, provide additional protection by reducing blood clotting and arrhythmias, which often precipitate heart attacks and strokes.

The cholesterol myth

The medical, scientific and nutritional research literature published over the past ten years in the field of the prevention and treatment of cardiovascular disease slowly erodes conventional wisdom. Pure cholesterol found in all animal fats may not damage blood vessels after all. There is no connection whatsoever between cholesterol in the food and cholesterol in the blood. This was proven by many studies, amongst others, two South African studies on the effect of high egg intake in rural communities.^{12,13} The culprit is most likely an oxidised polyunsaturated vegetable oil that forms a harmful by-product, which damages arteries and contributes to arteriosclerosis.

The recently popularised low-fat diets can be misleading. People who practicably live on olive oil, such as those in Crete, or on fish oil, such as the

Eskimos, have had the lowest incidence of heart disease in the world. Foods such as eggplant, garlic, onions and Soya beans will counteract the cholesterol elevating effect of fatty foods if eaten at the same meal. The key to a healthy cardiovascular system is balance, freshness, and variety, differentiating fat types, whole foods and wine in moderation. There is mounting evidence that wine, specifically red wine, has a favourable influence on the lipoprotein profile and platelet aggregation.¹⁴

It has been well established that soluble fibres lower serum cholesterol, although the mechanism of action has continued to be elusive.¹⁵ The Mediterranean diet contains sufficient amounts of soluble fibre to influence the cholesterol concentration in the blood. It was, in fact, Ancel Keys, the father of the Mediterranean diet concept, that first reported the cholesterol lowering effect of fibre 40 years ago!¹⁶

It is now convincingly clear that it is the saturated animal fat that is the dietary risk factor in raising cholesterol concentrations. With the onset of the Industrial Revolution, saturated fat intake rose dramatically with the increased availability of red meat and hydrogenation of polyunsaturated fatty acids (PUFAs), largely for margarine.

The plant based omega-6 fatty acids also have increased as the public has been repeatedly admonished to increase intake of PUFAs. Meanwhile, the omega-3 polyunsaturated fatty acids have been largely disappearing from our diets in Western industrialized countries, so that the ratio of omega-6 to omega-3 PUFAs is now estimated to be 15 to 1. This compares very unfavourably to the 4 to 1 ratio of our ancestors. For decades doctors have recommended low fat diet and promoted polyunsaturated oils from grains. This low fat diet is unfortunately

overloaded with omega-6 fatty acids which is linked with serious cardiovascular risks such as increased platelet aggregation and arteriolar vasoconstriction, it also has pro-inflammatory-, as well as pro-arrhythmic effects.

In contrast, the omega-3 class of essential fatty acids has potent anti-arrhythmic

effects preventing fatal ventricular arrhythmias.¹⁷ Furthermore; it has anti-inflammatory properties, and decreases insulin resistance as well as platelet aggregation. Another consistent finding is that the omega-3 PUFAs reduces plasma triglycerides, and increases HDL cholesterol concentration in a dose dependant fashion. There is evidence that omega-3 PUFAs reduce blood pressure

particularly in patients with mild essential hypertension.

All this information indicates that we have to increase our intake of green leafy vegetables and some vegetable oils such as linseed canola, soy, as well as fish and fish oils: all good sources of omega-3 PUFAs. Dietary factors must be very important, but they extend beyond cholesterol.

Conclusion

In solving the clinical problem or pathophysiological puzzle of coronary heart disease, we may be like the denizens of Plato's Cave, barely discerning the shadows on the wall. New risk factors identified, old risks reassessed, uncertainty about every medical study ever published – it all seems so confusing, and misinformation in the lay press create the impression that there is no clear vision forward.

The truth is, the road from ignorance to knowledge through the scientific method, works that way. We do

sometimes have to take a step backwards for every two steps forward, but that doesn't mean that we did not progressed on the road to a better understanding of CHD. Since Ancel Keys published his first paper, linking diet and lifestyle to CHD, 40 years worth of research points to a consistent theme: eat a balanced diet that includes lots of fruit and vegetables and fewer animal based foods; don't smoke; deal effectively with stress, and get as much exercise as you can comfortably maintain. As for drug therapy, there is consensus that it should only be

introduced after a prior trial of vigorous lifestyle modification.²⁰

What has become crystal clear is that we can rely on natural treatment strategies such as diet, exercise, music and meditation, advocated by Pythagoras to prevent heart disease. The patient has to take control of his/her life again, and listen to the clear message of nature. The problem should be seen holistically, implementing a multifactorial approach for lifestyle counselling and risk modification.

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