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A Historical Perspective of the Understanding of the Link between Diet and Coronary Heart Disease

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Abstract

The development of the understanding of the underlying causes of coronary heart disease has undergone several stages. Ecological studies, such as the Seven Countries' Study, showed a possible relationship between mortality in coronary heart disease and intake of saturated fats. The investigated area with the lowest rates of cardiovascular disease was the island of Crete, Greece. A discussion soon started to evolve around the Mediterranean diet, which at the time consisted of mainly foods of vegetable origin, olive oil and cereals of unrefined nature. Several clinical trials have been undertaken since, including the Lyon Heart Diet Study where it was clearly shown that both mortality and morbidity in coronary heart disease was substantially lowered by Mediterranean food compared to controls. Dean Ornish proved that an extreme regimen actually could reduce already existing sclerotic plaques, while the WHI study showed that a more modest diet change diet not cause the intended reduction in heart disease in middle-aged women. Another prospective study of a similar age group of women showed that a diet with a low glycemic load gave a good reduction in coronary heart disease. Multiple studies of different components of food have shown no positive result, pointing at the whole diet rather than its components of nutrients being of importance. Today, the experts agree on the optimal diet to prevent not only heart disease but also cancer forms and other chronic disease such as type 2 diabetes mellitus. This diet is consisting of a lot of fruit and vegetables, lots of fish, less salt and sugar, more unrefined cereals, beans and nuts. Going from a general notion of Mediterranean food to testing that food in clinical settings and testing nutrients as preventative agents, we can conclude that a generally healthy lifestyle, including a healthy diet, appropriate amounts of physical activity, good sleep and less stress, is the way to a heart healthy life.

Keywords

Nutrition; epidemiology; clinical trials; heart disease; guidelines

Introduction

Age-adjusted mortality from coronary heart disease has been rapidly decreasing in most Western countries. Heart disease is, however, still the biggest killer in the proportion of the US population over 65 years of age¹. Coronary heart disease as well as several other chronic conditions is currently not equally distributed over the population, with differences due to several socio-economic factors such as income, race/ethnic background and educational level, with the highest prevalence found among those with low socio-economic status. A lower socio-economic status can also be related to risk factors for coronary heart disease, for example being physically inactive or having type 2 diabetes mellitus. There is a considerable reason for concern regarding not only coronary heart disease, but also other related chronic conditions, such as type 2 diabetes mellitus, hypertension, stroke and obesity.

Serious warnings were issued more than ten years ago from the World Health Organization (WHO) regarding the increasing burden of cardiovascular disease (CVD) in developing countries. CVD is the broader term, including also vascular problems such as stroke, while Coronary Heart Disease (CHD) only includes diseases involving the heart vessels. Developing countries, low- and middle-income countries account for 86% of the DALYs (Disability Adjusted Life Years) lost to CVD world wide in 1998. In a statement from WHO ² we could read “*In the next two decades, the increasing burden of CVD will be borne mostly by developing countries*”.

This chapter will provide a brief background on some of the cornerstones, including some of the most important portal figures, of research leading to today's understanding of the link between diet and coronary heart disease. Some of the more important studies of the link between diet and coronary heart disease and different approaches to the problem are presented here, as well as some recent reviews, recommendations and guidelines.

Ansel Keys, Henry Blackburn and the Seven Countries' study

Dr Ansel Keys (1904-2004) was one of the most important scientists in the pursuit of the link between diet and coronary heart disease. He was a physiologist who during early years initiated and ran some of the more important studies in the field. The Seven Countries' study included Finland, Greece, US, Italy, Yugoslavia, Netherlands and Japan investigated links between coronary heart disease mortality and lifestyle factors, especially the intake of saturated fatty acids. The results from the study pointed out major differences in disease rates in relation to the amount of saturated fat intake, as a percentage of total caloric intake, where the countries with a high intake of saturated fats also had a significantly higher number of CHD deaths in relation to population size ³. Ansel Keys for many years worked with another interesting and groundbreaking scientist, Henry Blackburn who originally was his apprentice. The two of them became extremely important interventionists for many years to come at the Laboratory of Physiological Hygiene at the University of Minnesota and. Henry Blackburn is an MD, who besides his important contributions to the Minnesota Heart Health Programme also inspired the author of this paper to consider and further develop his views of why disagreements arise in CVD prevention.

Dr Blackburn described ⁴ three different viewpoints that often are the cause of disagreement:

- the clinical view where screening, the risk perspective, secondary prevention, treatment and clinical trials dominate
- the public health view, where the population perspective prevails and where theories and frameworks for change are formulated by public health professionals and health promotion is the most important concept, and
- the basic or mechanistic science view, where genetics, receptors, antioxidants, and molecular nutrition is dominant.

When trying to develop the concepts of coronary heart disease prevention and general health promotion, we need to keep the three viewpoints in mind, keeping up-to-date with all three aspects and navigating between the disciplines, integrating concepts and constantly updating our evidence-base in regards to clinical as well as basic and public health science.

Dietary Modification trials

The optimal diet in the Seven Countries' Study seemed to be the Cretan diet of the 1950's and 1960's. This diet was called the Mediterranean diet and was characterized by being primarily vegetarian, containing a large range of vegetables, fruits and beans plus nuts, seeds and cereals

of unrefined types. This food pattern typically included a high level of antioxidants and had olive oil as the primary source of fat, while the intake of meat and dairy foods was low and some fish was included. The fat profile of the food pattern turned out to be consistent with very low levels of saturated fats and high levels of mono- and n-3 polyunsaturated fatty acids.

The *Lyon Diet Heart Study* was a clinical trial building on the findings from the Seven Countries' Study, which asked the question: Can a Mediterranean type diet reduce the rate of recurrences after a first myocardial infarction? The study included 605 patients, assigned to intervention or control group after a first myocardial infarction, where the intervention group was given a Mediterranean type diet and the control group was given a diet in accordance with the recommendations from the American Heart Association (AHA). The characteristics of the two diets are described below.

Mediterranean type diet

- Dietary fat olive oil and Canola-based margarine (high oleic, alpha-linolenic (n-3) acids and an n-3/n-6 ratio of 1/5)
- Wide variety of vegetables and fruits (high dietary antioxidants)
- Moderate intake of chicken, fish and wine

AHA step 1 diet

- Total fat <30%, saturated fat <10% of energy intake
- Major dietary fatty acid linoleic acid (n-6)

The intervention lasted for 46 months and an intermediate analysis was made after 27 months. The study showed an amazing result⁵ – a 72% reduction in cardiac deaths and non-fatal acute myocardial infarction in the intervention group compared to controls. Furthermore, the study showed a 65% reduction in coronary heart disease mortality altogether and a 55% reduction in all-cause mortality. These are amazing and ground-breaking results of a nicely performed study.

Several other clinicians ran trials of similar type over years to come. Dean Ornish⁶ was one of them, and his contribution to the understanding was that a rigorous lifestyle regimen including meditation, low-fat vegetarian food, smoking cessation and regular exercise could not only stop the progression of coronary arterial disease but actually reverse it. His regimen was rather invasive but was effective for reducing sclerotic plaques in the coronary arterial wall.

The Women's Health Initiative is a still ongoing major set of trials, looking at several diseases of importance for women's health. One of these trials looked low-fat dietary patterns and the risk of cardiovascular disease⁷ in a randomized controlled dietary modification trial in postmenopausal women. This study was including a massive number of participants, almost 50,000, and went on for a mean of 8.1 years before the results were published in 2006. The results were rather disappointing, probably due⁸ to the fact that the dietary modification was not as successful as intended and the level of dietary change set out in the study design was not reached. Modest effects were identified on cardiovascular disease risk factors. These findings suggest that a more rigorous intervention needs to take place for results to be shown.

Another study⁹ of women, performed in the Netherlands, hit the headlines in 2007. It was a prospective cohort study over nine years including the impressive number of 15,700 Dutch women. This study gave echo in the journal of the American College of Cardiology, where Frank Hu in an editorial¹⁰ stated a need for a paradigm shift. The young scientist Beulens showed that a high dietary glycaemic load and glycaemic index increased the risk of

cardiovascular disease among middle-aged women. This was found to be particularly important among overweight women, already consuming modest glycemic load diets.

Mechanistic research

While the clinicians were performing clinical trials, obviously some serious activity was ongoing in the area of mechanistic research. These trials often examined the effects of one micronutrient or antioxidant or other compounds. The most investigated areas were those of folate, often in relation to homocysteine levels as a proxy for folate status, magnesium, selenium and the antioxidant hypothesis in general with including vitamins C, E and Betacarotene, where several trials were performed. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Trial ¹¹ study and the Carotene and Retinal Efficacy Trial (CARET) ¹² study both clearly showed that a dietary change was needed to reduce cardiovascular disease, rather than the addition of separate micronutrients or phytochemicals. Other interesting compounds where more research is needed include phytoestrogens and sitostanols.

The life course perspective

The Barker Hypothesis ¹³ was introduced in the 1990's, when David Barker from University of Southampton published several papers and books on the concept of fetal programming of adult disease, for example coronary heart disease. Barker's group originally studied the prevalence of coronary heart disease in a group of middle-aged men from the Hertfordshire area in the United Kingdom, where accurate records existed regarding anthropometric measures at birth and growth data during infancy. In brief, Barker showed that fetal undernutrition as such or fetal undernutrition followed by a rapid weight gain in the first few months, lead to a higher risk of coronary heart disease. His hypothesis has since been supported or debated by an endless number of studies.

The life course perspective as an overall concept, looking at fetal growth as well as tracking of lifestyle habits or anthropometric data through life, is often quoted in modern publications on nutrition and health ¹⁴ and point at the importance of remembering that there are windows in time when tracking of lifestyle or health outcomes are more or less important and the inter-generational aspects of the origins of disease.

Published guidelines, a selection

Several recent guidelines point at the fact that what is good for preventing coronary heart disease is also good for preventing several forms of cancer, stroke and respiratory disorders. Modern sets of guidelines point at a reduced total fat intake and a shift from saturated fats to unsaturated, with a reasonably high ratio of n-3 to n-6 fatty acids. A high intake of dietary fibre in the form of unrefined cereals, bread, beans and legumes is suggested. An increased fruit and vegetable consumption and fish consumption, more physical activity and a healthy weight is also highlighted, as well as a reduced intake of salt and a reduction of “free” sugars in the diet ^{2 15 16}.

Final comments

Several important scientists ^{3 5 13 17} have paved the way to today's understanding of how to prevent coronary heart disease. We have clearly understood the significance of the life course perspective in regards to coronary heart disease. We have understood the importance of integrating the concepts of clinical, mechanistic and public health research into a holistic view of health promotion and coronary heart disease prevention. We have also noted that previous research, which was dominated performed on men, may not provide results that are applicable

to women⁹¹⁸. Finally, significantly more attention than earlier is paid to healthy eating as a part of an overall healthy lifestyle, including good sleep, a low stress level and a generally happy life.

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