THE DENTAL CLINICS OF NORTH AMERICA

Dent Clin N Am 47 (2003) 411–423

Nutrition for health promotion: phytochemicals, functional foods, and alternative approaches to combat obesity

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People have been bombarded with public health messages about the importance of diet and lifestyle and their impact on health. Modifications of the United States population's dietary habits could potentially decrease morbidity and mortality significantly. For example, the American Cancer Society estimated that diet relates to one of every three cancer deaths and, for Americans who do not smoke, dietary choices and physical activity are the most important modifiable determinants of cancer risk [1].

Functional foods and phytochemicals

The terminology surrounding the area of health risk reduction and disease prevention can be very confusing to the general public. Although differences exist, the term *functional foods* is often used in the press interchangeably with the terms *chemopreventive agents*, *designer foods*, *nutraceuticals*, *pharmafoods*, and *phytochemicals*.

Functional foods are a new area of interest because of their potential health benefits. Functional foods contain significant levels of biologically active components that impart health benefits when consumed in optimal serving sizes. Individual components added to food items by enhancement, fortification, manipulation, or bioengineering could also be considered functional [2] (eg, enhancement through genetic engineering of foods such as vitamin C–enriched oranges or lycopene-enriched tomatoes, fortification of milk and dairy products with vitamins A and D, and fortification of flour products with folic acid).

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doi:10.1016/S0011-8532(02)00109-X

Individuals consuming functional foods meet the requirements for nutrients while consuming other naturally occurring health-promoting phytochemicals that act synergistically within the food to enhance health. Potentially, biotechnology, food fortification, and plant breeding could enhance the amount and presence of health-associated phytochemicals found in functional foods.

To date, there is no legal definition for functional foods; however, several organizations have provided working definitions. The International Food Information Council defines functional foods as foods that provide health benefits beyond basic nutrition [3]. Thus, broccoli (with sulforaphane, indoles, and so forth) and tomatoes (with lycopene) can be considered functional foods. The International Life Sciences Institute of North America defines functional foods as foods that, by virtue of physiologically active food components, provide health benefits beyond basic nutrition [4]. The Institute of Medicine of the National Academy of Sciences limits functional foods to those foods in which the concentrations of one or more ingredients have been manipulated or modified to enhance their contribution to a healthful diet [5].

Based on the above definitions,

- Unmodified whole foods (eg, fruits and vegetables) represent the simplest example of functional foods.
- Modified foods, including those that have been fortified with nutrients or enhanced with phytochemicals or botanicals, also fall within the realm of functional foods.
- Genetic engineering and biotechnology will continue to provide new avenues for functional food development.

The following are examples of functional foods:

- β glucan in oats may protect against cardiovascular disease.
- Conjugated linoleic acid in dairy and meat products may lower risk of cancer and coronary artery disease and may affect body composition.
- Fructo-oligosaccharides in Jerusalem artichokes, shallots, onion powder, bananas, garlic, and tomatoes may affect intestinal flora. Fructo-oligosaccharides are the preferred colonic fuel, changing colonic pH.
- Lactoferrin in milk and dairy products appears to stimulate the immune system and act as an antimicrobial agent.
- The probiotics lactobacillus and bifido-bacter in selected dairy products may be protective in colon cancer and improve the microflora of the gastrointestinal tract.

Scientific research has provided a rationale for functional foods:

- Epidemiologic research shows strong beneficial association between increased dietary intake of fruits, vegetables, grains, fish, and legumes and reduced risk for various chronic diseases.

- Significant correlations have been identified between (1) dietary fiber and fat and colon cancer, (2) folate and neural tube defect prevention, (3) calcium and osteoporosis, (4) dietary fat and psyllium and altered blood lipids, and (5) sodium and hypertension.

In their 1999 position statement, the American Dietetic Association stated that "functional foods, including whole foods and fortified, enriched, or enhanced foods, have a potentially beneficial effect on health when consumed as part of a varied diet on a regular basis, at effective levels" [6].

Phytochemicals are components of plants that convey healthful properties beyond their use as macronutrients or micronutrients. Scientists have identified thousands of phytochemicals in vegetables, fruits, grains, legumes, and other plant sources.

Phytochemicals include antioxidants such as carotenoids (beta-carotene, lutein, or lycopene), vitamin C, vitamin E, and folic acid. They also include flavonoids, glucosinolates (isothiocyanates and indoles), phenolic acids, phytates, and phytoestrogens (isoflavones and lignans), to name a few. Within each of these phytochemical groups, hundreds to thousands of individual compounds exist. For this reason, eating a wide variety of plant foods is essential to achieving the maximum benefit from the myriad of beneficial phytochemical components available.

A growing body of evidence exists for other diet-disease relationships including the health-promoting effects of several phytochemicals. For example, sulforaphane, a phytochemical found in high concentrations in broccoli sprouts, has been shown to reduce tumor size and number in rats exposed to chemical carcinogens and to induce antiangiogenesis and apoptosis [7]. Recently, it was reported that sulforaphane inhibits *Helicobacter* infections and blocks gastric tumor formation, potentially functioning synergistically to provide diet-based protection against gastric cancer in humans [8].

Although most scientific evidence to date supports a positive role for nutrients and phytochemicals in the prevention and treatment of disease, additional evidence indicates that select nutrients and phytochemicals, particularly when consumed in excess, may be harmful to overall health [9,10]. Therefore, it is prudent to consume these health-promoting components when feasible through a varied diet rather than as concentrated levels in pills or supplements.

One of the functions of phytochemicals is to protect cells and tissues within the body from the oxidation-reduction reactions that occur continuously from normal activities such as respiration, exercise, and exposure to environmental pollutants, ultraviolet light, and other potentially carcinogenic agents. When oxidation occurs, oxygen molecules lose an electron, becoming highly reactive and unstable. These oxygen, hydroxyl, or other free radicals then seek electrons to stabilize or neutralize themselves. As a result, they damage cell membranes, alter cell structures and functions,

depress immune functions, damage the genetic material in the cell nucleus (DNA), and inactivate antioxidant enzymes.

Our bodies have several defense mechanisms that work synergistically against this free-radical assault. Antioxidant enzymes, nutrients, and non-nutrient scavengers are examples of our body's response to these free radicals. Antioxidant enzymes function inside and outside the cell. Zinc, copper, manganese, and selenium act as cofactors for these enzyme systems. These enzymes are genetically predetermined. When adequate amounts of a given trace mineral are unavailable, the enzyme might not function optimally.

The multistep carcinogenesis model is now a well-accepted conceptual basis for cancer development [11]. Initiation of a normal cell occurs when exposure to chemical carcinogens, viruses, radiation, replication errors, dietary factors, and other causes damages the membrane or the DNA material within the cell. DNA repair mechanisms usually restore the cell to its normal status. If the cell is unable to repair itself, it then becomes initiated, or mutated. An initiated cell is still able to carry out its function or maintain its structure, and may pass on its mutation when it replicates, thus advancing from initiation to promotion. At this stage, the cell may experience spontaneous remission back to initiation or be exposed to growth inhibitors or antipromoters that will allow regression back to initiation. If the mutated cell continues to be exposed to potential carcinogens, however, it may eventually lose its integrity and develop into a premalignant lesion such as dysplasia, carcinoma in situ, or polyps. As the cell loses more of its control over function and structural integrity, it will continue to progress to the clinical stage of cancer.

Chemoprevention offers hope that if the cell cannot be protected at initiation (which would be ideal but not always possible), then at least it could be protected during the promotion stage. Cells can remain in the promotion stage for years or decades before cancers such as breast, prostate, or colorectal cancers manifest themselves. During this promotional phase, chemopreventives may be able to delay, regress, or inhibit cells from advancing to the clinical stage. There is a potentially wonderful opportunity to provide a means through improved nutrition and diet to decrease an individual's risk of developing cancer.

The damage caused by free radicals and oxidation also increases the risk of cardiovascular disease and other chronic illnesses so prevalent in our society today.

From epidemiologic studies in vitro and from animal research and human clinical trials, dietary compounds have been identified that can be initiators/promoters or anti-initiators/antipromoters. Lifestyle issues such as obesity and inadequate physical activity contribute to health risks.

The basis for these concepts comes from epidemiologic research. One of the first groups to explore the relationship between fruits/vegetables and the risk of various cancers was Block et al [12], who reviewed over 200 studies.

They found that there is no singular magic vegetable or fruit. They also found that individuals who consumed few fruits/vegetables had twice the risk of developing cancer as those individuals who ate more. Steinmetz and Potter [13] reviewed 206 epidemiologic studies and 22 animal studies also evaluating the relationship between vegetable and fruit consumption and cancer incidence. Their conclusions were consistent with Block et al [12]. The problem remains that people do not want to change their lifestyle. Individuals would rather take a pill or do nothing at all. Americans eat too many calories, too little fruits/vegetables and fiber, and are too sedentary. To effect change, individuals will need to

- Maintain a healthy weight
- Increase fruits and green/yellow vegetable consumption
- Increase soluble and insoluble dietary fiber
- Increase certain micronutrients
- Select healthy fats
- Limit the amount of sugars and starches

The health professional's role is to provide the tools and resources for individuals who would benefit from changing their diet and lifestyle but do not know how to do it. Because 100% of Americans eat, improving dietary habits may have a dramatic impact on the future health and well-being of the United States population.

An alternative approach to combat obesity

We are all aware of the epidemic of obesity and diabetes exploding within the American population. Just before leaving office, Surgeon General Dr. David Satcher released *The Surgeon General's Call to Action to Prevent and Decrease Overweight and Obesity* [14]. Even though the consumption of fat has steadily decreased over the past decade as Americans have became a fat-phobic society, body weight has continued to rise. Clearly, health professionals need to consider options or alternatives to the only recommendation currently being offered (ie, low-fat, low-calorie, portion-controlled diets) because this method is not succeeding. It is time to consider thinking "out of the box" for another approach to this serious health problem.

In a provocative article in *Science* entitled "The Soft Science of Dietary Fat," Gary Taubes [15] notes that "mainstream nutritional science has demonized dietary fat, yet 50 years and hundreds of millions of dollars of research have failed to prove that eating a low-fat diet will help you live longer." In that same article, Taubes quotes Dr. Walter Willett who states, "NIH has spent over $100 [million] on the three Harvard-based studies yet not one government agency has changed its primary guidelines to fit these particular data. They say, 'you really need a high level of proof to change the

recommendations' which is ironic, because they never had a high level of proof to set them'' [15]. Dr. Willett and his colleagues studied the relationship between glycemic load and carbohydrate intake and the risk of heart disease. Their findings suggested that

> a high intake of rapidly digested and absorbed carbohydrate increases the risk of coronary heart disease independent of conventional coronary disease risk factors. These data add to the concern that the current low-fat, high carbohydrate diet recommended in the United States may not be optimal for the prevention of coronary heart disease and could actually increase the risk in individuals with high degrees of insulin resistance and glucose tolerance [16].

Despite the fact that significant numbers of individuals have successfully lost weight and improved their health status using the low-carbohydrate approach, we continually hear from conventional health care professionals and see in the media dire predictions of what will happen to an individual who considers such options. Concerns about the dangers of developing increased risk factors for heart disease, kidney disease, loss of muscle mass, and other negative effects are continually raised but are not supported by scientific evidence. In fact, a body of emerging research exists that shows the benefits of lowering carbohydrate intake and increasing the intake of healthy fats. To help those skeptics who are locked in their thinking that increasing fat and protein intake is counterintuitive to weight loss and good health, consider this: the human body has an essential nutrient requirement for both protein (amino acids) and fats but no essential requirement for carbohydrate.

For an individual with high triglycerides (TGs), low high-density lipoprotein (HDL) levels, and truncal obesity, insulin resistance (Syndrome X or hyperinsulinemia) should be considered. Testing for this condition includes reading glucose and insulin levels (fasting and 2-hour postprandial after a carbohydrate challenge). When possible, a 5-hour glucose tolerance test with insulin levels checked every 2 hours may be beneficial. For individuals with high cholesterol, low HDL, and high low-density lipoprotein (LDL), a complete lipid profile (including lipoprotein-A subfractions, C-reactive protein, homocysteine, and fibrinogen) and an ultra-fast computed tomography scan along with other appropriate studies based on the patient's clinical history can be useful in supporting proper diagnosis and decisions for appropriate treatment. An individualized diet and nutritional support best suited to the individual can then be implemented. A single diet will not fit all patients. Some individuals might do best on an Ornish-type or Pritikin-type (very low fat, high-carbohydrate) diet. Others might respond favorably to a vegetarian or vegan-type approach. Identifying specific needs and conditions is key to successful application of the best approach and management of each patient.

The controlled-carbohydrate diet is one viable alternative dietary approach. Many clinicians presume that this diet will increase patients'

potential risk of heart disease. There are scores of scientific studies, however, that validate the use of limiting sugars and refined carbohydrates as a means of reducing the risk of developing heart disease and controlling serum glucose levels in type 2 diabetes mellitus patients. Clearly, there are benefits of a controlled-carbohydrate diet in preventing heart disease (versus reversing the effects of the disease process). This distinction is a crucial one because many critics of this approach use the lack of science in reversing or curing heart disease as a justification for not using a controlled-carbohydrate diet for the millions of individuals who are overweight or obese and are at increased risk of developing heart disease or diabetes.

A review of existing, ongoing, and soon-to-be published research, common sense, and an obvious public health crisis mandates a new look at the impact of current nutritional recommendations that stress low-fat, low-calorie diets limiting saturated fats and emphasizing complex carbohydrates. If this approach succeeds, then it should be encouraged and supported. If individuals respond to this approach and their metabolic and physiologic values improve, then this is clearly a successful approach.

Despite this universal approach, however, heart disease continues to take more lives annually (950,000) [17] than other diseases and the American population has reached an all-time high overweight/obesity level of 61%. Diabetes, which affects 17 million Americans, has increased 49% in the last decade and is expected to increase similarly in this decade [18]. Clearly, reevaluating the dietary advice given to overweight and obese individuals who are at risk for these chronic diseases is in order. Although this point seems obvious, it is not supported by many practitioners.

One of the most dramatic findings of the controlled-carbohydrate diet is its beneficial effect on TGs. Among the large number of studies showing the impact of TGs on cardiovascular disease is the large meta-analysis of 17 studies including 10,864 women followed for 11.4 years and 46,413 men followed for 8.4 years. TG elevation of 1 mmol/L (88 mg %) increased cardiovascular risk in men by 32% and in women by 76% [19]. One of the studies in this meta-analysis showed that cholesterol levels were less harmful in subjects whose TG levels were in the lowest quartile. Other studies found that a high TG level was an extremely predictive risk factor.

In a recent study by Tanne et al [20], high TGs were shown to be an independent risk factor for ischemic stroke/transient ischemic attack across subgroups of age, sex, patient characteristics, and cholesterol fractions, whereas high-percent HDL was an independent protective factor among patients with coronary heart disease (CHD). The investigators concluded that their findings supported the role of blood lipids, including TGs, as important modifiable stroke risk factors [20].

In a study by Stavenow and Kjellstrom [21], 12,500 men were followed for risk of myocardial infarction using the interaction between cholesterol and TGs. The lowest quartiles of both cholesterol and TGs were the most protective; however, those who had very low TG levels (<100 mg/dL) but

high cholesterol levels (>245 mg/dL) still had very few myocardial infarction incidences [21]. Another study evaluating the effects of TGs and LDL-cholesterol/HDL-cholesterol on heart disease found that when the LDL/HDL ratio was high and TG levels were low, there was an increase in events compared to when the LDL/HDL ratio was low. When the LDL/HDL ratio was high and TG levels were high, however, the number of events quadrupled, again supporting the hypothesis that TGs play a significant role in CHD risk [22]. Assmann et al [23] looked at CHD events by serum LDL-cholesterol and TG concentrations. In light of the recent National Cholesterol Education Program (NCEP) recommendations, this study is very interesting. Although LDL levels <130 mg/dL were the most protective, patients with TG levels >200 mg/dL had more than twice the incidences of those with TG levels <200 mg/dL. As the LDL increased, so did the number of events, with higher TG levels always producing more events in each LDL quartile than lower TG values. The highest quartile of LDL (>190 mg/dL) showed almost 2.5 times the events with high TG levels compared with TG levels <200 mg/dL. In light of the recent recommendations about the use of statin drugs with LDL values >130 mg/dL, decreasing TG levels may be more appropriate than use of statin drugs for management of these high-risk individuals [23]. Another large-scale study that evaluated the impact of HDL-cholesterol versus TGs as indicators of ischemic heart disease found that TGs were a stronger predictor of ischemic heart disease than HDL-cholesterol. This finding was borne out by the tertile of high TG levels that indicated more incidences of ischemic heart disease even with a high HDL value [24]. In a study done by Gaziano and colleagues [25] at Harvard Medical School and Brigham and Women's Hospital, high TGs combined with low HDL levels were more predictive than any other risk factor combined. Persons in the highest quartile were 16 times more likely to have a coronary event than those in the lowest quartile [25]. The combination of high TGs and low HDL levels has a common cause: hyperinsulinemia.

In a study conducted at Johns Hopkins University looking at 780 subjects who had baseline angiograms and then were followed for 18 years, subjects with a TG level <100 mg/dL had the greatest protection against conronary events. As the TG level increased, the risk that a coronary event would occur also increased [26].

These studies illustrate what a large number of research findings have proved: TGs are an independent risk factor. These findings need to be addressed and then applied in the context of individuals with hyperinsulinism, insulin resistance, prediabetes, and syndrome X—all of which are affected by dietary constituents that elevate serum glucose levels with concomitant elevation of serum insulin. Studies supporting the relationship between insulin, TGs, and CHD have been done. One example is the finding by the Harvard Nurses Health Study where glycemic load was measured against the risk of CHD in 75,000 women [16]. Women who consumed more

carbohydrates and a greater glycemic load had significantly more coronary events. The highest quartile exceeded the bottom two quartiles by over 25%. The authors concluded that

> a high intake of rapidly digested and absorbed carbohydrate increases the risk of CHD independent of conventional coronary disease risk factors. These data add to the concern that the current low fat, high carbohydrate diet recommended in the United States may not be optimal for the prevention of CHD and could actually increase the risk in individuals with degrees of insulin resistance and glucose intolerance [16].

What is happening, then, to the millions of individuals who are following the low-fat, high-carbohydrate diet recommended by most health professionals today? What is happening to their TG levels, and what impact are TG levels having on their overall health? One study by Abbasi et al [27] looked at high-carbohydrate diets and their effect on TGs using 60% versus 40% carbohydrate in their diets. Serum TG levels were almost 100 mg/dL higher on the 60% carbohydrate diet [27].

Carbohydrates contribute to the elevation of serum glucose, insulin secretion, and fat mobilization. In an interview, Dr. Walter Willett stated that "the typical American will have some degree of insulin resistance, and in this setting a high intake of highly refined carbohydrates can result in serious health problems, such as diabetes and heart disease" [28].

With so much evidence to support the important role of TGs in reducing the risk of many chronic diseases, recommending a controlled-carbohydrate diet would seem to be a prudent clinical alternative to the current recommendations in those patients identified as appropriate candidates.

What about the effect on heart disease from fats that would increase on a controlled-carbohydrate diet? There is ample evidence to show that lipid profiles improve on a controlled-carbohydrate diet. Dietary studies have been performed consistently in the context of high levels of carbohydrate. When carbohydrates are controlled for, lipid levels improve, as seen in a recent study on adolescents comparing a low-fat, calorie-controlled diet to an unrestricted-calorie intake, low-carbohydrate diet. The investigators found that all lipid parameters improved on the controlled-carbohydrate diet even though the caloric intake was over 700 calories more than the low-fat study diet [29]. These results have been repeated in several other studies that achieve the same results when the carbohydrate level is reduced enough. Two recent dietary studies on adults presented at nutrition conferences showed that the controlled-carbohydrate diet resulted in greater weight loss, better compliance, and improved overall lipid profiles [30–32]. Another recent study showed improved body composition and hormonal balance [31].

Many concerns such as ketosis or hepatic and renal damage have been refuted or never substantiated in the scientific literature. Ketosis is very well controlled in normal individuals [33]. In ketosis, the body defends against abnormal pH levels similar to its control of acid/base balance, temperature

fluctuations, or regulation of serum glucose levels. The brain's ability to effectively utilize ketones for energy has been accepted for many decades. No hepatic or renal damage has been seen with controlled-carbohydrate intake [33]. Therefore, these claims, like many of the erroneous statements about a controlled-carbohydrate diet, are unfounded and should not deter a practitioner from selecting such a regimen when faced with a patient who has been unsuccessful in controlling obesity using a low-fat, low-calorie approach and is becoming frustrated and discouraged.

Dozens of diet books abound with a similar theme of decreasing carbohydrates and increasing protein and fat in varying degrees. By redistributing carbohydrates (55%–65%), proteins (12%–15%), and fats (20%–30%) as currently recommended to a lower carbohydrate and higher protein/fat ratio, the body will begin to burn stored fat and suppress lipolysis. Excess calories, especially from high carbohydrate consumption in combination with fat, predisposes individuals to fat accumulation, especially truncally.

Dr. Robert Atkins' approach begins with low carbohydrate levels that "kick start" the fat-burning metabolic process and limit insulin secretion. The Atkins approach calls for individuals to reduce carbohydrate intake to 20 g (predominantly in the form of vegetables). The remaining foods consist of healthy fats, proteins, and a lot of water and fluids, along with exercise and some supplements to obtain optimal nutrition. What most practitioners fail to appreciate is that this phase is of short duration and allows the person not only to begin to lose weight (specifically truncally) but also to become sensitized to the excess carbohydrate consumption one typically eats when not aware of carbohydrates. After several weeks, the individual is encouraged to slowly and gradually introduce additional vegetables, nuts, seeds, beans, whole grains, and low-glycemic fruits to the food selection. By gradually introducing these foods in small amounts, individuals become aware of appropriate amounts of carbohydrate-containing foods that are appropriate for them to eat, as well as the total amount of carbohydrate that will prevent weight from being regained. By the time individuals reach this maintenance level, they should be eating a very healthy, nutritionally complete diet.

Other controlled-carbohydrate approaches have a similar theme, with modifications or gradations of allowed carbohydrates. Protein Power by two physicians and the Eades diet advocate reducing carbohydrates, starting with 30 g in the initial phase and then advancing to 55 g in the second phase. These diets stress the intake of proteins, using 0.5 g to 0.9 g or more of protein per pound of lean body mass per day. Healthy fats are also allowed and more frequent feedings are encouraged versus three set meals.

The Zone Diet by Dr. Barry Sears balances the three macronutrients in a 40:30:30 ratio of carbohydrate:protein:fat. Sears encourages the use of lean protein, low glycemic-index carbohydrates, and the use of monounsaturated fats (olive and peanut oil) and omega-3-fatty acids (fish oil).

Sears also suggests three meals and two snacks daily. Although his carbohydrate intake is higher than the Atkins and Eades approaches, he likewise stresses the need to limit sugars and refined carbohydrates. What many health professionals along with consumers do not realize is that refined carbohydrates include breads and flour products, white potatoes, rice, and pasta, erroneously thought of by many as being healthy complex carbohydrates.

Another well-known diet is the Carbohydrate Addict's Diet by Rachel Heller, MPh, PhD and Richard Heller, MS, PhD. These authors focus on the number of times a day carbohydrates are consumed, with the belief that insulin levels that are elevated several times a day cause individuals to lose control of their eating and their cravings. They allow one meal of short duration (consumed within an hour) when carbohydrates are not limited. In this way, insulin production is not excessive and hyperinsulinemia is not a problem. The other meals contain lean protein, vegetables, and limited fat intake. This program aims for a low-carbohydrate, low-fat, high-fiber intake.

Other controlled-carbohydrate diets suggest restricting the sugar and refined carbohydrate content of the diet without restricting the total carbohydrate intake. Another unique approach, Neanderthin, is advocated by Ray Audette and Troy Gilchrist. Their premise is that our bodies are still functioning metabolically as our Paleolithic ancestors did—as hunters and gatherers before agriculture and technology drastically changed our food selection and intake. Consumption of meat, poultry, fish, fruits, vegetables, nuts, seeds, and berries are what this approach suggests as being appropriate for our body's most effective functioning; we are not metabolically efficient in digesting refined grains, potatoes, sugar, dairy products, and all the modern-day processed foods so abundantly prevalent today.

There are many other variations on this same theme. Maybe we need to consider that there may be some basis for so many books advocating a similar approach. The effectiveness of restricting carbohydrates has been known for over 100 years. Current research, more sophisticated than that available in the 1800s, is corroborating the metabolic rationale for this approach. The obesity problem is not being solved with current methods and recommendations. A new paradigm is needed. Individual needs and clinical parameters, such as syndrome X or a lipoprotein subclass pattern that genetically predisposes an individual to increased risk with a low-fat intake as shown by Dr. D.M. Dreon [34] and Dr. R.M. Krauss [35] and other researchers should be the focus. An exciting possibility lies ahead, with more options and greater potential to improve the quality of life and the health of at-risk individuals.

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