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Progress in Pediatric Cardiology 17 (2003) 179–186

Progress  
in  
Pediatric  
Cardiology

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## Current concepts of diet therapy for children with hypercholesterolemia

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Accepted 1 May 2003

### Abstract

Substantial evidence now exists that the origins of atherosclerosis begin in childhood. Therapeutic efforts early in life may delay formation of advanced atherosclerotic lesions and enhance early opportunities for lifelong acquisition of heart healthy eating habits. Diet therapy is the cornerstone of clinical management of children with hypercholesterolemia. The National Cholesterol Education Program targets lowering elevated LDL-cholesterol as the primary aim of diet therapy. Recommended dietary modifications for children with elevated LDL-cholesterol include lowering total fat to 30% or less of calories, saturated fat to less than 10% of calories, cholesterol to less than 300 mg/d, and consuming enough calories to achieve or maintain desirable body weight. For children with severe hypercholesterolemia (persistent LDL-cholesterol >130 mg/dl), a further reduction in saturated fat and cholesterol are advised. Parents play a powerful role in promoting adoption of heart healthy eating habits at home. Feeding strategies parents can use to promote acceptance of low fat foods include increasing the availability and accessibility and exposure to these foods, modeling healthy food habits, and presenting healthy foods to their child in a relaxed non-pressured manner. Adherence to a low fat diet can safely lower LDL-cholesterol levels and provide optimal calories and nutrients to support normal growth and development in childhood and adolescence.

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**Keywords:** Diet therapy; Children; Hypercholesterolemia; Step-one diet; Saturated fat

### 1. Introduction

Several important developments have occurred in the area of medical nutrition therapy for pediatric hypercholesterolemia over the last decade. First, the rationale for early intervention has been strengthened by well-designed pathobiological studies documenting that the juvenile fatty streak, an innocuous cluster of lipid filled cells, can progress to advanced atherosclerotic lesions within a few decades. Second, there is now consensus among major health organizations, including the expert panel of the National Cholesterol Education Program (NCEP), the American Heart Association (AHA), and the American Academy of Pediatrics (AAP) that controlling the type and amount of dietary fat after the age of 2 years has the potential to reduce atherosclerotic vascular disease in adulthood. Third, repeated studies have demonstrated the safety and efficacy of fat-modi-

fied diets in children, and successful family-based and school-based programs have been developed to modify children's food intake. The purpose of this review is to discuss the current rationale for early dietary intervention for childhood dyslipidemia, provide guidelines and strategies for implementing low fat diets in childhood, and review the evidence suggesting that dietary changes that lower fat intake in children can be acceptable, safe and efficacious.

### 2. Rationale for treating hypercholesterolemia in childhood

There is substantial evidence to show that the presence of complicated fibrous plaques or raised lesions on coronary vessels determines the risk of coronary heart disease (CHD) and associated clinical sequelae. The fatty streak, a lesion composed predominantly of non-obstructive lipid-filled cells (macrophages) in the arterial intima, is considered the predecessor of the raised lesion. Fatty streaks begin to appear in the aorta in the

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first decade of life, and in the coronary arteries by the end of the first into the second decade [1]. Histologic studies of the coronary arteries of approximately 500 persons from birth to age 29 have documented the progression of atherosclerosis by age from the simple clustering of macrophage foam cells in about a third of children <9 years of age, to the larger accumulation of foam cells, extracellular lipid and lipid in smooth muscle cells in about half of children by early adolescence [2]. These same studies documented that about one-third of young adults have advanced lesions containing extracellular lipid and cholesterol ester crystals with a thick fibromuscular cap. Importantly, comparisons of the localization of lesions in the coronary arteries showed a close correspondence between the localization of fatty streaks in young persons and that of raised lesions in older persons [3]. These data are strongly suggestive that the atherosclerotic process has its origins in childhood.

An elevated low-density lipoprotein (LDL) cholesterol concentration has been shown to be the most common determinant of the progression of atherosclerosis. Pathobiological studies of coronary arteries of some 3000 persons aged 15–34 years, who died prematurely from accidental injury, homicide or suicide have shown that the percentage of surface involved by fatty streaks and fibrous plaques in the coronary arteries was positively associated with LDL-cholesterol concentration [4]. Similar findings were reported by a smaller observational study [5]. Complex molecular and cellular mechanisms involving the endothelium, oxidized LDL and scavenger receptors can now explain the physiologic process by which elevated plasma LDL concentrations may transform the innocuous fatty streak into a pathological lesion under certain conditions [4]. The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study demonstrated that the third decade of life (20–24 years) is the timeframe when elevated LDL-cholesterol concentrations begin to significantly affect raised lesion formation [4]. For this reason, critics of therapeutic interventions to lower elevated LDL-cholesterol concentrations in children suggest that intervention efforts are not likely to alter risk of developing atherosclerosis until young adulthood. While it is true, with the exception of homozygous familial hypercholesterolemia that dyslipidemia in childhood is not associated with CHD morbidity or mortality during childhood, chronic exposure to elevated atherogenic lipoproteins may accelerate the age at which fibrous plaque formation occurs. Proponents of early interventions for childhood dyslipidemia suggest that therapeutic efforts early in life may delay lesion development [6]. Furthermore, proponents also suggest that dietary intervention for dyslipidemia in childhood is likely to enhance early opportunities for lifelong acquisition of heart healthy lifestyle habits [7,8]. Evidence to support this latter claim is discussed below.

Results from the PDAY study also indicated that elevated body mass index and low HDL-cholesterol concentrations, were positively correlated with the increased histologic extent of atherosclerosis [4]. Almost all coronary risk factors are increased with obesity, including elevated total and LDL-cholesterol levels, reduced HDL-cholesterol levels, hypertension and insulin resistance. Importantly, even small amounts of weight loss have been shown to result in the normalization of the lipid profile in obese adolescents [9]. As overweight/obesity becomes more common in children and adolescents [10], the number of children with both dyslipidemia and obesity who are seen in clinical practice is increasing [11]. For this reason, it is important that overweight/obesity management be considered an integral component of the dietary treatment protocol for children with a BMI >85<sup>th</sup> percentile. The NCEP also suggests that obesity be considered a discretionary criterion for screening children for the presence of dyslipidemia [12].

### 3. Criteria for therapeutic intervention

Given the strength of the evidence that elevated LDL-cholesterol concentrations contribute to the pathogenic process of atherosclerosis, there is consensus among health organizations that therapeutic interventions should focus on normalizing LDL-cholesterol levels in children above the age of 2 years. The NCEP currently recommends that children with elevated LDL-cholesterol, be provided with dietary instruction to lower excess consumption of saturated fatty acids, total fat and cholesterol [13]. More specifically, the NCEP recommends that children with LDL-cholesterol concentrations in the borderline high range (110–129 mg/dl) should initiate the AHA step-one diet (as described below), and be counseled on managing other risk factors for CHD (e.g. smoking, obesity, diabetes, high blood pressure). For children with LDL-cholesterol concentrations in the high range (>130 mg/dl), the NCEP recommends that they be screened for secondary causes of hypercholesterolemia (renal and hepatic disease, endocrine disorders or as a result of medication ingestion) and familial disorders, and that they initiate the step-one diet, followed by the step-two diet, if necessary. A summary of the NCEP criteria for diet therapy can be found in Table 1.

Although the goal of dietary therapy is to lower the LDL-cholesterol level to less than 110 mg/dl, in some cases this will not be possible. Potential reasons include the fact that a child may already be consuming a heart healthy diet, so further improvement is not possible or that the elevation in LDL-cholesterol may be so severe that the percentage of reduction achieved by dietary modification still may not lower LDL-cholesterol to the target goal. In this latter case, the NCEP suggests that a target goal for LDL-cholesterol should be set at 130

Table 1  
LDL-cholesterol cutpoints for dietary intervention

Category	LDL-cholesterol (mg/dl)	Dietary intervention
Borderline	110–129	Advice on the step-one diet and other risk factors by an appropriately trained health professional.
High	≥ 130	Detailed assessment of current eating patterns and instruction on the step-one diet by an appropriately trained health professional. Reevaluate after 3 months. If good adherence but has not reached target LDL-cholesterol goal, instruction on the step-two diet should be provided.

Modified from Ref. [13].

mg/dl. Importantly, because lowering LDL-cholesterol levels reduces the progression of CHD, any lowering of LDL-cholesterol levels is valuable, even if the goal is not accomplished.

A large body of evidence suggests that a low HDL-cholesterol concentration is a powerful independent predictor of increased risk of premature coronary artery disease [14,15]. However, it has not been conclusively shown that increases in HDL-cholesterol resulting from diet and lifestyle modifications lead to reduce CHD risk. For this reason, the AHA has not made HDL-cholesterol a target of diet therapy [16]. Since obesity and inactivity are believed to increase CHD risk in part through their association with reduced HDL-cholesterol levels, efforts to manage adiposity and increase physical activity should be emphasized in the clinical management of children and adolescents with low HDL-cholesterol levels (NCEP criteria-HDL-cholesterol <35 mg/dl).

#### 4. Diet therapy considerations

##### 4.1. A step-wise approach

Leading health organizations including the NCEP [13], the AHA [17] and the AAP [18] recommend the step-one diet as the primary approach to lowering elevated LDL-cholesterol concentrations. Although this diet has been shown to be effective for lowering blood lipids and promoting optimal growth and development in children <1 year of age [19,20], current recommendations do not support use of the diet for children <2 years. The nutrient composition of the diet is 30% or less of calories from total fat, less than 10% of calories from saturated fat, and less than 300 mg/day of cholesterol with adequate energy to support growth and development. A precise percentage of dietary intakes of fat that supports normal growth while optimally reducing LDL-cholesterol in children are not known. Neverthe-

less, the NCEP and AHA recommend a total fat intake of approximately 30% of calories as a means to achieve a sufficiently low saturated fat intake while contributing adequate essential fatty acids, fat soluble vitamins and calories for normal growth and development [13,17]. In a recent revision to the AAP dietary recommendations for children with high cholesterol, the AAP specified that the 30% recommendation for total fat is not intended to be a daily recommendation but an average over several days, thus allowing for daily variation in this macronutrient [18]. Further, this organization has set a lower limit of 20% of calories from fat with the intent of preventing parents from over restricting fat in their children's diets.

The step-one diet may normalize LDL-cholesterol concentrations in children with LDL-cholesterol in the borderline high range. The reported responses to the diet in children with LDL-cholesterol levels <130 mg/dl have ranged from 3 to 10% [21–25]. For children with persistent LDL-cholesterol levels above 130 mg/dl (after 3 to 6 months of dietary compliance on the step-one diet), the NCEP recommends a step-two diet to reduce progressively saturated fatty acids and cholesterol to levels of <7% of calories and <200 mg/d, respectively [13]. These nutrients are targeted, because they are known to be the major nutrients that affect LDL-cholesterol levels [13,26–28]. Additional LDL-cholesterol reductions while on the step-two diet have ranged from 4 to 14% [22–25].

For many children with moderately or severely elevated LDL-cholesterol, diet alone will not lower their cholesterol values to the acceptable or even borderline values. Long-term drug therapy is associated with decreased incidence of both heart disease and overall mortality in adults [29]. However, long-term efficacy of drug treatment in children has not been studied. For this reason, the pediatric panel of the NCEP recommends using medication only in patients who are at least 10

years of age and who have failed on aggressive dietary treatment over a 6–12 month period [13].

Given that childhood overweight/obesity may result in elevated LDL-cholesterol, weight management should be a goal of diet therapy for children with a BMI >85<sup>th</sup> percentile. Weight reduction approaches should focus on decreasing the child's weight for height percentile, while maintaining linear growth [11]. Moderate caloric restriction can be achieved by following the step-one diet. Increased physical activity should be encouraged and sedentary activities, such as watching television, using computers for recreation or playing video games should be discouraged.

#### 4.2. Translating dietary prescriptions into food selections

From the practical point of view, when the step-one or step-two diet is recommended for a child, it is the rare parent that can translate a dietary prescription of 10% or 7% of calories from saturated fat into food selections for their family. In the Report of the Expert Panel on Blood Cholesterol levels in Children and Adolescents [13], the NCEP provides dietary implementation guidelines that outline recommended food choices and number of servings from different food groups necessary to achieve the step-one and step-two dietary total fat, saturated fat and cholesterol goals. To summarize, the report recommends achieving reasonable intakes of lean meats (e.g. 5–6 oz per day) and low-fat dairy products (24–32 oz per day). Meat, poultry and fish provide protein, iron, zinc and B12 to the diet, but are also significant sources of total fat, saturated fat and cholesterol. Meat selections should be from lean cuts (round or loin), and should be well trimmed before cooking. Skin should be removed from chicken or turkey and ground poultry should contain white meat only. Processed meats (e.g. hot dogs and bologna) that contain less than 3 g of fat per ounce are acceptable, as are all types of fresh or frozen unbreaded fish. Liver and other organ meats are high in cholesterol and should be limited to once per month. Like the meat group, dairy products provide important nutrients to the diet of children (calcium, phosphorus and protein), but contribute substantial amounts of saturated fat and cholesterol as whole milk products. Children should be encouraged to consume low fat or non-fat milk, yogurt, cottage cheese and frozen desserts. Acceptable cheeses are those that contain less than 6 g per ounce on the step-one diet, and less than 2 g per ounce on the step-two diet. Eggs should be limited to less than 4 per week on the step-one diet, and less than 2 per week on the step-two diet, because of their high cholesterol content. Breads, cereals, grains, fruits and vegetables should comprise the largest proportion of calories in the child's diet. Most choices within these food groups are low in fat, cholesterol free and high in fiber, and will help to displace

energy sources containing saturated fat. Children should be encouraged to choose whole-grain cereals, breads and pasta, rice and beans, and to consume at least five servings of fruits and vegetables per day.

Although obvious fats in the diet should be limited, enough should be consumed to allow for normal growth and development. In particular, unsaturated fats including canola, corn, soybean, sunflower and peanut oils should be used in cooking in place of lard and shortening. Soft tub margarines should be used in place of butter. Foods high in saturated fat and low in nutrient density such as bakery goods, candies and fast foods should be avoided. Recently, a new class of margarines and other fat derived products (salad dressing, mayonnaise) containing plant sterols and sterol esters that are intended to lower blood cholesterol levels have been introduced into the marketplace. Although, these products have been shown to decrease LDL-cholesterol by 9 to 20% in children, when consumed at levels of ~2 g/d [30–33], there are some observations of decreased fat soluble vitamin status as a result of the consumption of these foods [34,35]. The AHA recommends that, although these margarines can be used as a dietary adjunct in moderate to severely hypercholesterolemic children, fat soluble vitamin status should be monitored in these patients [36].

Snack foods are an important part of the diet of a child. Thus, educating the family about low calorie, healthy snack foods like fruits and vegetables should be a focus of dietary intervention. Diets that are high in sucrose, likely from excess sugared snack food and beverage consumption, have been associated with low HDL-cholesterol and high triglyceride levels in children [37]. Thus, snack foods should be recommended that are low in sugar, such as pretzels, graham crackers and vanilla wafer cookies. Additionally, nearly 60% of US school children obtain 25–30% of their saturated fat and cholesterol intake in the school lunch program [28]. Parents should be encouraged to become familiar with their child's school lunch menus and assist their child in incorporating school meal choices into the recommended diet. Importantly, to assist parents in meal planning, the NCEP recommends that families should receive consultation with a registered dietitian after being diagnosed with high cholesterol. Registered dietitians are trained to appropriately assist children, and their families in translating dietary recommendations into practice.

#### 4.3. Child-feeding strategies

Current research suggests that feeding strategies parents use to get their children to eat certain foods play a powerful role in determining food intake and consumption patterns in childhood [38,39]. Parents can promote heart healthy food consumption at home by making

these foods available and accessible to their children [40–42]. Children choose to eat foods that are served most often, and prefer what is available and accessible in the parental household [43]. Increased availability and accessibility of low fat, nutritious foods in the home provides opportunities for children to try and become familiar with these foods early in life. These experiences with heart healthy foods may be particularly important, because familiarity is central to a child's acceptance of foods [43]. Increased availability and accessibility of low fat foods also enhances a child's preference for these foods by allowing them repeated opportunities to taste these foods. Children tend to reject unfamiliar foods, but initial rejection can be modified through repeated exposure. A minimum of 8–10 exposures (each including at least a taste) to new foods [44,45] increased preference for these foods among young children. Thus, parents and child-care providers may provide opportunities for children to learn to like a variety of low fat nutritious foods by exposing them to these foods early in childhood.

A second strategy parents can use to promote compliance to a heart healthy diet is through modeling appropriate eating behaviors. Children's acceptance of foods follows the example of parents [46]. In a study of children between the ages of 3 and 5 years, Oliveria et al. [47] demonstrated that the fat intake of children was related to that of parents. Children whose parents ate high amounts of saturated fat were 5.5 times more likely to eat a high amount of saturated fat than children in families where parents were not consuming a diet high in saturated fats. Likewise, Hertzler [48] noted that children were more likely to eat a food when they saw an adult eating it, and that a child's acceptance of a food was more likely to follow the example of parents and familiar adults. Children tended to sample an unfamiliar food more readily when an adult was eating it, than when they were merely offered the food [46]. Thus, modeling specific eating behaviors by parents can have a powerful effect on food selection of a child.

Meal structure and parents food socialization practices may also impact children's dietary quality. For young children, parents control when and whether families eat together. Increased frequency of a family dinner was associated with more healthful dietary patterns among children, i.e. higher consumption of fruits and vegetables, and a lower consumption of fried foods [49]. Food socialization practices are the process by which a parent's beliefs and attitudes about food shape their children's food related beliefs and attitudes, which in turn influence their intake of certain foods [50]. Research shows that parents who convey a positive attitude about healthy foods increase their children's preference for these foods [51]. Additionally, parents who offered nutrition explanations or talked more specifically about the nutritional value of food had children who reported

greater nutrition knowledge [52], and increased acceptance of healthful foods [53].

Many parents restrict the availability and accessibility of unhealthy foods through use of controlling child-feeding practices. Research suggests that parents who use controlling child feeding strategies to limit foods that are high in fat, sugar and energy may inadvertently increase their child's preference for these foods. Parental control can take several different forms including restricting access to foods, encouraging (verbally or by rewarding) the amount and type of food that the child eats, and keeping track of the child's consumption of energy-dense foods. Several studies [54–56] have demonstrated that using foods high in sugar or fat as a reward for eating or performing a task increases a child's preference for these foods. Fischer and Birch [57] found that maternal restriction of a child's access to snack foods was related to over-consumption of those same foods in an unrestricted setting. Birch [58] also found that children whose parents were more controlling in the amounts and types of foods they ate, were less able to regulate energy intake and the amount of food consumed. Given the fact that foods that are restricted are frequently high fat, energy-dense foods, parents who use these strategies may unintentionally increase their child's consumption of calories and fat, and potentially contribute to increased blood cholesterol levels and weight gain.

## 5. Effectiveness of diet therapy

Repeated studies have shown the safety and efficacy of cholesterol lowering diets in children with elevated LDL-cholesterol levels. The Dietary Intervention Study in Children (DISC) is considered the best-controlled and longest outpatient study of hypercholesterolemia in children [59]. In this study, 663 children, aged 8 to 10 years, with high LDL-C levels were randomly assigned to a behavioral intervention group or a usual care group. The behavioral intervention provided frequent sessions (4–12 times per year for 3 years) to families to promote adherence to a step-two diet (approx. 7% of energy from saturated fat and 200 mg cholesterol); the usual care group was provided with pamphlets on heart-healthy eating. After 3 years, dietary intake of total fat, saturated fat and cholesterol was lower in the intervention group vs. the usual care group. Levels of LDL-cholesterol decreased by 15.4 mg/dl in the intervention group and 11.9 mg/dl in the usual care group, a mean difference of 3.23 mg/dl, which was significant. There were no significant differences between groups for adjusted mean height or serum ferritin. A 7-year follow-up report to this study showed that the intervention/usual care differences in total and saturated fat and LDL-cholesterol could be maintained in families who had continuous exposure to the DISC intervention [60].

Thus, adherence to a step-two diet can safely lower LDL-cholesterol levels during the critical growth period of adolescence. Importantly, ongoing intervention may be necessary to produce lasting decreases in LDL-cholesterol levels.

Results from the DISC study have been corroborated by other clinic-based studies. Jacobson et al. [61] reported LDL-cholesterol levels and growth data on 138 children aged 2 to 15 years (54% boys), who were referred to three pediatric centers in the New York City vicinity for hyperlipidemia. A step-one diet was prescribed and patients received at least 3 counseling sessions by a registered dietitian per year for 3 years. Total serum cholesterol was reduced from an initial mean value of 262 mg/dl to 249 mg/dl (4.6%). There were no adverse effects on growth when compared with the National Health and Nutrition Examination Survey II data. Kuehl et al. [22] conducted a 4-month dietary fat intervention project for 295 children with hypercholesterolemia aged 2–15 years. Children were randomly assigned to one single or four multiple 90-minute sessions of family oriented nutrition education on the step-one diet. Total cholesterol was lowered equally in the intervention groups by ~9%, and there were no disturbances of linear growth. Tershakovec et al. [21] compared two educational approaches for administering the step-one diet to children enrolled in a Cholesterol Treatment Center; one approach was a parent-child autotutorial program (PCAT) and the other, standard nutrition counseling by a registered dietitian. Children were randomly assigned to one of the two intervention groups or an ‘at risk’ control group. Both intervention methods were equally effective at lowering total and saturated fat consumption, and the mean LDL-cholesterol decline was significantly greater for intervention groups compared to the controls (–8% in the PCAT group, –3.4% in the dietary counseling group, and –2.6% in the at-risk control group). Also, normal growth was maintained in children receiving either type of nutrition education approach to achieve the step-one diet.

It should be mentioned that several reports have been published of nutritional inadequacies [62] and growth failure [63,64], resulting from children following low fat diets. These reports, however, were for children who were following medically unsupervised, parent-imposed low fat diets. Parents in these cases severely restricted their children’s energy and fat intake, which had a negative effect on the overall nutritional quality of the children’s diets and on their growth and development. While no health organization is suggesting that extremely low-fat, low energy diets that are nutritionally inadequate and restrict linear growth are appropriate for children, these reports remind us that care must be taken when administering low fat diets to assure adequate intake of all nutrients, particularly those sentinel nutri-

ents required for growth (e.g. zinc, iron, calcium). Nutrition education and counseling by trained professionals for a well-balanced, heart healthy diet is an integral part of ensuring the safety and efficacy of dietary therapy for the management of pediatric hyperlipidemia.

In addition to clinically-based studies, school based intervention programs to lower dietary fat have been shown to be safe and efficacious. In the NHLBI-sponsored Child and Adolescent Trial for Cardiovascular Health (CATCH), 5000 third grade students participated in a food service modification and education intervention to reduce saturated fat and total fat intake levels to those specified in the US dietary guidelines [65]. Both intervention and control groups decreased their total fat and saturated fat intakes, and neither linear growth nor body weight were adversely affected in either group [65,66]. The intervention group decreased their total fat and saturated fat intake from baseline levels of 33 and 13%, respectively, to 30 and 11%, respectively, at the end of fifth grade. Dietary adequacy of all vitamins and minerals was maintained on the low fat diet. In a similar cardiovascular risk reduction project for younger children, Williams et al. [67] modified preschool meals and snacks to reduce total and saturated fat levels to step-one diet levels. Preliminary data after 1 year of intervention showed that school meal modifications could reduce blood cholesterol levels without compromising growth in 2-to 5-year-old children. In total, these data support the fact that a healthy, fat controlled diet during childhood can be safely and effectively achieved through the application of a wide variety of fat-reduction strategies and in many different settings.

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