Published in final edited form as:
Int J Obes (Lond). 2008 August ; 32(8): 1297–1304. doi:10.1038/ijo.2008.89.

Serum Phospholipid and Cholesteryl Ester Fatty Acids and Estimated Desaturase Activities are Related to Overweight and Cardiovascular Risk Factors in Adolescents

Lyn M. Steffen[1], **Bengt Vessby**[2], **David R. Jacobs Jr.**[1,3], **Julia Steinberger**[4], **Antoinette Moran**[4], **Ching-Ping Hong**[1], and **Alan R. Sinaiko**[4]

[1]Division of Epidemiology and Community Health, University of Minnesota School of Public Health; Minneapolis, Minnesota

[2]Section of Clinical Nutrition and Metabolism, Department of Public Health and Caring Sciences, Faculty of Medicine, Uppsala University, Uppsala, Sweden

[3]affiliated with the Department of Nutrition, University of Oslo, Norway

[4]Department of Pediatrics, University of Minnesota School of Medicine; Minneapolis, Minnesota

Abstract

Aim/Hypothesis—The objective of this study was to describe the relation of serum fatty acids and DA to overweight, insulin sensitivity, and CVD risk factors in adolescents.

Methods—The relations of % serum phospholipid (PL) and cholesteryl ester (CE) fatty acids and estimated desaturase activity (DA) with cardiovascular risk factors were examined in 264 adolescents (average age 15 years). Fatty acids were determined by gas liquid chromotography. Surrogate measures of DA were expressed as ratios of serum fatty acids: Δ9DA= 16:0/16:1; Δ6DA=20:3,n6/18:2,n6 (PL) or 18:3,n6/18:2,n6 (CE); and Δ5DA=20:4,n6/20:3,n6. Spearman partial correlations of fatty acids (%) and DA ratios with CVD risk factors were reported, adjusting for age, sex, race, Tanner stage, energy intake and physical activity.

Results—Overweight adolescents compared to normal weight had more adverse levels of CVD risk factors, composition of PL and CE fatty acids in serum, and Δ6 DA and Δ5 DA ratios. Linoleic acid was inversely related to BMI, waist circumference and triglycerides ($p \leq 0.01$). Dihomo-gamma linolenic acid was positively related to BMI, waist, insulin, and triglycerides, and inversely related to HDL-c levels ($p \leq 0.01$). Δ6 DA was adversely associated with most of the risk factors ($p \leq 0.01$), while triglycerides and fasting insulin were beneficially related to Δ5 DA ($p \leq 0.01$).

Conclusion—These findings support those observed in adults, that factors, such as type of dietary fat, physical activity, and obesity, may influence fatty acid metabolism and are important in the development of adverse CVD risk factors as early as adolescence.

INTRODUCTION

Fatty acids play a key role in energy balance, carbohydrate and lipid metabolism, and regulation of gene transcription (1). Epidemiologic studies have shown associations of amount and type of dietary fat intake with the development of chronic disease in adults, including obesity (2), insulin resistance (3–5), and cardiovascular disease (CVD) (6,7). Furthermore, experimental

Corresponding author: Lyn M. Steffen, PhD, MPH, University of Minnesota School of Public Health, Division of Epidemiology and Community Health, 1300 South Second St, Suite 300, Minneapolis, MN 55454, Phone: (612) 625-9307, Fax: (612) 624-0315, steffen@epi.umn.edu.

studies in adults demonstrate that changes in the type of dietary fatty acid intake may result in changes in insulin action (7), lower blood pressure (8), and lower total cholesterol, LDLcholesterol, and triglycerides and higher HDL-cholesterol (9,10).

The composition of fatty acids in the body reflects dietary fat intake and endogenous fatty acid metabolism (11). Plasma or serum fatty acid composition partly reflects dietary fat intake during the past 2–6 weeks and the fatty acids in body fat tissue represents diet in the past several months or years (12). Desaturase enzyme activity (modulating fatty acid degree of saturation) (11,13) includes Delta (Δ) 9, Δ6, and Δ5 desaturase activities, the rate-limiting steps for transforming shorter chain fatty acids into longer essential fatty acid metabolites. Desaturase activities cannot readily be measured in humans in vivo but can be estimated from relevant product/precursor ratios in plasma or serum. High Δ9 DA and Δ6 DA are associated with adiposity and the metabolic syndrome (14–18). High Δ5 DA has been associated with normal weight and insulin sensitivity in adults (15,19).

Few studies have assessed the relations of serum lipid fatty acid composition with overweight and CVD risk factors in adolescents and none have included measures of insulin resistance. In the present study serum phospholipid (PL) and cholesteryl ester (CE) fatty acids were measured in adolescents participating in a longitudinal study of cardiovascular risk. The objective was to describe the relation of serum fatty acids and DA to overweight, insulin sensitivity, and CVD risk factors in adolescents. Similar to adult studies, we hypothesize that palmitic, palmitoleic, and dihomo-gamma linolenic acids and desaturase Δ6 and Δ9 will be adversely associated and linoleic acid and desaturase Δ5 will be beneficially associated with overweight, insulin sensitivity, and CVD risk factors.

METHODS

Study Population

Approval for this study was obtained from the University of Minnesota Institutional Review Board Human Subjects Committee. Consent for participation was obtained from all participants and their parents or guardians.

Methods of recruitment and study procedures have been previously described (20). After blood pressure screening of 12,043 fifth to eight grade Minneapolis, Minnesota Public School students, participants were randomly selected by strata of sex, race (black or white), and blood pressure percentiles (one-half of study participants had blood pressures in the upper 25 percentiles and the other one-half of study participants had blood pressures in the lower 75 percentiles). The cohort for the present study includes 264 adolescents (mean age 15 years, range 13–17) who had fasting blood specimens available for analysis of fatty acids at mean age 15 years and who had an euglycemic hyperinsulinemic clamp study, clinical examination, and a timed overnight urine collection.

Measurements

Physical measurements—Height was measured using a wall-mounted stadiometer to the nearest 0.5 cm and weight was measured using a balance scale to the nearest 0.1 kg by trained staff. Blood pressure was recorded twice using a random-zero sphygmomanometer while the participant was seated after a 5-minute rest; the average of the two measurements was used in the analysis. Waist circumference was measured with a cloth tape to the nearest 0.5 cm. Tanner stage was assessed by a board-certified pediatrician based on pubic hair development in boys and pubic hair and breast development in girls.

The euglycemic insulin clamp has previously been described in detail (21). Insulin sensitivity (M) was determined from the final 40 minutes of a 3-hour insulin clamp and expressed as M_{lbm} (mg glucose uptake/kg lean body mass [lbm]/minute).

Laboratory measurements—Blood specimens for fasting insulin and fasting glucose were obtained at 15, 10 and 5 minutes prior to starting the insulin clamp, and the means of the three values were used in the data analyses. Serum glucose levels were measured immediately at the bedside during the euglycemic clamp procedure using a Beckman Glucose Analyzer II (Beckman Instruments, Fullerton, CA). Analyses for insulin and lipids were performed in the laboratory of the University of Minnesota Hospital, as previously described (20).

The fatty acid composition of the serum lipids (cholesteryl ester and phospholipids) were analyzed by gas-liquid chromatography (GLC) as previously described in detail (22). The GLC system consists of a GC 5890, an automatic 7671 sampler, a 3392A integrator (all Hewlett-Packard, Avondale, PA), and a 25-m Nordion fused silica capillary column NS-351(HNU Systems Inc, Finland), with helium as the carrier gas. The temperature is programmed to 100–210° C. Standards from NuCheck Prep (Elysian, MN) are used for identification of the individual fatty acids and as a control for the GLC system. Fatty acid phospholipids and cholesteryl esters were identified from 14:0 through 22:6,n3 and expressed as a percentage of total fatty acids. The CV for all reported fatty acids are <1.0–5.5%, except for 18:0 in the cholesteryl esters (9.9%) and 17:0 (6.3%) and 18:3 n-3 in phospholipids (8.2%).

Statistical Analysis

All analyses were conducted using SAS Version 9.1 (SAS Institute, Inc., Cary, North Carolina). Body mass index (BMI) was computed as weight in kg divided by height in meters squared (kg/m^2). Overweight in adolescents is defined as ≥85%ile of BMI for age and sex according to the CDC growth charts (23). The distribution of triglycerides was highly skewed and log transformed prior to analysis. Means were back log-transformed and reported as geometric means. M_{lbm} was further corrected for steady-state plasma insulin concentration (I) to account for differences in clamp insulin levels (M_{lbm}/I) (24). To represent DA, we used previously defined ratios Δ9 DA: 16:1,n7/16:0; Δ6 DA: 18:3,n6/18:2,n6 (CE) and 20:3,n6/18:2,n6 (PL) as 18:3,n6 in PL is too low to allow an adequate determination (assuming that the elongase responsible for the elongation of 18:3,n6 to 20:3,n6 is not rate limiting); and Δ5 DA: 20:4,n6/20:3,n6 (13,15,16). Spearman partial correlation coefficients evaluated the relations of serum fatty acids and DA with cardiovascular risk factors and measures of insulin sensitivity, adjusting for age, sex, race, Tanner stage, energy intake, and physical activity. Because multiple comparisons were performed, Spearman partial correlations were considered significant at $p \leq 0.01$. Differences in relations between overweight and normal weight children were significant at $p \leq 0.05$.

RESULTS

Among 264 adolescents, 42% was female, 17% African American, average age was 15±1.2 years and Tanner stage 4.5±0.7. DA ratios and the relative content (%) of PL fatty acids were similar between boys and girls (data not shown). However, the proportions of CE fatty acids suggested an adverse fatty acid pattern in the boys with greater palmitic (11.1 vs. 10.8%) and stearic (1.2 vs. 1.0%) acids and lower linoleic acid (53.5 vs. 55.2%) than girls (all $p < 0.01$).

When stratified by weight status and adjusted for age, sex, race, Tanner stage, energy intake, and physical activity, overweight adolescents had more adverse cardiovascular risk factors than adolescents who were normal weight, including higher levels of BMI, waist circumference, fasting insulin, triglycerides, glucose, systolic blood pressure, total cholesterol, and LDL-cholesterol and lower HDL-cholesterol (Table 1).

In addition, the relative content (%) of several individual fatty acids in serum was significantly higher in overweight than normal weight adolescents, including myristic (14:0), palmitoleic (16:1) stearic acid (18:0), gamma linolenic acid (18:3,6) and dihomo-gamma linolenic acid (20:3,n6) (Table 2).

Normal weight adolescents had a higher percent of heptadecanoic acid (17:0), oleic acid (18:1), and linoleic acid (18:2,n6) than overweight individuals. PL and CE fatty acid ratios for Δ6 DA (20:3,n6/18:2,n6 and 18:3, n6/18:2,n6, respectively) and CE Δ9 DA (16:1/16:0) were significantly higher, while PL Δ5 (20:4,n6/20:3,n3) was significantly lower in overweight than normal weight adolescents (Table 3).

As shown in table 4, Spearman partial correlations evaluate the associations between the CVD risk factors and the PL and CE fatty acids.

As expected, correlations for the saturated fatty acids myristic (14:0), palmitic (16:0), and stearic (18:0) in PL and CE were adversely associated with lipids. PL stearic acid was also positively related to BMI, waist circumference, and fasting insulin. However, PL heptadecanoic acid (17:0) was significantly and inversely associated with triglycerides. The monounsaturated PL palmitoleic acid (16:1, n7) was positively related to triglycerides, while CE palmitoleic acid was positively related to BMI, fasting insulin, triglycerides, and total cholesterol. Both PL and CE oleic acid (18:1) were inversely associated with adiposity measures. The polyunsaturated fatty acids (PUFA) gamma-linolenic (18:3,n6) and dihomo-gamma linolenic (20:3,n6) acids were adversely associated with most CVD risk factors. In contrast, PUFA linoleic acid (18:2,n6) in PL was beneficially inversely associated with most CVD risk factors, while CE linoleic acid was inversely associated with fasting insulin and triglyceride levels. Interestingly, the very long PUFA EPA CE (20:5,n3) was positively associated with BMI, triglycerides, and total cholesterol and both PL and CE EPA were positively associated with fasting insulin. CE DHA (22:6,n3) was positively associated with BMI and waist circumference, while PL DHA was unrelated to all risk factors. Insulin sensitivity (M_{lbm}) was not significantly related to any of the individual PL or CE fatty acids (data not shown). However, M_{lbm}/I showed significant relations with PL and CE fatty acids at $p<0.05$ for 18:2,n6 ($r=0.15$ and 0.14, respectively); 18:3,n6 (both r= -0.14); and 20:3,n6 ($r=-0.17$ and -0.14, respectively).

After further adjustment for BMI, relations of PL and CE fatty acids with CVD risk factors remained significant, although somewhat attenuated; an exception was waist circumference which only remained significantly related to PL stearic acid. The CE ratio for Δ9 DA (16:1/16:0) was significantly and positively associated with lipids and fasting insulin; while PL Δ9 DA was not related to them (Table 5).

PL Δ6 (20:3,n6/18:2,n6) was positively associated with most risk factors. CE Δ6 (18:3,n6/18:2,n6) was positively associated with triglycerides, total cholesterol, and fasting insulin. PL and CE Δ5 DA (20:4,n6/20:3,n6) were inversely related to triglycerides and fasting insulin. PL Δ6 was inversely associated ($r=-0.19$, $p=0.004$), while PL Δ5 was positively associated with M_{lbm}/I ($r=0.14$, $p=0.05$). Systolic blood pressure, glucose, and M_{lbm} were not related to Δ9, Δ6, or Δ5 DA. With further adjustment for BMI, most relations of DA with the CVD risk factors remained significant, although slightly attenuated.

DISCUSSION

We found that adolescent overweight is associated with an adverse fatty acid profile and specific patterns of the DA. Compared to normal weight adolescents, overweight adolescents had significantly higher proportions of palmitoleic and dihomo-gamma linolenic acids and lower linoleic acid, but a similar proportion of palmitic acid. This pattern was similar to that

in another study of adolescents (18). DAs Δ9 and Δ6 were higher, while Δ5 DA was lower in overweight adolescents compared to normal weight adolescents. We also observed that high activities of Δ9 and Δ6 DA were positively associated with most CVD risk factors in adolescents. Moreover, linoleic acid and Δ5 DA were inversely associated with triglycerides, insulin, and several other CVD risk factors, which in previous studies of adults were related to lower body fat (4,19) and insulin sensitivity (14,19). Although, neither proportions of the individual fatty acids nor DAs were significantly related to insulin resistance (M_{lbm}), Mlbm/I was positively associated with linoleic acid and Δ5 and inversely associated with dihomo-gamma-linolenic acid and Δ6.

Adverse pattern of fatty acids

Several observational and experimental studies have found dietary and plasma or serum fatty acids to be related to insulin resistance (3,14) and serum lipids (9). Insulin resistance and adiposity have been characterized by an abnormal fatty acid pattern, including a high relative % of palmitic, palmitoleic, and dihomo-gamma linolenic acids and low % of linoleic acid in adults (3,4,14,19,25,26). A similar pattern was observed in obese children in our study and others (16,27), although study results have been inconsistent (18).

Desaturase activity

Consistent with most previous studies of adults (4,11,14,28) and children (16,18), we found the estimated activities of Δ6 an Δ9 DA were positively associated with adiposity and insulin measures in our study of adolescents. Further, Δ6 DA was also adversely associated with other CVD risk factors, including triglycerides, total cholesterol, LDL-and HDL-cholesterol. An inverse relation was observed of Δ5 DA with fasting insulin and triglycerides, independent of BMI, which is consistent with some studies conducted in adults (4,14,26,28) and in adolescents (18).

Insulin resistance

M_{lbm} was not related to DA ratios or any of the individual serum PL or CE fatty acids in our study. However, individual fatty acids may influence insulin action in adults (19,29). In elderly men, peripheral insulin sensitivity was significantly correlated to the proportion of palmitic ($r=-0.31$, $p<0.001$), palmitoleic ($r=-0.25$, $p<0.001$) and di-homo-gamma-linolenic ($r=-0.33$, $p<0.001$) acids and positively to the content of linoleic ($r=0.28$, $p<0.001$) acid in the serum CE. A stronger negative relation to the proportion of palmitic acid was observed in the skeletal muscle PL of these elderly men ($r = -0.45$, $p < 0.004$)(29). In adult Pima Indians maximal insulin stimulation level (MZ) was positively related to C20-22 PUFAs measured in muscle ($r=0.46$, $p<0.001$) and Δ5 DA ($r= 0.45$, $p<0.001$) (19). The lack of association of M_{lbm} with the fatty acids in adolescents, especially palmitic, palmitoleic, di-homo-gamma-linolenic, and linoleic, may result from the lesser severity or shorter duration of metabolic abnormality compared to an older population or a high risk population, such as the PIMA Indians. However, after correcting for steady-state insulin, M_{lbm}/I (24) was significantly and positively related to linoleic and Δ5, while di-homo-gamma-linolenic acid and Δ6 were both inversely related to M_{lbm}/I, confirmation of a pattern related to both obesity and insulin action (19). Adverse risk factors, including insulin resistance, have been observed 7 or more years prior to the development of CVD and type 2 diabetes (30,31). Therefore, as adolescents get older, a chronically abnormal fatty acid pattern may further promote increased severity of insulin resistance.

Saturated fatty acids

The saturated fatty acids myristic, palmitic, and stearic were positively correlated with total cholesterol, LDL-cholesterol, triglycerides, or fasting insulin, even after adjustment for body

mass, in this adolescent cohort. About 40 years ago, Ancel Keys related dietary saturated fat intake to heart disease (32). Since then, studies in adults have shown that lauric, myristic, and palmitic acids raise both LDL- and HDL- cholesterol levels (9) and adversely influence measures of glucose metabolism (3). Although stearic acid was not shown to effect lipid concentrations, insulin action or glucose tolerance in some studies (9,33), replacement of linoleic acid by stearic acid in clinical studies has been reported to lower HDL-cholesterol and raise LDL-cholesterol levels (34). Lauric and myristic fatty acids has also been correlated with increased LDL-cholesterol among urban and rural adolescents (beta coeff = 3.6, 1.7, $p < 0.05$) (35).

In contrast, an intake of fatty acids in milk, as mirrored by a high proportion of pentadecanoic (15:0) or heptadeconoic acid (17:0) in plasma, seems to be beneficially related to health (36). This is consistent with our finding that PL heptadecanoic acid (17:0) was inversely related to triglycerides. The estimated intake of milk fat was lower in adults with acute myocardial infarction compared to controls (36), and PAI-ag, t-PA-ag, triacylglycerols, fasting insulin, pro-insulin, and leptin all were inversely correlated to milk-fat serum lipid esters. Whether the associations between estimated intake of milk fat or milk products and disease risk reflect causal relationships, or whether these relationships are confounded by other lifestyle-related factors, is at present unknown.

Monounsaturated fatty acids (MUFA)

MUFA intake has been associated with an improved lipid profile and increased insulin sensitivity (37). Oleic acid is found in a variety of animal and vegetable sources and is also the product of Δ6 desaturation of stearic acid (18:0 → 18:1). The proportion of palmitoleic acid in plasma depends mainly upon the conversion of palmitic acid via Δ9 (16:0 → 16:1), while palmitoleic acid is not often found in the food supply (11). This makes the ratio between 16:1/16:0 a useful indicator of Δ9 activity, in contrast to the ratio between 18:1/18:0 which is to a high extent directly influenced by the high content of oleic acid in the diet and thus not a useful reflection of the Δ9 activity. Also consistent with data from adult studies, the present study showed a significant and positive relation of palmitoleic acid, particularly in CE to many CVD risk factors (25) and an inverse relation of oleic acid with BMI and waist circumference (38).

Polyunsaturated fatty acids (PUFA)

Similar to studies in adults (9,14,26), we observed significant and beneficial relations between the polyunsaturated fat (PUFA) linoleic acid with CVD risk factors. An earlier study in 3–18 year old Finnish children reported that linoleic acid was inversely associated with serum triglycerides, total- and LDL-cholesterol levels and positively associated with HDL-cholesterol (39). Long-chain PUFAs EPA and DHA are known to be inversely associated with CVD risk factors and fish consumption to the risk of myocardial infarction (40–42). However, in the present study and others (26,43,44), EPA was positively related to some CVD risk factors. It has been suggested that the positive relation between the proportion of EPA in plasma and CVD risk factors may be explained by the fatty acid composition of the diet and competition for the same enzymes in the process of elongation and desaturation (13,26). A low content of linoleic acid in the diet, as in a diet containing a high proportion of saturated fat, will allow for an efficient endogenous formation of long chain n3 fatty acids from alpha linolenic acid (18:3,n3). A high intake of linoleic acid would, on the contrary, inhibit this conversion leading to a lower proportion of EPA in plasma. Another point is the EPA in PL was positively related to fasting insulin only, while EPA in CE was related to several risk factors. As PLs take part in a more functional role, while CEs operate as transport structures, the FA pattern in PLs is more regulated and is probably closer to that of cell membranes.

A few limitations of our study deserve comment. Because of the cross-sectional study design, the temporal relationships are unknown. Actual desaturase activity was not directly measured, which is difficult to do in vivo in humans, but estimated from the ratio of specific substrate to the corresponding product of the respective enzyme (product/substrate ratio) (5,14,15,45). Nevertheless, the estimated desaturase activity ratios Δ9, Δ6, and Δ5 are useful in sorting out the relations between fatty acid metabolism and CVD risk factors. Diverging relationships between the fatty acid composition of phospholipids and cholesteryl esters, respectively, and cardiovascular risk factors may be related to differences in post intake metabolism of fatty acids. Confounding was assessed in our statistical models by including several variables known to influence fatty acid metabolism-CVD risk factor associations in adolescents; however, the possibility for residual confounding cannot be excluded.

There are also specific strengths of our study. Gender differences have been reported for Δ9 DA, with higher activity in women than men (28). There was a large number of boys and girls enrolled, enabling us to show no gender difference in Δ9 DA in this age group. An important strength is the measurement of insulin sensitivity using the ‘gold standard’ euglycemic hyperinsulinemic clamp. Although we further adjusted our models for body mass, this was probably an overadjustment of our statistical models since body mass is in the causal pathway of developing adverse CVD risk factors and insulin resistance (14,15,45).

In summary, this study shows that adverse patterns of fatty acids and DA are already associated with overweight and insulin resistance prior to adulthood. Results of observational and clinical studies conducted in humans have shown that a diet high in total or saturated fat is associated with abnormal glucose concentrations (3,46,47) or insulin resistance (3,48), while diets enriched in monounsaturated fat (39,49) or linoleic acid (50) improve insulin sensitivity. Beneficial changes in the cholesteryl ester fatty acid profile and DA ratios were related to improved insulin sensitivity in a population at risk for type 2 diabetes (51). Lowering the intake of dietary total and saturated fat and increasing physical activity promotes reductions in Δ9 and Δ6 DAs at the same time Δ5 increases. Type of dietary fatty acid intake plays an important role in modulating fatty acid metabolism. It is also possible, however, that the adverse fatty acid pattern observed in this and other studies is not only, or mainly, related to dietary fat intake. It may alternatively be secondary to early metabolic changes, e.g. related to insulin resistance, or due to genetic predisposition or early pre- or perinatal environmental influence affecting fatty acid metabolism later in life. Our study findings of serum fatty acids in adolescents support those observed in adults; i.e., that type of fat may be important in the development of adverse CVD risk factors as early as adolescence. These findings emphasize the importance of promoting healthy eating patterns prior to adulthood.

Acknowledgments

This research received funding from the National Institutes of Health by grants #HL52851 and #MO1RR00400.

REFERENCES

1. Storlien LH, Hulbert AJ, Else PL. Polyunsaturated fatty acids, membrane function and metabolic diseases such as diabetes and obesity. Curr Opin Clin Nutr Metab 1998;1:559–563.
2. Bray GA, Paeratakul S, Popkin BM. Dietary fat and obesity: a review of animal, clinical and epidemiological studies. Physiology and Behavior 2004;83:549–555. [PubMed: 15621059]
3. Lichtenstein AH, Schwab US. Relationship of dietary fat to glucose metabolism. Atherosclerosis 2000;150:227–243. [PubMed: 10856515]
4. Warensjö E, Risérus U, Vessby B. Fatty acid composition of serum lipids predicts the development of the metabolic syndrome in men. Diabetologia 2005;48:1999–2005. [PubMed: 16132958]

5. Borkman M, Storlien LH, Pan DA, Jenkins AB, Chisholm DJ, Campbell LV. The relationship between insulin sensitivity and the fatty acid composition of phospholipids of skeletal muscle. N Engl J Med 1993;328:238–244. [PubMed: 8418404]
6. Wang L, Folsom AR, Eckeldt JH. Plasma fatty acid composition and incidence of coronary heart disease in middle aged adults: The Atherosclerosis Risk in Communities (ARIC) Study. Nutr Metab Cardiovasc Dis 2003;13:256–266. [PubMed: 14717057]
7. Hu FB, Manson JE, Willett WC. Types of dietary fat and risk of coronary heart disease: a critical review. J Am Coll Nutr 2001;20:5–19. [PubMed: 11293467]
8. Beilin LJ. Dietary fats, fish, and blood pressure. Ann NY Acad Sci 1993;683:35–45. [PubMed: 8352460]
9. Katan MB, Zock PL, Mensink RP. Effects of fats and fatty acids on blood lipids in humans: an overview. Am J Clin Nutr 1994;60:1017S–1022S. [PubMed: 7977143]
10. Berry EM, Hirsch J, Most J, McNamara DJ, Thornton J. The relationship of dietary fat to plasma lipid levels as studied by factor analysis of adipose tissue fatty acid composition in a free-living population of middle-aged American men. Am J Clin Nutr 1986;44:220–231. [PubMed: 3728359]
11. Nakamura MT, Nara TY. Structure, function, and dietary regulation of Δ6, Δ5, and Δ9 desaturases. Ann Review Nutr 2004;24:345–376.
12. Katan MJ, Deslypere JP, van Birgelen AP, Penders M, Zegwaard M. Kinetics of the incorporation of dietary fatty acids into serum cholesteryl esters, erythrocyte membranes, and adipose tissue: an 18-month controlled study. J Lipid Res 1997;38:2012–2022. [PubMed: 9374124]
13. Vessby B, Gustafsson IB, Tengblad S, Boberg M, Andersson A. Desaturation and elongation of fatty acids and insulin action. Ann NY Acad Sci 2002;967:183–195. [PubMed: 12079847]
14. Pan DA, Hulbert AJ, Storlien LH. Dietary fats, membrane phospholipids and obesity. J Nutr 1994;124:155–165.
15. Ntambi JM. Regulation of stearoyl-CoA desaturase (SCD). Prog Lipid Res 1994;34:139–150. [PubMed: 7480063]
16. Okada T, Furuhashi N, Kuromori Y, Miyashita M, Iwata F, Harada K. Plasma palmitoleic acid content and obesity in children. Am J Clin Nutr 2005;82:747–750. [PubMed: 16210702]
17. Guesnet P, Bourre JM, Guerre-Millo, Pascal G, Durand G. Tissue phospholipid fatty acid composition in genetically lean (Fa/-) or obese (fa/fa) Zucker female rats on the same diet. Lipids 1990;25:517–522. [PubMed: 2250587]
18. Decsi T, Csabi G, Torok K, et al. Polyunsaturated fatty acids in plasma lipids of obese children with and without metabolic cardiovascular syndrome. Lipids 2000;35:1179–1184. [PubMed: 11132177]
19. Pan DA, Lillioja S, Milner MR, et al. Skeletal muscle membrane lipid composition is related to adiposity and insulin action. J Clin Invest 1995;96:2802–2808. [PubMed: 8675650]
20. Sinaiko AR, Jacobs DR, Steinberger J, et al. Insulin resistance syndrome in childhood: associations of the euglycemic insulin clamp and fasting insulin with fatness and other risk factors. J Pediatr 2001;139:700–707. [PubMed: 11713450]
21. DeFronzo RA, Tobin JD, Andres R. Glucose clamp techniques: a method for quantifying insulin secretion and resistance. Am J Physiol 1979;237:E214–E223. [PubMed: 382871]
22. Boberg M, Croon LB, Gustafsson I-B, Vessby B. Platelet fatty acid composition in relation to fatty acid composition in plasma and to serum lipoprotein lipids in healthy subjects with special reference to the linoleic acid pathway. Clinical Science 1985;68:581–587. [PubMed: 3919990]
23. National Center for Health Statistics. CDC Growth Charts: United States. 2000 [Accessed 7/06/07]. Available from http://www.cdc.gov/growthcharts/
24. Ferranninia E, Marib A. How to measure insulin sensitivity. J Hypertension 1998;16:895–906.
25. Lovejoy JC, Champagne CM, Smith SR, et al. Relationship of dietary fat and serum cholesteryl ester and phospholipid fatty acids to markers of insulin resistance in men and women with a range of glucose tolerance. Metabolism: Clinical & Experimental 2001;50:86–92. [PubMed: 11172480]
26. Vessby B. Dietary fat, fatty acid composition in plasma and the metabolic syndrome. Curr Opin Lipidol 2003;14:15–19. [PubMed: 12544656]

27. Klein-Platat C, Drai J, Oujaa M, Schlienger JL, Simon C. Plasma fatty acid composition is associated with the metabolic syndrome and low-grade inflammation in overweight adolescents. Am J Clin Nutr 2005;85:1178–1184. [PubMed: 16332649]
28. Warensjo E, Ohrvall M, Vessby B. Fatty acid composition and estimated desaturase activities are associated with obesity and lifestyle variables in men and women. Nutr Metab & CVD 2006;16:128–136.
29. Vessby B, Tengblad S, Lithell H. Insulin sensitivity is related to the fatty acid composition of serum lipids and skeletal muscle phospholipids in 70-year-old men. Diabetologia 1994;37:1044–1050. [PubMed: 7851683]
30. Haffner SM, Miettinen H, Gaskill SP, Stern MP. Decreased insulin secretion and increased insulin resistance are independently related to the 7-year risk of NIDDM in Mexican-Americans. Diabetes 1995;44:1386–1391. [PubMed: 7589843]
31. Haffner SM, Stern MP, Hazuda HP, Mitchell BD, Patterson JK. Cardiovascular risk factors in confirmed prediabetic individuals. Does the clock for coronary heart disease start ticking before the onset of clinical diabetes? JAMA 1990;263:2893–2898. [PubMed: 2338751]
32. Keys A, Anderson JT, Grande F. Serum cholesterol response to changes in the diet. Metabolism 1965;13:759–765.
33. Louheranta AM, Turpeinen AK, Schwab US, Vidgren HM, Parviainen MT, Uusitupa MI. A high-stearic acid diet does not impair glucose tolerance and insulin sensitivity in healthy women. Metabolism 1998;47:529–534. [PubMed: 9591742]
34. Zock PL, Katan MB. Hydrogenation alternatives: effects of trans fatty acids and stearic acid versus linoleic acid on serum lipids and lipoproteins in humans. J Lipid Res 1992;33:399–410. [PubMed: 1569387]
35. Monge-Rojas R, Campos H, Fernandez Rojas X. Saturated and cis- and transunsaturated fatty acids intake in rural and urban Costa Rican adolescents. J Am Coll Nutr 2005;24:286–293. [PubMed: 16093406]
36. Warensjo E, Jansson JH, Berglund L, et al. Estimated intake of milk fat is negatively associated with cardiovascular risk factors and does not increase the risk of a first acute myocardial infarction. A prospective case-control study. Brit J Nutr 2004;91:635–642. [PubMed: 15035691]
37. Vessby B, Uusitupa M, Hermansen K, et al. Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women; the KANWU study. Diabetologia 2001;44:312–319. [PubMed: 11317662]
38. Luscombe-Mar ND, Noakes M, Wittert GA, Keogh JB, Foster P, Clifton PM. Carbohydrate-restricted diets high in either monounsaturated fat or protein are equally effective at promoting fat loss and improving blood lipids. Am J Clin Nutr 2005;81:762–772. [PubMed: 15817850]
39. Moilanen T, Solakivi-Jaakkola T, Viikari J, et al. Fatty acid composition of serum cholesteryl esters in relation to serum lipids and apolipoproteins in 3–18-year-old Finnish children and adolescents. Atherosclerosis 1986;59:113–119. [PubMed: 3964339]
40. Kris-Etherton PM, Harris WS, Appel LJ. for the American Heart Association Nutrition Committee. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Circulation 2002;106:2747–2757. [PubMed: 12438303]
41. Mortensen JZ, Schmidt EB, Nielsen AH, Dyerberg J. The effect of N-6 and N-3 polyunsaturated fatty acids on hemostasis, blood lipids and blood pressure. J Thrombosis & Haemostasis 1983;50:543–546.
42. Kromhout D. N-3 fatty acids and coronary heart disease: epidemiology from Eskimos to Western populations. J Int Med 1989;225:47–51.
43. Zheng ZJ, Folsom AR, Ma J, Arnett DK, McGovern PG, Eckfeldt JH. Plasma fatty acid composition and 6-year incidence of hypertension in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Am J Epidemiol 1999;150:492–500. [PubMed: 10472949]
44. Dewailly E, Blanchet C, Gingras S, Lemieux S, Holub BJ. Cardiovascular disease risk factors and n-3 fatty acid status in the adult population of James Bay Cree. Am J Clin Nutr 2002;76:85–92. [PubMed: 12081820]
45. Kim YC, Ntambi JM. Regulation of stearoyl-CoA desaturase genes: role in cellular metabolism and preadipocyte differentiation. Biochem Biophys Res Comm 1999;266:1–4. [PubMed: 10581155]

46. Feskens EJ, Kromhout D. Habitual dietary intake and glucose tolerance in euglycaemic men: the Zutphen Study. Int J Epidemiol 1990;19:953–959. [PubMed: 2084027]

47. Tsunehara CH, Leonetti DL, Fujimoto WY. Diet of second-generation Japanese-American men with and without non-insulin-dependent diabetes. Am J Clin Nutr 1990;52:731–738. [PubMed: 2403066]

48. Mayer-Davis EJ, Monaco JH, Hoen HM, et al. Dietary fat and insulin sensitivity in a triethnic population: the role of obesity. The Insulin Resistance Atherosclerosis Study (IRAS). Am J Clin Nutr 1997;65:79–87. [PubMed: 8988917]

49. Perez-Jimenez F, Lopez-Miranda J, Pinillos MD, et al. A Mediterranean and a high-carbohydrate diet improve glucose metabolism in healthy young persons. Diabetologia 2001;44:2038–2043. [PubMed: 11719836]

50. Summers LK, Fielding BA, Bradshaw HA, et al. Substituting dietary saturated fat with polyunsaturated fat changes abdominal fat distribution and improves insulin sensitivity. Diabetologia 2002;45:369–377. [PubMed: 11914742]

51. Corpeleijn E, Feskens EJM, Jansen EH, et al. Improvements in glucose tolerance and insulin sensitivity after lifestyle intervention are related to changes in serum fatty acid profile and desaturase activities: the SLIM study. Diabetologia 2006;49:2393–2401.

Table 1

Cardiovascular risk factors in normal- and overweight adolescents, n=264

Cardiovascular Risk Factors	Normal Weight (n=190) mean	Overweight (n=74) mean	p-value
BMI, kg/m^2	20.5	28.2	<0.001
Waist, cm	73.2	90.8	<0.001
Insulin, mU/L	12.0	20.0	<0.001
Triglyceride, mg/dl[1]	72.2	96.5	<0.001
HDL-chol, mg/dl	44.9	40.6	<0.001
Glucose, mg/dl	97.4	99.8	0.05
Systolic blood pressure	107	112	<0.001
Total cholesterol, mg/dl	140.6	159.8	<0.001
LDL-cholesterol, mg/dl	79.8	96.8	0.001
M_{lbm}, mg/kg/min	12.2	12.6	0.46

Adjusted for age, sex, race, Tanner stage, energy intake, and physical activity

Overweight = age-gender specific ≥85%ile CDC growth charts

[1] log transformed, geometric mean

Mlbm =mg glucose uptake/kg lean body mass/minute

Table 2

% Serum phospholipid and cholesterol ester fatty acids in adolescent normal- and overweight adolescents, n=264

% Plasma Fatty Acids	Normal Weight (n=190) mean	Overweight (n=74) mean	p-value
Phospholipids			
14:0 myristic acid	0.41	0.44	0.008
15:0 pentadecanoic acid	0.22	0.21	0.53
16:0 palmitic acid	27.4	27.5	0.52
16:1 palmitoleic acid	0.84	0.86	0.26
17:0 heptadecanoic acid	0.47	0.45	0.04
18:0 stearic acid	14.2	14.8	<0.001
18:1 oleic acid	14.0	13.6	0.05
18:2, n6 linoleic acid	24.7	23.7	0.002
18:3, n3 α-linolenic acid	0.20	0.20	0.71
18:3, n6 γ-linolenic acid	0.07	0.11	<0.001
20:3, n6 dh-γ-linolenic acid	3.22	3.53	<0.001
20:4, n6 arachidonic acid	10.60	10.82	0.19
20:5, n3 EPA	0.43	0.44	0.96
22:6, n3 DHA	2.28	2.28	0.99
Cholesterol Esters			
14:0 myristic acid	0.83	0.89	0.05
15:0 pentadecanoic acid	0.20	0.20	0.76
16:0 palmitic acid	11.04	11.01	0.72
16:1 palmitoleic acid	3.10	3.46	0.001
17:0 heptadecanoic acid	0.11	0.10	0.04
18:0 stearic acid	1.13	1.13	0.18
18:1 oleic acid	18.6	18.1	0.02
18:2, n6 linoleic acid	54.4	53.9	0.23
18:3, n3 α-linolenic acid	0.49	0.50	0.28
18:3, n6 γ-linolenic acid	0.93	1.05	0.009
20:3, n6 dh γ-linolenic acid	0.80	0.88	.001
20:4, n6 arachidonic acid	7.58	7.97	0.02
20:5, n3 EPA	0.38	0.44	0.002
22:6, n3 DHA	0.37	0.41	0.08

Adjusted for age, sex, race, Tanner stage, energy intake, and physical activity

Overweight = age-gender specific ≥85%ile CDC growth charts

EPA: eicosapentenoic acid; DHA: docosahexenoic acid

Table 3

Desaturase activity in normal- and overweight adolescent girls and boys, n=264

Desaturase activity	**Normal Weight (n=190) mean**	**Overweight (n=74) mean**	**p-value**
Phospholipids			
Δ 9 DA 16:1/16:0	0.03	0.03	0.34
Δ 6 DA 20:3,n6/18:2,n6	0.13	0.15	<0.001
Δ 5 DA 20:4,n6/20:3,n6	3.41	3.18	0.04
Cholesterol esters			
Δ 9 DA 16:1/16:0	0.28	0.31	<0.001
Δ 6 DA 18:3,n6/18:2,n6	0.017	0.02	<0.001
Δ 5 DA 20:4,n6/20:3n6	9.73	9.35	0.23

Adjusted for age, sex, race, Tanner stage, energy intake, and physical activity

Overweight = age-gender specific ≥85%ile CDC growth charts

DA: desaturase activity

Table 4

Spearmen partial correlations between serum fatty acids and cardiovascular risk factors in adolescents, n=264

% *Plasma Fatty Acids*	BMI kg/m^2	Waist cm	Insulin mU/L	Triglyc mg/dL	HDL-c mg/dL	Glucose Mg/dL	SBP mmHg	Tchol mg/dL	LDL-c mg/dL
Phospholipids									
14:0 myristic acid	NS	NS	**0.23**	**0.21**	NS	NS	NS	**0.20**	NS
15: 0 pentadeconoic acid	NS	NS	NS	NS	NS	NS	NS	NS	NS
16:0 palmitic acid	NS	NS	NS	NS	NS	NS	NS	**0.13**	NS
16:1 palmitoleic acid	NS	NS	NS	**0.20**	NS	NS	NS	NS	NS
17:0 heptadecanoic acid	NS	NS	NS	**−0.20**	NS	NS	NS	NS	NS
18:0 stearic acid	**0.24**	**0.15**	**0.31**	**0.21**	NS	NS	NS	**0.27**	**0.24**
18:1 oleic acid	**−0.17**	**0.13**	NS	NS	NS	NS	NS	NS	NS
18:2, n6 linoleic acid	**−0.20**	**0.19**	NS	**−0.20**	NS	NS	NS	**−0.25**	**−0.26**
18:3, n3 α-linolenic acid	NS	NS	NS	NS	**0.17**	NS	NS	NS	NS
18:3, n6 γ linolenic acid	**0.16**	**0.10**	**0.22**	**0.33**	NS	NS	NS	**0.28**	NS
20:3, n6 dh-γ-linolenic acid	**0.24**	**0.22**	**0.20**	**0.31**	**0.14**	NS	NS	**0.15**	NS
20:4, n6 arachidonic acid	**0.15**	**0.14**	NS	**−0.16**	NS	NS	NS	NS	NS
20:5, n3 EPA	NS	NS	**0.18**	NS	NS	NS	NS	NS	NS
22:6, n3 DHA	NS	NS	NS	NS	NS	NS	NS	NS	NS
Cholesterol Esters									
14:0 myristic acid	NS	NS	NS	**0.31**	NS	NS	NS	**0.19**	NS
15: 0 pentadeconoic acid	NS	NS	NS	NS	NS	NS	NS	NS	NS
16:0 palmitic acid	NS	NS	NS	**0.16**	**−0.17**	NS	NS	NS	NS
16:1 palmitoleic acid	**0.17**	NS	**0.26**	**0.35**	NS	NS	NS	**0.22**	NS
17:0 heptadecanoic acid	NS	NS	NS	NS	NS	NS	NS	NS	NS
18:0 stearic acid	NS	NS	NS	NS	**−0.18**	NS	NS	NS	NS
18:1 oleic acid	**0.18**	**−0.15**	NS	NS	NS	NS	NS	NS	NS
18:2, n6 linoleic acid	NS	NS	**0.15**	**−0.24**	NS	NS	NS	NS	NS
18:3, n3 α-linolenic acid	NS	NS	NS	**0.17**	NS	NS	NS	NS	NS
18:3, n6 γ-linolenic acid	NS	NS	**0.18**	**0.29**	NS	NS	NS	**0.22**	NS
20:3, n6 dh-γ-linolenic acid	**0.22**	**0.24**	**0.27**	**0.24**	**−0.17**	NS	NS	NS	NS
20:4, n6 arachidonic acid	NS	NS	NS	NS	NS	NS	NS	NS	NS

% *Plasma Fatty Acids*	BMI kg/m^2	Waist cm	Insulin mU/L	Triglyc mg/dL	HDL-c mg/dL	Glucose Mg/dL	SBP mmHg	Tchol mg/dL	LDL-c mg/dL
20:5, n3 EPA	**0.20**	NS	**0.18**	**0.15**	NS	NS	NS	**0.19**	NS
22:6, n3 DHA	**0.17**	**0.18**	NS	NS	NS	NS	NS	NS	NS

Adjusted for age, sex, race, Tanner stage, energy intake and physical activity;
Spearmen correlations are significant at $p<0.01$.

BMI = body mass index
Triglyc = triglyceride
SBP = systolic blood pressure
Tchol = total cholesterol
EPA: eicosapentenoic acid; DHA: docosahexenoic acid
NS = not significant

Table 5

Spearmen partial correlations between desaturase activity (DA) ratios and cardiovascular risk factors in adolescents, n=264

Desaturase Activity	BMI kg/m^2	Waist (cm)	Insulin mU/L	Triglyc mg/dL	HDL-c mg/dL	Glucose Mg/dL	SBP mmHg	Tchol mg/dL	LDL-c mg/dL
Phospholipids									
Δ9 DA (16:1/16:0)	NS	NS	NS	NS	NS	NS	NS	NS	NS
Δ6 DA (20:3,n6/18:2,n6)	**0.31**	**0.27**	**0.21**	**0.31**	**−0.20**	NS	NS	**0.22**	**0.22**
Δ5 DA (20:4,n6/20:3,n6)	NS	NS	**−0.21**	**−0.29**	NS	NS	NS	NS	NS
Cholesterol Esters									
Δ9 DA (16:1/16:0)	NS	NS	**0.27**	**0.35**	NS	NS	NS	**0.24**	**0.16**
Δ6 DA (18:3,n6/18:2,n6)	NS	NS	**0.18**	**0.30**	NS	NS	NS	**0.22**	NS
Δ5 DA (20:4,n6/20:3,n6)	NS	NS	**−0.17**	**−0.24**	NS	NS	NS	NS	NS

Adjusted for age, sex, race, Tanner stage, energy intake and physical activity;
Spearmen correlations are significant at $p<0.01$.

BMI = body mass index
Triglyc = triglyceride
SBP = systolic blood pressure
Tchol = total cholesterol
NS = not significant

Int J Obes (Lond). Author manuscript; available in PMC 2010 March 4.