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REVIEW

Effects of Dietary Lipids on Lipoprotein Profile

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Summary

Cholesterol, fats and oils belongs to the family of lipids. Lipids are important source of energy and, beside that, they are biologically active molecules that have many important roles in organism. Fat and cholesterol can't dissolve in blood, so they are transported in the plasma as triglicerydes or by large complexes called lipoproteins. In this paper an overview of dietary lipids, sources of diffrent dietary lipids and lipoprotein metabolism is presented as well as adverse effects of over consumption of cholesterol and fat on body weight and health.

Key words: fatty acids, lipoproteins, cholesterol, lipoprotein metabolism

Sažetak

Kolesterol, masne kiseline i ulja pripadaju u obitelj lipida. Lipidi su važan izvor energije i osim toga važne biološki aktivne molekule koje imaju mnoge funkcije u organizmu. Masti i kolesterol se ne mogu otapati u krvi pa se transportiraju kao trigliceridi ili u lipoproteinskim kompleksima. U ovom radu prikazan je pregled masnih kiselina koje su najzastupljenije u hrani, metabolizma lipoproteina te negativnih utjecaja pretjerane konzumacije kolesterola i masti na tjelesnu težinu i zdravlje.

Ključne riječi: masne kiseline, lipoproteini, kolesterol, metabolizam lipoproteina

Introduction

A low-fat and low-cholesterol diet has been proposed as healthful eating for decades. To lose weight and prevent or control heart disease millions of people have tried to follow this advice. But, on the other hand, despite reduction of fat and oils in diet, percent of obese persons and type 2 diabetes patients is ever increasing. Research shows that the type of fat in the diet rather than the total amount of fat is really linked with weight or disease (Beresford et al., 2006; Howard et al., 2006). This finding raises a question about ″healthful eating″ guidelines concerning fat and cholesterol in diet.

Fat is important source of energy as well as a great depot for storing it. Moreover, fats are biologically active molecules that influence muscles respond to insulin's signal and are an important part of cell membranes, controlling what gets into cells and what comes out. Cholesterol is a wax-like substance, which together with fats and oils belongs to the family of lipids. It is essential to all our body cells and has a special role in the formation of brain cells, nerve cells and as precursor for estrogen, testosterone, vitamin D, and other vital compounds synthesis. Although some foods contribute ready-made cholesterol, the majority of cholesterol in the body is manufactured by the liver.

Fat and cholesterol can't dissolve in blood, so the bulk of the body's lipids (cholesterol, phospholipids and triacylglycerols), are transported in the plasma by large complexes called lipoproteins that mix easily with blood and flow with it. These lipoproteins consist of a core of triacylglycerols and cholesteryl esters surrounded by a layer of amphipathic phospholipids, unesterified cholesterol and apoproteins. The apoproteins have specific structural domains that are recognized by cell receptors. All of the apoproteins have amphipathic α-helixes with the hydrophobic side chains facing the lipid interior of the lipoprotein and the hydrophilic residues interacting with the polar head groups of the phospholipids or with the aqueous solvent. The affinities of the apoproteins for the surface components of the lipoprotein change during lipoprotein metabolism so they often diffuse from one lipoprotein to another.

Lipoproteins are classified according to their density (lipids to proteins ratio in the complex). Lipoproteins with higher protein content have higher density. The lowest density lipoproteins are the chylomicrons followed by the chylomicron remnants, very low density lipoproteins VLDLs, intermediate density lipoproteins, IDLs, low density lipoproteins, LDLs, and high density lipoproteins, HDLs (Brewer et al., 1988).

Saturated fatty acid and cholesterol intakes above an identified UL (Tolerable Upper Intake Level) indicate a potential risk of an adverse health effects. There is a positive linear trend between total saturated fatty acid intake and total and LDL cholesterol concentration and increased risk of coronary heart disease (CHD). A UL is not set for saturated fatty acids because any incremental increase in saturated fatty acid intake increases CHD risk. It is neither possible nor advisable to achieve zero percent of energy from saturated fatty acids in typical whole-food diets. This is because all fat and oil sources are mixtures of fatty acids, and consuming zero percent of energy would require extraordinary changes in patterns of dietary intake, such as the inclusion of fats and oils devoid of saturated fatty acids, which are presently unavailable. Such extraordinary adjustments may introduce undesirable effects (e.g., inadequate intakes of protein and certain micronutrients) and unknown and unquantifiable health risks.

Dietary lipids and cholesterol

Dietary fat is often divided into saturated and unsaturated fat. It has been shown that trans and saturated fats increase the risk for certain diseases while monounsaturated and poly-

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unsaturated fats do just the opposite. Mesnik et al. (2003) examined the effects of carbohydrates and various fats on blood lipid levels. In trials in which polyunsaturated and monounsaturated fats were eaten in place of carbohydrates, these good fats decreased levels of harmful LDL and increase protective HDL (Mensink et al., 2003). Randomized trial known as the Optimal Macronutrient Intake Trial for Heart Health (Omni Heart) showed that replacing a carbohydrate-rich diet with one rich in unsaturated fat, predominantly monounsaturated fats, lowers blood pressure, improves lipid levels, and reduces the estimated cardiovascular risk (Appel et al., 2005). Concerning cholesterol in food, for most people, the mix of fats in the diet influences cholesterol in the bloodstream far more than cholesterol in food does. On the other hand, dietary cholesterol may act synergistically with dietary fatty acids in the mediation of plasma cholesterol concentrations (Connor et al., 1964; Hopkins, 1992; Lichtenstein et al., 1994; Oh and Miller, 1985). Interactive effects between dietary fatty acid composition and cholesterol with respect to the plasma lipoprotein response are still not well defined (Mensink and Katan, 1989; Oh and Miller, 1985).

Saturated Fatty Acids.

Sources of saturated fatty acids tend to be foods of animal sources, including whole milk, cream, butter, cheese, fatty meats such as pork and beef (USDA/HHS, 2000), lard (and foods made from these including pastries, cakes and biscuits) and meat products (e.g., salami, pies and sausages). Certain oils, however, such as coconut, palm, and palm kernel oil, also contain relatively high amounts of saturated fatty acids. Saturated fatty acids provide approximately 20 to 25 percent of energy in human milk. Human bodies can make all the saturated fat we need, so we do not need to intake the saturated fat at all. Minimizing dietary saturated fat intake has a beneficial impact on serum cholesterol levels. Calories from saturated fat can be replaced with either unsaturated fats or carbohydrates.

Unsaturated Fatty Acids.

Unsaturated fats are called good fats because they can improve blood cholesterol levels, ease inflammation, stabilize heart rhythms, and play a number of other beneficial roles. Unsaturated fats are predominantly found in vegetable oils, nuts, and seeds. They are liquids at room temperature. There are two types of unsaturated fats: monounsaturated fats (MUFAs) and polyunsaturated fats (PUFAs).

Monounsaturated fats (MUFAs) are found in high concentrations in canola, peanut, and olive oils; avocados; almonds, hazelnuts, pumpkin and sesame seeds. About 50 percent of monounsaturated fatty acids are provided by animal products, primarily meat fat (Jonnalagadda et al., 1995). Monounsaturated fatty acids provide approximately 20 percent of energy in human milk. The major monounsaturated fatty acid in the diet is oleic acid, which contains one double bond at the C9. Monounsaturated fatty acids are neutral with respect to their effects on plasma total cholesterol concentrations (Hegsted et al., 1965; Keys et al., 1965). Many investigators have shown that, when substituted for dietary saturated fatty acids, monounsaturated fatty acids have a hypocholesterolemic effect (Becker et al., 1983; Berry et al., 1992; Dreon et al., 1990; Lichtenstein et al., 1993; Masana et al., 1991; Mata et al., 1992; McDonald et al., 1989; Mensink and Katan, 1992; Valsta et al., 1992; Wardlaw and Snook, 1990). The overall data indicate that monounsaturated fats do not lower LDL or HDL cholesterol relative to saturated fat as much as does polyunsaturated fat (Mattson and Grundy, 1985; Mensink and Katan, 1992; Valsta et al., 1992; Wardlaw and Snook, 1990). The saturated fat and monounsaturated fat contents of most natural diets are similar, and when saturated fat is restricted, the monounsaturated fat content of the diet decreases.

Polyunsaturated fats (PUFAs) are found in high concentrations in sunflower, corn, soybean, and flaxseed oils, and also in foods such as walnuts, flax seeds, and fish. Dietary PUFAs are subclassified as ω-6 and ω-3, indicating the location of the carbon involved in the first double bond from the omega end of the carbon chain. The major ω-6 fatty acid in the diet is α-linoleic acid, which serves as the precursor for arachidonic acid (20:4n-6), which has important biological effects in the body. α-Linoleic acid is not synthesized by the body and is therefore an essential fatty acid. The other major essential fatty acid in the diet is α-linolenic acid (18:3n-3). This fatty acid can be rapidly converted in the body to eicosapentaenoic acid (20:5n-3), which can be further elongated, desaturated, and oxidized to docosahexaenoic acid (22:6n-3) (Siguel et al., 1987). Linoleic acid clearly has a hypocholesterolemic effect when substituted for dietary saturated fatty acids, reducing both LDL and HDL-cholesterol concentrations. However, dietary arachidonic acid has little or no effect on plasma lipoprotein concentrations (Nelson et al., 1997). Sources of ω-6 polyunsaturated fatty acids include nuts, seeds, certain vegetables, and vegetable oils such as soybean oil, safflower oil, and corn oil. Certain oils, such as blackcurrant seed oil and evening primrose oil, are high in γ-linolenic acid (18:3n-6). Arachidonic acid is formed from linoleic acid in animal cells, but not plant cells, and is present in the diet in small amounts in meat, poultry, and eggs. Arachidonic acid is not present in plant-derived fats and oils. Most (approximately 85 to 90 percent) ω-6 polyunsaturated fatty acids are consumed in the form of linoleic acid. Other ω-6 polyunsaturated fatty acids, such as arachidonic acid and γ-linolenic acid, are present in small amounts in the diet. ω-3 fats are an important type of polyunsaturated fat the human body can't make, so they must come from food. The major sources of ω-3 fatty acids include certain vegetable oils and fish (Kris-Etherton et al., 2000). Vegetable oils such as soybean and flaxseed oils contain high amounts of α-linolenic acid. Fish oils provide a mixture of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), so fatty fish are the major dietary sources of EPA and DHA. Smaller amounts are also present in meat and eggs. ω-3 Fatty acids found in fish oil, especially eicosapentaenoic acid, lower triacylglycerol concentrations significantly and reduce coronary heart disease risk as well, in part, independently of their influence on lipoprotein concentrations (Chee et al., 1990; Harris, 1997). Specifically, high intakes of ω-3 fatty acids are associated with lower platelet ag-

gregation, blood pressure, and immune response (Endres et al., 1989; Lichtenstein et al., 1990; Meydani et al., 1993; Norris et al., 1986; Urakaze et al., 1987).

Trans Fatty Acids

A relatively new concern involves the concentration of *trans* fatty acids in the diet (Lichtenstein et al., 1993; Lichtenstein et al., 1999; Mensink and Katan, 1990; Zock and Katan, 1992). *Trans* Fatty acids are formed during the hydrogenation process that converts vegetable oils to a semisolid state. During this process, α-linoleic acid (18:2n-6) is converted to either stearic acid, oleic acid, or elaidic acid. Elaidic acid (*trans* 18:1n-9) is the principal *trans* fatty acid in the diet. Reports listing the *trans* fatty acid level in selected food items are available from the United States (Enig et al., 1990; Litin and Sacks, 1993; Michels and Sacks, 1995) and Europe (Aro et al., 1998a, 1998b, 1998c; van Erp-Baart et al., 1998; van Poppel et al., 1998). More recently, a comprehensive U.S. database was compiled by the U.S. Department of Agriculture (ARS, 2001) that included a description of the methodology used to formulate the nutrient values (Schakel et al., 1997). *Trans* fatty acids are present in foods containing traditional stick margarine (3.04 g *trans* fatty acids/serving) and vegetable shortenings (2.54 g/serving) that have been subjected to hydrogenation, as well as in milk (0.22 g/serving), butter (0.40 g/serving) and meats (0.01 to 0.21 g/serving) (Emken, 1995). Human milk contains approximately 1 to 5 percent of total energy as *trans* fatty acids and similarly, infant formulas contain approximately 1 to 3 percent (Ratnayake et al., 1997). Estimating the amount of *trans* fatty acids in the food supply has been hampered by the lack of an accurate and comprehensive database from which to derive the data and the trend towards the reformulation of products over the past decade to reduce levels. This latter issue complicates analysis of historical food intake data. Additionally, the variability in the *trans* fatty acid content of foods within a food category is extensive and can introduce substantial error when the calculations are based on food frequency questionnaires that heavily rely on the grouping of similar foods (Innis et al., 1999). Early reports suggested a wide range of *trans* fatty acid intakes, from 2.6 to 12.8 g/d (Emken, 1995). The lower estimated intakes tended to be derived from food frequency data, whereas the higher estimated intakes tended to be derived from food availability data. Studies have shown that, compared with diets enriched in linoleic or oleic acid, diets enriched in elaidic acid do not have a beneficial effect on the plasma lipoprotein profile, elevating LDL-cholesterol and reducing HDL-cholesterol concentrations (Judd et al., 1994; Judd et al., 1998; Lichtenstein et al., 1993; Lichtenstein et al., 1999; Mensink and Katan, 1990; Mensink et al., 1992; Nestel et al., 1992; Zock and Katan, 1992). There is also evidence that increased *trans* fatty acid consumption, in contrast with consumption of saturated fat, increases plasma concentrations of lipoprotein(a), an independent risk factor for coronary heart desease (CHD) (Judd et al., 1998; Lichtenstein et al., 1999; Mensink et al., 1992).

Conjugated Linoleic Acid

The average concentration of conjugated linoleic acid (CLA) in dairy products and ruminant meats is approximately 5 mg of CLA/g of fat (Chin et al., 1992). Although numerous CLA isomers have been reported to be found in meat, milk, and dairy products (Ha et al., 1989), the cis-9,trans-11 isomer is the predominant form of CLA present in these foods (Ma et al., 1999). The conjugated linoleic acid content of milk can vary depending on a number of factors, such as animal feed diet, pasture grazing, supplement use, and number of lactations (MacDonald, 2000). Ma and coworkers (1999) reported values of 1.8 mg of CLA/g of fat for skim milk, 3.4 mg/g for whole milk, 4.3 mg/g for 1 percent milk, 5.0 mg/g for 2 percent milk, and 5.5 mg/g for half-and-half cream. In addition, values ranged from 2.7 to 6.2 mg of CLA/g of fat for various cheeses and 1.2 to 3.2 mg of CLA/g of fat for different types of raw and cooked beef products.

Dietary cholesterol

Some foods (eggs, liver, kidney and prawns) naturally contain cholesterol (dietary cholesterol). The cholesterol found in foods in most cases does not influence blood cholesterol levels as much as the amount and type of fat eaten, but some people might be sensitive to high cholesterol intakes. Minimizing dietary saturated fat intake has a beneficial impact on serum cholesterol levels.

Lipoprotein and triglycerides metabolism

Fat and cholesterol can't dissolve in blood, so the body's lipids are transported in the form of plasma lipoproteins or triglycerides. Lipoproteins are classified according to their density to chylomicrons, chylomicron remnants, very low density lipoproteins (VLDLs), intermediate density lipoproteins (IDLs), low density lipoproteins (LDLs), and high density lipoproteins (HDLs) (Brewer et al., 1988).

Chylomicrons

Dietary lipids are carried from the intestinal mucosa cells to other tissues by lipoproteins called chylomicrons. The principle apoproteins of nascent chylomicrons are apo B-48, apo A-I, apo A-II and apo-AIV. Apo B-48 is essential for chylomicron formation in the intestine. Apo B-48 is combined with lipid by the action of microsomal transfer protein. In circulation, the nascent chylomicrons acquire apo-C and apo-E from plasma HDL in exchange for phospholipids (Cohn et al., 1988; Cohn et al., 1993; Lichtenstein et al., 1992; Welty et al., 1999). apo-CII activate membrane bound lipoprotein lipase, LPL located on adipose and muscle tissues and bind chylomicrons to it. The fatty acids transported to the adipose cell are bound again into triacylglycerols and stored, while in the muscle the fatty acids are oxidized to provide energy. As the tissues absorb the fatty acids, the chylomicrons are reduced to cholesterol enriched remnants. As the chylomicron shrinks it transfers part of its phospholipids and apoproteins A and C to HDL. The apo-C proteins are continuously recycled between chylomicrons and HDL. The remnants lacking apo A and C proteins do not bind to the LPLs in the capillaries and are rapidly taken up by the liver via receptors that bind apo E (Welty et al., 1999).

Very Low Density Lipoproteins (VLDL)

The liver synthesizes fatty acids and cholesterol and packages them for transport in the blood plasma in VLDLs. Normally the cholesterol is unesterified and found as a surface

component of the lipoprotein. Apo B-100 is the major protein of VLDL. Apo B-100 is combined with lipid in the liver by the action of microsomal transfer protein (Cohn et al., 1988; Cohn et al., 1993; Lichtenstein et al., 1992; Welty et al., 1999).

The nascent VLDL acquires apo-C and E from HDL. VLDLs bind to the same membrane bound lipoprotein lipases (LPLs) located on adipose and muscle tissues as chylomicrons do. As the tissues absorb the fatty acids, the VLDLs progressively shrink to IDL and transfers a substantial portion of its phospholipids and apoprotein C to HDL. IDLs bind to receptors of liver cells where they are absorbed, or they can be further catabolized by LPLs, eventually loosing apo-E to form LDLs.

Low-density lipoproteins (LDL)

Low-density lipoproteins (LDL) is the major cholesterol-carrying lipoprotein that carry cholesterol from the liver to the rest of the body (Welty et al., 1999). The sole protein of LDL is Apo B-100. LDL is cleared from plasma in part through the action of the LDL receptor (LDLR) by both the liver and peripheral cells. The LDLR has five functionally distinct regions: an N-terminal ligand-binding region, an epidermal growth factor (EGF)-precursor homology region, a region containing O-linked sugars, a transmembrane domain and a C-terminal cytosolic domain (Francke et al., 1984; Sudhof et al., 1985). The ligand-binding region consists of seven cysteine rich repeats (R1–R7), so-called LDLR class A repeats (LDL-A, also known as complement-type repeats) (Sudhof et al., 1985). Besides LDL, the LDLR can bind VLDL particles that contain several copies of the apoE protein in addition to cholesteryl esters and a single apoB-100 molecule. The structural requirements for binding LDL and VLDL differ: LDL binds its receptor via apoB-100, VLDL via apoE. The second region in the LDLR shows homology to the EGF-precursor protein (Russell et al., 1984). Deletion of the EGF-precursor homology region does not affect VLDL binding, but instead prevents the acid-dependent dissociation of ligand in endosomes (Davis et al., 1987). The third region in the LDLR ectodomain is enriched in serine and threonine residues that function as acceptor sites for O-linked sugars. The role of O-linked glycosylation in LDLR function is still unclear. LDLR molecules lacking this region behave like wild-type receptors with respect to ligand binding, endocytosis and degradation (Davis et al., 1986). Possibly, glycosylation may protect the receptor from denaturation during recycling through the slightly acidic endosomal compartments (Tyko et al., 1982). Furthermore, O-glycosylation may modulate the rate of proteolytic cleavage by metalloproteases at the cell surface since variants of VLDLR lacking the O-linked glycosylation region are more prone to proteolytic cleavage than their full-length counterparts (Magrane et al., 1999; May et al., 2003). A hydrophobic domain of 24 amino acids anchors the LDLR in the lipid bilayer. Endocytosis and intracellular transport of the LDLR are regulated via its cytosolic domain.

After binding LDL the LDL receptors migrate to areas of the plasma membrane coated with the clathrin on the cytoplasmic side of it. The clathrin proteins promote endocytosis. Once the vesicle is inside of the cell, the clathrin spontaneously dissociates from the endosomal vesicle, and lowered pH of the vesicle results in LDL dissociation from the receptor. The LDL receptors are recycled to the cell surface. The vesicle fuses with a lysosome which then degrades the lipoprotein to its primary components, fatty acids, glycerol, cholesterol and amino acids. The cholesterol is incorporated into the intracellular cholesterol pool which is used for membrane or steroid synthesis. The liver also absorbs LDLs by the same endocytosis mechanism. Approximately 75% of the LDLs are absorbed by the liver.

When there is too much LDL cholesterol in the blood, these particles can form deposits in the walls of the coronary and other arteries. Such deposits narrow arteries and limit blood flow. When deposits breaks apart, it can cause a heart attack or stroke. Because of this, LDL cholesterol is often referred to as bad, or harmful, cholesterol.

High-density lipoproteins (HDL)

High-density lipoproteins (HDL) scavenge cholesterol from the bloodstream, from LDL, and from artery walls and ferry it back to the liver for disposal, so HDL cholesterol is often referred to as good, or protective, cholesterol. HDLs are secreted by liver and intestinal cells. The primary function of HDLs is to remove excess cholesterol and carry it to the liver to be metabolized into bile salts. HDL contains enzymes that either esterify cholesterol or transfer cholesteryl esters. Apo A-I is essential for HDL formation because in its absence no HDL is present in plasma (Lamon-Fava et al., 1987; Ordovas et al., 1989; Schaefer et al., 1982; Schaefer et al., 1984; Schaefer et al., 1985). The liver and intestine synthesize apolipoprotein A-I (apo A-I), which can interact with the adenosine triphosphate–binding cassette transporter A1 (ABCA1) located on the arterial macrophages, transporting free cholesterol to the extracellular HDL. Lipidation of the HDL particles generates nascent HDL (Curtiss et al., 2006). Subsequently, lechithin-cholesterol transferase (LCAT), enzyme that circulates with HDL, esterifies free cholesterol within nascent HDL with long chain fatty acids from phospholipids to produce mature HDL particles. These mature HDL particles can further take up free cholesterol. LCAT thus facilitating the storage and transport of excess cholesterol. Mature HDL has at least 2 metabolic fates. In the direct pathway, cholesteryl esters contained within HDL can undergo selective uptake by hepatocytes and steroid hormone–producing cells via the scavenger receptor type B1 and subsequent excretion into the bile (Lewis and Rader, 2005; Meyers and Kashyap, 2004). In the indirect pathway, cholesteryl esters within HDL can be exchanged for triglycerides in apolipoprotein B–rich particles (LDL and VLDL) through the action of cholesteryl ester transfer protein (CETP), which is another peripheral protein that circulates with HDL. CETP promotes the net transfer of cholesterol esters from HDL to LDL, IDL and VLDL. This process transforms VLDLs and IDLs into LDLs. The triglyceride-rich HDLcan then undergo hydrolysis

by hepatic lipase and endothelial lipase to form small HDL for further participation in transport (Lewis and Rader, 2005)

In addition to its major role in reverse cholesterol transport, HDL has other biological activities. These include antioxidant (counteracting LDL oxidation) effects, anti-inflammatory effects, antithrombotic/profibrinolytic (reducing platelet aggregation and coagulation) effects, and vasoprotective (facilitating vascular relaxation and inhibiting leukocyte chemotaxis and adhesion) effects (Assmann and Gotto, 2004; Chapman et al., 2004; Navab et al., 2004; Shah et al., 2001).

Triglycerides

Triglycerides make up most of the fat from food that travels through the bloodstream. As the body's main vehicle for transporting fats to cells, triglycerides are important for good health. But an excess of triglycerides can be unhealthy too.

Fasting triacylglycerol concentrations increase significantly with age: by 80% between the ages of 20 and 50 (Schaefer et al., 1995). LDL-cholesterol concentrations also increase, by 30% (Schaefer et al., 1995). The reasons for these alterations and delayed chylomicron remnant clearance in the elderly compared with the young are elevated VLDL apo B-100 secretion and delayed LDL apo B-100 clearance, accounting for the increases in triacylglycerol and LDL cholesterol (Krasinski et al., 1990; Millar et al., 1995). In the very elderly, both triacylglycerol and LDL cholesterol are significantly lower than in middle-aged persons due to decreased apo B-100 production in these subjects (Schaefer et al., 1995). It is well known that women have significantly higher concentrations of HDL cholesterol and apo A-I than do men, and premenopausal women also have higher apo A-I secretion rates than do men (Schaefer et al., 1982). Estrogen increases HDL apo A-I production and liver APOA1 gene expression (Lamon-Fava et al., 1999; Schaefer et al., 1983). Shematic owerwiew of lipoprotein metabolism is shown in Fig.1 (Schaefer, 2002).

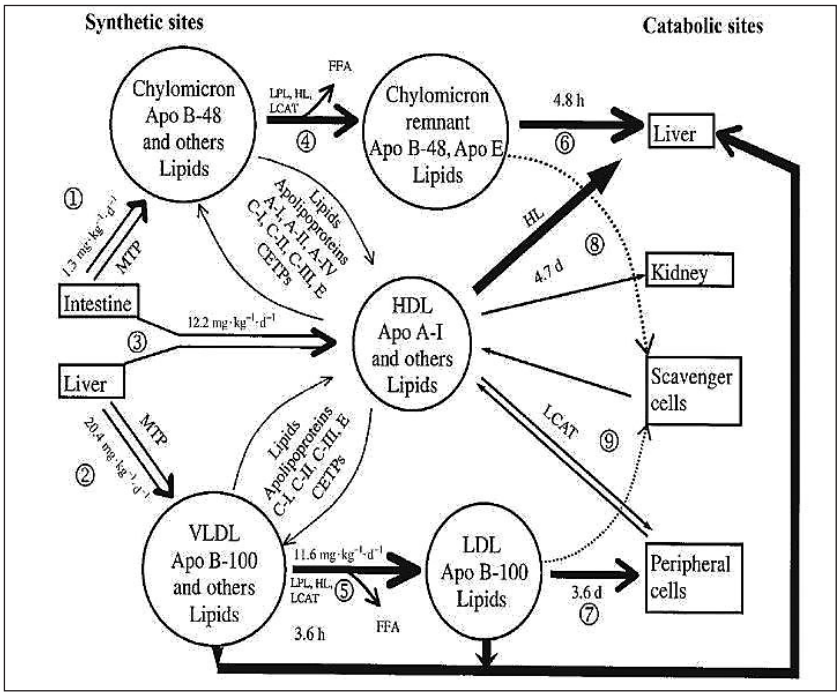

Figure 1. *Shematic owerwiew of lipoprotein metabolism (Schaefer, 2002).*

Adverse Effects of Over Consumption of Cholesterol and Fat

The Effects of Dietary Cholesterol on Plasma Total, HDL, and LDL Cholesterol Concentrations.

Numerous studies in humans have examined the effects of dietary cholesterol on plasma total and lipoprotein cholesterol concentrations, and empirical formulas have been derived to describe these relationships. Between 1957 and 1993, Keys and Hegsted independently developed several equations to predict changes in total-C and LDL-C that would accompany changes in dietary fat and cholesterol intake (Hegsted et al., 1965; Hegsted et al., 1986; Hegsted et al., 1993; Keys et al., 1957; Keys et al., 1965; Keys et al., 1984). Each of these predictive equations consistently suggested that polyunsaturated fats lowered serum total-C and LDL-C levels, whereas monounsaturated fats had a neutral effect. These findings were challenged in 1985 when Mattson and Grundy reported results indicating that both types of unsaturated fat lowered LDL-C levels when they replaced saturated fat. Their results also indicated that polyunsaturated fat lowered HDL-C, whereas monounsaturated did not. This study is now frequently cited as evidence that monounsaturated are preferred over polyunsaturated (Artaud-Wild et al., 1993; Garg et al., 1994; Reaven et al., 1993). Although most studies have reported a linear relationship between changes in dietary cholesterol and total serum cholesterol concentration, other studies, including a meta-analysis of 27 controlled metabolic feeding studies of added dietary cholesterol (Hopkins, 1992), have indicated a curvilinear univariate relationship that is quasilinear in the range from 0 to 300 to 400 mg/d of added dietary cholesterol. The range of added dietary cholesterol in the studies was 17 to 4,800 mg/d. The meta-analysis also identified a diminishing increment of serum cholesterol with increasing baseline dietary cholesterol intake. With a baseline cholesterol intake of 0, the estimated increases in serum total cholesterol concentration for intakes from 100 to 400 mg/d of added dietary cholesterol were 0.16 to 0.51 mmol/L, whereas for a baseline cholesterol intake of 300 mg/d, the estimated increases in serum total cholesterol were 0.05 to 0.16 mmol/L (Hopkins, 1992). Another meta-analysis showed that dietary cholesterol raises the ratio of total cholesterol to high density lipoprotein (HDL) cholesterol, therefore adversely affecting the cholesterol profile (Weggemans et al., 2001).

Other predictive formulas for the effect of 100 mg/d of added dietary cholesterol, which did not consider baseline cholesterol intake and are based on compilations of studies with a variety of experimental conditions, have yielded estimates of 0.1 mmol/L (Hegsted, 1986), 0.057 mmol/L (Howell et al., 1997), and 0.065 mmol/L (Clarke et al., 1997), the latter two involving meta-analyses with adjustment for other dietary variables. Furthermore, pooled analyses of the effects of 100 mg/d of added

dietary cholesterol on plasma lipoprotein cholesterol concentrations (Clarke et al., 1997) indicated an estimated increase of 0.05 mmol/L in low density lipoprotein (LDL) and 0.01 mmol/L in HDL (ratio of 5 LDL:1 HDL). There is evidence that the increase in HDL is largely accounted for by higher levels of apoE-containing HDL particles (Mahley et al., 1978), but the significance in atherosclerosis protection is not established. Hegsted and coworkers (1993) reported that the majority of the increase in serum total cholesterol concentration with increased cholesterol intake was due to an increase in LDL cholesterol concentration.

There is increasing evidence that genetic factors underlie a substantial portion of interindividual variation in response to dietary cholesterol. An instructive case is that of the Tarahumara Indians, who in addition to consuming a diet low in cholesterol, have both low intestinal cholesterol absorption and increased transformation of cholesterol to bile acids (McMurry et al., 1985). However, with an increase in dietary cholesterol from 0 to 905 mg/d, their average plasma cholesterol concentration increased 0.88 mmol/L (from 2.92 to 3.8 mmol/L), the same value predicted by the formula of Hopkins (1992), indicating the likelihood of above-average responsiveness of other aspects of cholesterol or lipoprotein metabolism.

Variations in several genes have been associated with altered responsiveness to dietary cholesterol. The common E4 polymorphism of the apoE gene has been associated with increased cholesterol absorption (Kesäniemi et al., 1987) and with increased plasma LDL cholesterol response to dietary saturated fat and cholesterol in some, but not all studies (Dreon and Krauss, 1997). The recent finding that apoE is of importance in regulating cholesterol absorption and bile acid formation in apoE knockout mice lends support to a possible role for this gene in modulating dietary cholesterol responsiveness in humans. The A-IV-2 variant allele of the apo A-IV gene has been found to attenuate the plasma cholesterol response to dietary cholesterol (McCombs et al., 1994). Recently, the A-IV-2 allele has been associated with reduced intestinal cholesterol absorption in diets high in polyunsaturated fat but not in diets high in saturated fat (Weinberg et al., 2000). However, this has not been confirmed in other studies (Weggemans et al., 2000). Finally, the recent discovery that defects in the ABCG5 and ABCG8 genes can lead to markedly increased intestinal absorption of both cholesterol and plant sterols (Berge et al., 2000) points to the possibility that more common variants of these genes may contribute to variation in cholesterol absorption and dietary cholesterol response in the general population.

There are numerous other candidate genes that could modulate plasma lipid and lipoprotein response to dietary cholesterol by affecting cholesterol absorption, cellular cholesterol homeostasis, and plasma lipoprotein metabolism. Among the most likely candidates are those regulated by lipid-responsive nuclear transcription factors, including sterol regulatory element-binding proteins, peroxisome proliferator-activated receptors, and orphan nuclear receptors. Studies in animal models have generated data in support of the possibility that variations among these genes may be of importance in influencing dietary cholesterol response in humans, but to date such human data are lacking. Nevertheless, the existence of marked interindividual variability in dietary cholesterol response among and within various animal models points to the likelihood that some of the mechanisms underlying this variability will also apply to humans.

The Effects of Dietary Total Fat on Plasma Total, HDL, and LDL Cholesterol Concentrations.

A Tolerable Upper Intake Level (UL) was not set for total fat because of the lack of a defined intake level at which an adverse effect, such as obesity, can occur. An Acceptable Macronutrient Distribution Range (AMDR) for fat intake, however, has been estimated based on adverse effects from consuming low fat and high fat diets. Several hundred studies have been conducted to assess the effect of saturated fatty acids on serum cholesterol concentration. In general, the higher the intake of saturated fatty acids, the higher the serum total and low density lipoprotein (LDL) cholesterol concentrations. Regression analyses of such studies have suggested that for each 1 percent increase in energy from saturated fatty acids, serum LDL cholesterol concentration increases by 0.033 mmol/L (Mensink and Katan, 1992), 0.036 mmol/L (Clarke et al., 1997), or 0.045 mmol/L (Hegsted et al., 1993). Although all fats will increase serum high density lipoprotein (HDL) cholesterol concentration relative to carbohydrate, the increase attributable to saturated fats is greater than that observed for monounsaturated and polyunsaturated fatty acids. Serum HDL cholesterol concentration increases by 0.011 to 0.013 mmol/L for each 1 percent increase in saturated fat (Clarke et al., 1997; Hegsted et al., 1993; Mensink and Katan, 1992).

The Effects of Dietary Elevated LDL Cholesterol Concentration and Risk of CHD.

Similar to that observed for saturated fatty acid intake and LDL cholesterol concentration, there is a positive linear relationship between serum total and LDL cholesterol concentrations and risk of coronary heart disease (CHD) (Jousilahti et al., 1998; Neaton and Wentworth, 1992; Sorkin et al., 1992; Stamler et al., 1986; Weijenberg et al., 1996). It has been estimated that a 10 percent reduction in serum cholesterol concentration would reduce CHD mortality by 20 percent (Jousilahti et al., 1998).

A number of epidemiological studies have reported an association between saturated fatty acid intake and risk of CHD. The majority of these studies have reported a positive relationship between saturated fatty acid intake and risk of CHD and CHD mortality (Goldbourt et al., 1993; Hu et al., 1997, 1999a, 1999c; Keys et al., 1984; McGee et al., 1984).

Although all saturated fatty acids were originally considered to be associated with increased adverse health outcomes, including increased blood cholesterol concentrations, it later became apparent that saturated fatty acids differ in their metabolic effects (e.g., potency in raising blood cholesterol concentrations). In general, stearic acid has been shown to have a neutral effect on total and LDL cholesterol concentrations (Bonanome and Grundy, 1988; Denke, 1994; Yu et al., 1995; Zock and Katan, 1992). While palmitic, lauric, and myristic acids increase cholesterol concentrations (Mensink et al., 1994),

stearic acid is more similar to oleic acid in its neutral effect (Kris-Etherton et al., 1993). Furthermore, a stearic acid-rich diet has been shown to improve thrombogenic and atherogenic risk factor profiles (Kelly et al., 2001). However, it is impractical at the current time to make recommendations for saturated fatty acids on the basis of individual fatty acids.

The World Health Organization (WHO) has estimated that amongst Europeans the average total cholesterol levels in men are about 4.5 mmol/l and in women, average total cholesterol levels are around 4.6 mmol/l (WHO, 2006). For most people, the recommended total cholesterol level is <5.0 mmol/l, but for people who already have some degree of cardiovascular disease, this recommended level is <4.5 mmol/l (Policy Analysis Centre, 2007). There are several factors that influence blood cholesterol levels. Eating a balanced diet, being of healthy weight and keeping physically active, in particular, can help to keep cholesterol levels normal. Minimizing dietary saturated fat intake has a beneficial impact on serum cholesterol levels. Calories from saturated fat can be replaced with either unsaturated fats or carbohydrates. Concerning unsaturated fats, it is currently unclear whether monounsaturated or polyunsaturated are preferable for optimal serum lipid levels. Foods containing unsaturated fats include vegetable and seed oils and spreads (e.g., rapeseed oil, olive oil, soya spread), oily fish (e.g., mackerel, salmon and herring), nuts and avocado.

Another type of fat, *trans* fat, is sometimes found in foods that contain partially hydrogenated fats (e.g., some pastry and biscuits), although many companies in Europe have reduced levels of *trans* fats in their products to a minimum. *Trans* fats can raise LDL (bad) cholesterol levels. Unlike saturated fats, *trans* fats also lead to a fall in HDL (or good) cholesterol and raise blood triglyceride levels, both of which are associated with an increased risk of CHD. These negative effects may occur with long-term intakes of trans fats of 5-10 g per day (Hunter, 2006; Stender et al., 2006). In addition to the type of fat we eat, other foods can also help to keep cholesterol levels healthy. Eating plenty of fruits and vegetables, foods containing soluble fibre (e.g., oats, lentils, beans and peas), tree nuts (e.g., almonds) and soya can be useful. Products containing added plant stanols or plant sterols are designed for people who have excessive cholesterol levels and are not necessary for people with healthy cholesterol levels. Eating a healthy low-fat diet, including a 'portfolio' of the foods mentioned above, can reduce cholesterol levels by up to 20% (Jenkins et al., 2005). Foods that can lower cholesterol and protect heart are:

1. Oatmeal, oat bran and high-fiber foods - Oatmeal contains soluble fiber, which reduces low-density lipoprotein (LDL), the "bad" cholesterol. Soluble fiber is also found in such foods as kidney beans, apples, pears, barley and prunes. Soluble fiber can reduce the absorption of cholesterol into bloodstream. Five to 10 grams or more of soluble fiber a day decreases total and LDL cholesterol (Flight et al., 2006).

2. Fish and ω-3 fatty acids - Eating fatty fish can be heart-healthy because of its high levels of ω-3 fatty acids, which can reduce blood pressure and risk of developing blood clots. In people who have already had heart attacks, fish oil or ω-3 fatty acids reduces the risk of sudden death. Doctors recommend eating at least two servings of fish a week. The highest levels of ω-3 fatty acids are in: Mackerel, Lake trout, Herring, Sardines, Albacore tuna, Salmon and Halibut.

3. Walnuts, almonds and other nuts - Walnuts, almonds and other nuts can reduce blood cholesterol. Rich in polyunsaturated fatty acids, walnuts also help keep blood vessels healthy. According to the Food and Drug Administration, eating about a handful (42.5 grams) a day of most nuts, such as almonds, hazelnuts, peanuts, pecans, some pine nuts, pistachio nuts and walnuts, may reduce risk of heart disease (Kris-Etherton et al., 2008; King et al., 2008).

4. Olive oil - Olive oil contains a potent mix of antioxidants that can lower "bad" (LDL) cholesterol but leave "good" (HDL) cholesterol untouched. The Food and Drug Administration recommends using about 2 tablespoons (23 grams) of olive oil a day in place of other fats in diet to get its heart-healthy benefits (Covas et al., 2006; Covas et al., 2008).

5. Foods with added plant sterols or stanols - Foods are now available that have been fortified with sterols or stanols - substances found in plants that help block the absorption of cholesterol. Margarines, orange juice and yogurt drinks with added plant sterols can help reduce LDL cholesterol by more than 10 percent. The amount of daily plant sterols needed for results is at least 2 grams. Plant sterols or stanols in fortified foods don't appear to affect levels of triglycerides or of high-density lipoprotein (HDL), the "good" cholesterol (Fassbender et al., 2008; Abumweis et al., 2008).

Obesity.

A number of studies have attempted to ascertain the relationship between saturated fatty acid intake and body mass index, and these results are mixed. Saturated fatty acid intake was shown to be positively associated with body mass index or percent of body fat (Doucet et al., 1998; Gazzaniga and Burns, 1993; Larson et al., 1996; Ward et al., 1994). In contrast, no relationship was observed for saturated fatty acid intake and body weight (González et al., 2000; Ludwig et al., 1999; Miller et al., 1994).

Impaired Glucose Tolerance and Risk of Diabetes.

Epidemiological studies have been conducted to ascertain the association between the intake of saturated fatty acids and the risk of diabetes. A number of these studies found no relationship (Colditz et al., 1992; Costa et al., 2000; Salmerón et al., 2001; Sevak et al., 1994; Virtanen et al., 2000). Several large epidemiological studies, however, showed increased risk of diabetes with increased intake of saturated fatty acids (Feskens et al., 1995; Hu et al., 2001; Marshall et al., 1997; Parker et al., 1993). The Normative Aging Study found that a diet high in saturated fatty acids was an independent predictor for both fasting and postprandial insulin concentration (Parker et al., 1993). A reduction in saturated fatty acid intake from 13.9 to 7.8 percent of energy was associated with an 18 percent decrease in fasting insulin and a 25 percent decrease in postprandial insulin concentrations.

Findings from short-term intervention studies tend to suggest a lack of adverse effect of saturated fatty acids on risk indicators for diabetes in healthy individuals. Postprandial glucose

and insulin concentrations were not significantly different in men who ingested three different levels of saturated fatty acids (Roche et al., 1998). Fasching and coworkers (1996) reported no difference in insulin secretion or sensitivity in men who consumed a 33 percent saturated, monounsaturated, or polyunsaturated fatty acid diet. There was no difference in postprandial glucose or insulin concentration when healthy adults were fed butter or olive oil (Thomsen et al., 1999). Louheranta and colleagues (1998) found no difference in glucose tolerance and insulin sensitivity in healthy women fed either a high oleic or stearic acid diet. In contrast, results of the study indicate that consumption of high levels (18 percent of energy) of saturated fats can significantly impair insulin sensitivity (Vessby et al., 2001).

Conclusions

Fatty acids are important source of energy and biologically active molecules. Cholesterol is essential to all our body cells and has a special role in the formation of brain cells, nerve cells and as precursor for estrogen, testosterone, vitamin D, and other vital compounds synthesis. Fat and cholesterol can't dissolve in blood, so they are transported in the plasma as triglicerydes or by large complexes called lipoproteins. Metabolism of fatty acids, lipoproteins and cholesterol is quite well studied so far, while effects of dietary fats and cholesterol on the level and distribution of lipoproteins to VLDL, LDL and HDL is still under examination worldwide. Prevention of CHD through risk factor control - smoking cessation and control of blood pressure, blood glucose, and LDL cholesterol and raising of HDL cholesterol - remains the most effective long-term option for treatment. Obesity has an adverse effect on all these risk factors except smoking and therefore requires treatment. Emerging risk factors requiring attention are elevated concentrations of lipoprotein(a), remnant lipoproteins, and homocysteine. Dietary treatment can clearly decrease CHD risk, especially when the food supply is altered. It is recommend to decrease saturated fat to < 7% of energy, decrease total fat to 15–30% of energy, decrease dietary cholesterol to < 200 mg/d, decrease sugar intake to < 10% of energy, having an ω-6 fatty acid intake of 5–10% of energy, having an ω-3 fatty acid intake of ≥1% of energy, minimize trans fatty acid intake, and increase the intake of vegetables, fruit, and grains. It is important to maintain an adequate intake of essential fatty acids while restricting intakes of saturated fat and cholesterol.

References

Abumweis S.S., Jones P.J. (2008) Cholesterol-lowering effects of plant sterols. *Current Atherosclerosis Reports.* 10, 467.

Appel L.J., Sacks F.M., Carey V.J. (2005) Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the Omni Heart randomized trial. *The Journal of the American Medical Association.* 294, 2455-64.

Aro A., Amaral E., Kesteloot H., Rimestad A., Thamm M., van Poppel G. (1998a) *Trans* fatty acids in French fries, soups, and snacks from 14 European countries: The TRANSFAIR Study. *Journal of Food Composition and Analysis.* 11, 170–177.

Aro A., Antoine J.M., Pizzoferrato L., Reykdal O., van Poppel G. (1998b) *Trans* fatty acids in dairy and meat products from 14 European countries: The TRANSFAIR Study. *Journal of Food Composition and Analysis.* 11, 150–160.

Aro A., Van Amelsvoort J., Becker W., van Erp-Baart M.A., Kafatos A., Leth T., van Poppel G. (1998c) *Trans* fatty acids in dietary fats and oils from 14 European countries: The TRANSFAIR Study. *Journal of Food Composition and Analysis.* 11, 137–149.

Artaud-Wild S.M., Connor S.L., Sexton G., Connor W.E. (1993) Differences in coronary mortality can be explained by differences in cholesterol and saturated fat intakes in 40 countries but not in France and Finland: a paradox. *Circulation.* 88, 2771-2779.

Assmann G., Gotto A.M. Jr. (2004) HDL cholesterol and protective factors in atherosclerosis. *Circulation.* 109, 8-14.

Becker N., Illingworth D.R., Alaupovic P., Connor W.E., Sundberg E.E. (1983) Effects of saturated, monounsaturated, and omega-6 polyunsaturated fatty acids on plasma lipids, lipoproteins, and apolipoproteins in humans. *The American Journal of Clinical Nurition.* 37, 355–64.

Beresford S.A., Johnson K.C., Ritenbaugh C. (2006) Low-fat dietary pattern and risk of colorectal cancer: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *The Journal of the American Medical Association.* 295, 643-54.

Berge K.E., Tian H., Graf G.A., Yu L., Grishin N.V., Schultz J., Kwiterovich P., Shan B., Barnes R., Hobbs H.H. (2000) Accumulation of dietary cholesterol in sitosterolemia caused by mutations in adjacent ABC transporters. *Science.* 290, 1771–1775.

Bonanome A., Grundy S.M. (1989) Intestinal absorption of stearic acid after consumption of high fat meals in humans. *Journal of Nutrition.* 119, 1556–1560.

Brewer H.B., Gregg R.E., Hoeg J.M. and Fojo S.S. (1988) Apolipoproteins in human plasma: An overview. *Clinical Chemistry.* 34, 4-8.

Chapman M.J., Assmann G., Fruchart J.C., Shepherd J., Sirtori C. (2004) Raising high-density lipoprotein cholesterol with reduction of cardiovascular risk: the role of nicotinic acid—a position paper developed by the European Consensus Panel on HDL-C. *Current Medical Research and Opinion.* 20, 1253-1268.

Chee K.M., Gong J.X., Rees D.M. (1990) Fatty acid content of marine oil capsules. *Lipids.* 25, 523–8.

Chin S.F., Liu W., Storkson J.M., Ha Y.L., Pariza M.W. (1992) Dietary sources of conjugated dienoic isomers of linoleic acid, a newly recognized class of anti-carcinogens. *Journal of Food Composition and Analysis.* 5, 185–197.

Clarke R., Frost C., Collins R., Appleby P., Peto R. (1997) Dietary lipids and blood cholesterol: Quantitative meta-analysis of metabolic ward studies. *British Medical Journal.* 314, 112–117.

Cohn J.S., McNamara J.R., Cohn S.D., Ordovas J.M., Schaefer E.J. (1988) Plasma apolipoprotein changes in the triglyceride-rich lipoprotein fraction of human subjects fed a fat-rich meal. *Journal of Lipid Research.* 29, 925–36.

Cohn J.S., McNamara J.R., Cohn S.D., Ordovas J.M., Schaefer E.J. (1988) Postprandial plasma lipoprotein changes in human subjects of different ages. *Journal of Lipid Research.* 29, 469–78.

Cohn J.S., Johnson E.J., Millar J.S. (1993) The contribution of apoB-48 and apoB-100 triglyceride-rich lipoproteins to post-prandial increases in plasma triglycerides and retinyl esters. *Journal of Lipid Research.* 34, 2033–40.

Colditz G.A., Manson J.E., Stampfer M.J., Rosner B., Willett W.C., Speizer F.E. (1992) Diet and risk of clinical diabetes in women. *The American Journal of Clinical Nurition.* 55, 1018–1023.

Connor W.E., Stone D.B., Hodges R.E. (1964) The interrelated effects of dietary cholesterol and fat upon human serum lipid levels. *The Journal of Clinical Investigation.* 43, 1691–702.

Costa M.B., Ferreira S.R.G., Franco L.J., Gimeno S.G.A., Iunes M. (2000) Japanese-Brazilian Diabetes Study Group. Dietary patterns in a high-risk population for glucose intolerance. *The Journal of Epidemiology.* 10, 111–117.

Covas M.I., Nyyssönen K., Poulsen H.E., Kaikkonen J., Zunft H.J., Kiesewetter H., Gaddi A., Torre R., Mursu J., Bäumler H., Nascetti S., Salonen J.T., Fitó M.,Virtanen J., Marrugat J. (2006) The effect of virgin and refined olive oils on heart disease risk factors. *Annals of Internal Medicine.* 145, 333.

Covas M.I. (2008) Bioactive effects of olive oil phenolic compounds in humans: Reduction of heart disease factors and oxidative damage. *Immunopharmacology.* 16, 216.

Curtiss L.K., Volenta D.T., Hime N.J., Rye K.A. (2006) What is so special about apolipoprotein AI in reverse cholesterol transport? *Arteriosclerosis Thrombosis Vascular Biology.* 26, 12-19.

Davis C.G., Elhammer A., Russell D.W., Schneider W.J., Kornfeld S., Brown M.S. (1986) Deletion of clustered O-linked carbohydrates does not impair function of low density lipoprotein receptor in transfected fibroblasts. *J. Biol. Chem.* 261, 2828–2838.

Davis C.G., Goldstein J.L., Sudhof T.C., Anderson R.G., Russell D.W., Brown M. S. (1987) Acid-dependent ligand dissociation and recycling of LDL receptor mediated by growth factor homology region. *Nature.* 326, 760–765.

Denke M.A. (1994) Effects of cocoa butter on serum lipids in humans: Historical highlights. *The American Journal of Clinical Nurition.* 60, 1014–1016.

Doucet E., Alméras N., White M.D., Després J.P., Bouchard C., Tremblay A. (1998) Dietary fat composition and human adiposity. *European Journal of Clinical Nurition.* 52, 2–6.

Dreon D.M., Vranizan K.M., Krauss R.M. (1990) The effects of polyunsaturated fat vs monounsaturated fat on plasma lipoproteins. *The Journal of the American Medical Association.* 263, 2462–70.

Dreon D.M., Krauss R.M. (1997) Diet-gene interactions in human lipoprotein metabolism. *Journal of the American College of Nutrition.* 16, 313–324.

Emken E.A. (1995) Physiochemical properties, intake, and metabolism. *The American Journal of Clinical Nurition.* 62, 659–669.

Endres S., Ghorbani R., Kelley V.E. (1989) Dietary n-3 polyunsaturated fatty acids suppress synthesis of interleukin-1 and tumor necrosis factor. *The New England Journal of Medicine.* 320, 265–71.

Enig M.G., Atal S., Keeney M., Sampugna J. (1990) Isomeric trans fatty acids in the U.S. diet. *Journal of the American College of Nutrition.* 5, 471–486.

Fassbender K., Fassbender K., Lütjohann D., Dik M.G., Bremmer M., Konig J., Walter S., Liu Y., Letiembre M., von Bergmann K., Jonker C. (2008) Moderately elevated plant sterol levels are associated with reduced cardiovascular risk — The LASA study. *Atherosclerosis.* 196, 283.

Feskens E.J.M., Virtanen S.M., Räsänen L., Tuomilehto J., Stengard J., Pekkanen J., Nissinen A., Kromhout D. (1995) Dietary factors determining diabetes and impaired glucose tolerance: A 20-year follow-up of the Finnish and Dutch cohorts of the Seven Countries Study. *Diabetes Care.* 18, 1104–1112.

Flight I., Clifton P. (2006) Cereal grains and legumes in the prevention of coronary heart disease and stroke: A review of the literature. *European Journal of Clinical Nutrition.* 60, 1145.

Francke U., Brown M.S., Goldstein J. L. (1984) Assignment of the human gene for the low density lipoprotein receptor to chromosome 19: synteny of a receptor, a ligand and a genetic disease. *Proceedings of the National Academy of Sciences.* 81, 2826–2830.

Garg A., Bantle J.P., Henry R.R., Coulston A.M., Griver K.A., Raatz S.K., Brinkley L., Chen Y.D., Grundy S.M., Huet B.A., Reaven G.M. (1994) Effects of varying carbohydrate content of diet in patients with non–insulin-dependent diabetes mellitus. *The Journal of the American Medical Association*. . 271, 1421-1428.

Gazzaniga J.M., Burns T.L. (1993) Relationship between diet composition and body fatness, with adjustment for resting energy expenditure and physical activity, in preadolescent children. *The American Journal of Clinical Nurition.* 58, 21–28.

Goldbourt U., Yaari S., Medalie J.H. (1993) Factors predictive of long-term coronary heart disease mortality among 10,059 male Israeli civil servants and municipal employees. A 23-year mortality follow-up in the Israeli Ischemic Heart Disease Study. *Cardiology.* 82, 100–121.

González C.A., Pera G., Quirós J.R., Lasheras C., Tormo M.J., Rodriguez M., Navarro C., Martinez C., Dorronsoro M., Chirlaque M.D., Beguiristain J.M., Barricarte A., Amiano P., Agudo A. (2000) Types of fat intake and body mass index in a Mediterranean country. *Public Health Nutrition.* 3, 329–336.

Ha Y.L., Grimm N.K., Pariza M.W. (1989) Newly recognized anticarcinogenic fatty acids: Identification and quantification in natural and processed cheeses. *Journal of Agricurtural and Food Chemistry.* 37, 75–81.

Harris W.S. (1997) n-3 Fatty acids and serum lipoproteins: human studies. *The American Journal of Clinical Nurition.* 65, 1645-53.

Hegsted D.M., McGandy R.B., Myers M.L., Stare F.J. (1965) Quantitative effects of dietary fat on serum cholesterol in man. *The American Journal of Clinical Nurition.* 17, 281-295.

Hegsted D.M. (1986) Serum-cholesterol response to dietary cholesterol: A re-evaluation. *The American Journal of Clinical Nurition.* 44, 299–305.

Hegsted D.M., Ausman L.M., Johnson J.A., Dallal G.E. (1993) Dietary fat and serum lipids: an evaluation of the experimental data. *The American Journal of Clinical Nurition.* 57, 875-883.

Hopkins P.N. (1992) Effects of dietary cholesterol on serum cholesterol: A meta-analysis and review. *The American Journal of Clinical Nurition.* 55, 1060–1070.

Howard B.V., Manson J.E., Stefanick M.L. (2006) Low-fat dietary pattern and weight change over 7 years: the Women's Health Initiative Dietary Modification Trial. *The Journal of the American Medical Association.* 295, 39-49.

Howard B.V., Van Horn L., Hsia J. (2006) Low-fat dietary pattern and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *The Journal of the American Medical Association.* 295, 655-66.

Howell W.H., McNamara D.J., Tosca M.A., Smith B.T., Gaines J.A. (1997) Plasma lipid and lipoprotein responses to dietary fat and cholesterol: A meta-analysis. *The American Journal of Clinical Nurition.* 65, 1747–1764.

Hu F.B., Stampfer M.J., Manson J.E., Ascherio A., Colditz G.A,. Speizer F.E., Hennekens C.H., Willett W.C. (1999a) Dietary saturated fats and their food sources in relation to the risk of coronary heart disease in women. *The American Journal of Clinical Nurition.* 70, 1001–1008.

Hu F.B., Stampfer M.J., Manson J.E., Rimm E., Colditz G.A., Rosner B.A., Hennekens C.H., Willett W.C. (1997) Dietary fat intake and the risk of coronary heart disease in women. *The New England Journal of Medicine.* 337, 1491–1499.

Hu F.B., Stampfer M.J., Rimm E., Ascherio A., Rosner B.A., Spiegelman D., Willett W.C. (1999c) Dietary fat and coronary heart disease: A comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. *American Journal of Epidemiology.* 149, 531–540.

Hu F.B., van Dam R.M., Liu S. (2001) Diet and risk of type II diabetes: The role of types of fat and carbohydrate. *Diabetologia.* 44, 805–817.

Hunter J.E. (2006) Dietary trans fatty acids: review of recent human studies and food industry responses. *Lipids.* 41, 967-92.

Innis S.M., Green T.J., Halsey T.K. (1999) Variability in the trans fatty acid content of foods within a food category: Implications for estimation of dietary trans fatty acid intakes. *Journal of the American College of Nutrition.* 18, 255–260.

Jenkins D.J.A., Kendall C.W.C., Marchie A., Faulkner D.A., Wong J.M.W., de Souza R., Emam A., Parker T.L., Vidgen E., Trautwein E.A., Lapsley K.G., Josse R.G., Leiter L.A., Singer W., Connelli P.W. (2005) Direct comparison of a dietary portfolio of cholesterol lowering foods with a statin in hypercholesterolemic participants. *American Journal of Clinical Nutrition.* 81, 380-7.

Jousilahti P., Vartiainen E., Pekkanen J., Tuomilehto J., Sundvall J., Puska P. (1998) Serum cholesterol distribution and coronary heart disease risk. Observations and predictions among middle-aged population in eastern Finland. *Circulation.* 97, 1087–1094.

Judd J.T., Baer D.J., Clevidence B.A. (1998) Effects of margarine compared with those of butter on blood lipid profiles related to cardiovascular disease risk factors in normolipemic adults fed controlled diets. *American Journal of Clinical Nutrition.* 68, 768–77.

Kelly F.D., Sinclair A.J., Mann N.J., Turner A.H., Abedin L., Li D. (2001) A stearic acid-rich diet improves thrombogenic and atherogenic risk factor profiles in healthy males. *European Journal of Clinical Nutrition.* 55, 88–96.

Kesäniemi Y.A., Ehnholm C., Miettinen T.A. (1987) Intestinal cholesterol absorption efficiency in man is related to apoprotein E phenotype. *The Journal of Clinical Investigation.* 80, 578–581.

Keys A., Anderson J.T., Grande F. (1957) Prediction of serum-cholesterol responses of man to changes in fats in the diet. *Lancet.* 2, 959-966.

Keys A., Anderson J.T., Grande F. (1965) Serum cholesterol response to changes in diet, IV: particular saturated fatty acids in diet. *Metabolism.* 14, 776-787.

Keys A. (1984) Serum-cholesterol response to dietary cholesterol. *The American Journal of Clinical Nurition.* 40, 351-359.

King J.C., Blumberg J., Ingwersen L., Jenab M., Tucker K.L. (2008) Tree nuts and peanuts as components of a healthy diet. *Journal of Nutrition.* 138, 1736.

Krasinski S.D., Cohn J.S., Schaefer E.J., Russell R.M. (1990) Post-prandial plasma retinyl ester response is greater in older subjects compared with younger subjects. *The Journal of Clinical Investigation.* 85, 883–92.

Kris-Etherton P.M., Derr J., Mitchell D.C., Mustad V.A., Russell M.E., McDonnell E.T., Salabsky D., Pearson T.A. (1993) The role of fatty acid saturation on plasma lipids, lipoproteins, and apolipoproteins: I. Effects of whole food diets high in cocoa butter, olive oil, soybean oil, dairy butter, and milk chocolate on the plasma lipids of young men. *Metabolism.* 42, 121–129.

Kris-Etherton P.M., Taylor D.S., Yu-Poth S., Huth P., Moriarty K., Fishell V., Hargrove R.L., Zhao G., Etherton T.D. (2000) Polyunsaturated fatty acids in the food chain in the United States. *The American Journal of Clinical Nurition.* 71, 179–188.

Kris-Etherton P.M., Hu F.B., Emilio Ros E., Sabaté J. (2008) The role of tree nuts and peanuts in the prevention of coronary heart disease: Multiple potential mechanisms. *Journal of Nutrition.* 138, 1746S.

Lamon-Fava S., Ordovas J.M., Mandel G. (1987) Secretion of apolipoprotein A-I in lipoprotein particles following transfection of the human apolipoprotein A-I gene into 3T3 cells. *Journal of Biological Chemistry.* 62, 8944–7.

Lamon-Fava S., Ordovas J.M., Schaefer E.J. (1999) Estrogen increases apolipoprotein (Apo) A-I secretion in Hep G2 cells by modulating transcription of the Apo A-I gene promoter. *Arteriosclerosis Thrombosis and Vascular Biology.* 19, 2960–5.

Larson D.E., Hunter G.R., Williams M.J., Kekes-Szabo T., Nyikos I., Goran M.I. (1996) Dietary fat in relation to body fat and intraabdominal adipose tissue: A cross-sectional analysis. *The American Journal of Clinical Nurition.* 64, 677–684.

Lewis G.F., Rader D.J. (2005) New insights into the regulation of HDL metabolism and reverse cholesterol transport. *Circulation Research.* 96, 1221-1232.

Lichtenstein A.H., Chobanian A.V. (1990) Effect of fish oil on atherogenesis in Watanabe heritable hyperlipidemic rabbits. *Arteriosclerosis.* 10, 597–605.

Lichtenstein A.H., Hachey D.L., Millar J.S. (1992) Measurement of human apolipoprotein B-48 and B-100 kinetics in triglyceride-rich lipoproteins using [5,5,5–2H3] leucine. *Journal of Lipid Research.* 33, 907–14.

Lichtenstein A.H., Ausman L.M., Carrasco W. (1993) Effects of canola, corn, and olive oils on fasting and postprandial plasma lipoproteins in humans as part of a National Cholesterol Education Program Step 2 diet. *Arteriosclerosis Thrombosis and Vascular Biology.* 13, 1533–42.

Lichtenstein A.H., Ausman L.M., Carrasco W., Jenner J.L., Ordovas J.M., Schaefer E.J. (1993) Hydrogenation impairs the hypolipidemic effect of corn oil in humans: hydrogenation, trans fatty acids, and plasma lipids. *Arteriosclerosis Thrombosis and Vascular Biology.* 13, 154–61.

Lichtenstein A.H., Ausman L.M., Carrasco W. (1994) Hypercholesterolemic effect of dietary cholesterol in diets enriched in polyunsaturated and saturated fat. *Arteriosclerosis Thrombosis and Vascular Biology.* 14, 168–75.

Lichtenstein A.H., Ausman L.M., Jalbert S.M., Schaefer E.J. (1999) Effects of different forms of dietary hydrogenated fats on serum lipoprotein cholesterol levels. *The New England Journal of Medicine.* 340, 1933–40.

Litin L., Sacks F. (1993) Trans-fatty-acid content of common foods. *The New England Journal of Medicine.* 329, 1969–1970.

Louheranta A.M., Turpeinen A.K., Schwab U.S., Vidgren H.M., Parviainen M.T., Uusitupa M.I.J. (1998) A high-steric acid diet does not impair glucose tolerance and insulin sensitivity in healthy women. *Metabolism.* 47, 529–534.

Ludwig D.S., Pereira M.A., Kroenke C.H., Hilner J.E., Van Horn L., Slattery M.L., Jacobs D.R. (1999) Dietary fiber, weight gain, and cardiovascular disease risk factors in young adults. *The Journal of the American Medical Association.* 282, 1539–1546.

Ma D.W.L., Wierzbicki A.A., Field C.J., Clandinin M.T. (1999) Conjugated linoleic acid in Canadian dairy and beef products. *Journal of Agricurtural and Food Chemistry.* 47, 1956–1960.

Mac Donald H.B. (2000) Conjugated linoleic acid and disease prevention: A review of current knowledge. *Journal of the American College of Nutrition.* 19, 111–118.

Magrane J., Casaroli-Marano R.P., Reina M., Gafvels M., Vilaro S. (1999) The role of O-linked sugars in determining the very low density lipoprotein receptor stability or release from the cell. *FEBS Letters.* 451, 56–62

Mahley R.W., Innerarity T.L., Bersot T.P., Lipson A., Margolis S. (1978) Alterations in human high-density lipoproteins, with or without increased plasma-cholesterol, induced by diets high in cholesterol. *Lancet.* 2, 807–809.

Marshall J.A., Bessesen D.H., Hamman R.F. (1997) High saturated fat and low starch and fibre are associated with hyperinsulinemia in a non-diabetic population: The San Luis Valley Diabetes Study. *Diabetologia.* 40, 430–438.

Masana L., Camprubi M., Sarda P., Sola R., Joven J., Turner P.R. (1991) The Mediterranean-type diet: is there a need for further modification? *The American Journal of Clinical Nurition.* 53, 886–9.

Mata P., Garrido J.A., Ordovas J.M. (1992) Effect of dietary monounsaturated fatty acids on plasma lipoproteins and apolipoproteins in women. *The American Journal of Clinical Nurition.* 56, 77–83.

Mattson F.H., Grundy S.M. (1985) Comparison of the effects of dietary saturated, monounsaturated, and polyunsaturated fatty acids on plasma lipids and lipoproteins in man. *Journal of Lipid Research.* 26, 194–205.

May P., Bock H.H., Nimpf J., Herz J. (2003) Differential glycosylation regulates processing of lipoprotein receptors by gamma-secretase. *Journal of Biological Chemistry.* 278, 37386–37392

Mc Combs R.J., Marcadis D.E., Ellis J., Weinberg R.B. (1994) Attenuated hypercholesterolemic response to a high-cholesterol diet in subjects heterozygous for the apolipoprotein A-IV-2 allele. *The New England Journal of Medicine.* 331, 706–710.

Mc Donald B.E., Gerrard J.M., Bruce V.M., Conner E.J. (1989) Comparison of the effect of canola oil and sunflower oil on plasma lipids and lipoproteins and on in vivo thromboxane A2 and prostacyclin production in healthy young men. *The American Journal of Clinical Nurition.* 50, 1382–91.

Mc Gee D.L., Reed D.M., Yano K., Kagan A., Tillotson J. (1984) Ten-year incidence of coronary heart disease in the Honolulu Heart Program. Relationship to nutrient intake. *American Journal of Epidemiology.* 119, 667–676.

Mc Murry M.P., Connor W.E., Lin D.S., Cerqueira M.T., Connor S.L. (1985) The absorption of cholesterol and the sterol balance in the Tarahumara Indians of Mexico fed cholesterol-free and high cholesterol diets. *The American Journal of Clinical Nurition.* 41, 1289–1298.

Mensink R.P., Katan M.B. (1989) Effect of a diet enriched with monounsaturated or polyunsaturated fatty acids on levels of low density and high density lipoprotein cholesterol in healthy women and men. *The New England Journal of Medicine.* 321, 436–44.

Mensink R.P., Katan M.B. (1990) Effect of dietary trans fatty acids on highdensity and low-density lipoprotein cholesterol levels in healthy subjects. *The New England Journal of Medicine.* 323, 439–45.

Mensink R.P., Katan M.B. (1992) Effect of dietary fatty acids on serum lipids and lipoproteins. A meta-analysis of 27 trials. *Arteriosclerosis Thrombosis and Vascular Biology.* 12, 911–919.

Mensink R.P., Zock P.L., Katan M.B. (1992) Effect of dietary cis and trans fatty acids on serum lipoprotein[a] levels in humans. *Journal of Lipid Research.* 33, 1493–501.

Mensink R.P., Temme E.H., Hornstra G. (1994) Dietary saturated and trans fatty acids and lipoprotein metabolism. *Annals of Medicine.* 26, 461–464.

Mensink R.P., Zock P.L., Kester A.D., Katan M.B. (2003) Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *The New England Journal of Medicine.* 77, 1146-55.

Meydani S.N., Lichtenstein A.H., Cornwall S. (1993) Immunologic effects of National Cholesterol Panel Step 2 diets with and without fish derived n-3 fatty acid enrichment. *The Journal of Clinical Investigation.* 92, 105–13.

Meyers C.D., Kashyap M.L. (2004) Pharmacologic elevation of high-density lipoproteins: recent insights on mechanism of action and atherosclerosis protection. *Current Opinion in Cardiology.* 19, 366-373.

Michels K., Sacks F. (1995) Trans fatty acids in European margarines. *The New England Journal of Medicine.* 332, 541–542.

Millar J.S., Lichtenstein A.H., Cuchel M. (1995) Impact of age on the metabolism of VLDL, IDL, and LDL apolipoprotein B-100. *Journal of Lipid Research.* 36, 1155–67.

Miller W.C., Niederpruem M.G., Wallace J.P., Lindeman A.K. (1994) Dietary fat, sugar, and fiber predict body fat content. *Journal of The American Dietetic Association.* 94, 612–615.

Navab M., Ananthramaiah G.M., Reddy S.T. (2004) The oxidation hypothesis of atherogenesis: the role of oxidized phospholipids and HDL. *Journal of Lipid Research.* 45, 993-1007.

Neaton J.D., Wentworth D. (1992) Serum cholesterol, blood pressure, cigarette smoking, and death from coronary heart disease. Overall findings and differences by age for 316,099 white men. *Archives of Internal Medicine.* 152, 56–64.

Nelson G.J., Schmidt P.C., Bartolini G. (1997) The effects of dietary arachidonic acid on plasma lipoprotein distributions, apoproteins, blood lipid levels, and tissue fatty acid composition in humans. *Lipids.* 32, 427–33.

Norris P.G., Jones C.J., Weston M.J. (1986) Effect of dietary supplementation with fish oil on systolic blood pressure in mild essential hypertension. *British Medical Journal.* 293, 104–15.

Oh S.Y., Miller L.T. (1985) Effect of dietary egg on variability of plasma cholesterol levels and lipoprotein cholesterol. *The American Journal of Clinical Nurition.* 42, 421–31.

Ordovas J.M., Cassidy E.K., Civeira F., Bisgaier C.L., Schaefer E.J. (1989) Familial apolipoprotein A-I, C-III, and A-IV deficiency with marked high density lipoprotein deficiency and premature atherosclerosis due to a deletion of the apolipoprotein A-I, C-III, and A-IV gene complex. *Journal of Biological Chemistry.* 264, 16339–42.

Parker D.R., Weiss S.T., Troisi R., Cassano P.A., Vokonas P.S., Landsberg L. (1993) Relationship of dietary saturated fatty acids and body habitus to serum insulin concentrations: The Normative Aging Study. *The American Journal of Clinical Nurition.* 58, 129–136.

Policy Analysis Centre (2007) European Cholesterol Guidelines Report. Available at: http://www.policy-centre.com/downloads/European-Cholesterol-Guidelines07.pdf Accessed: 03.11.2010.

Ratnayake W.M., Chardigny J.M., Wolff R.L., Bayard C.C., Sebedio J.L., Martine L. (1997) Essential fatty acids and their trans geometrical isomers in powdered and liquid infant formulas sold in Canada. *Journal of Pediatric Gastroenterology and Nutrition.* 25, 400–407.

Reaven P., Parthasarathy S., Grasse B.J., Miller E., Steinberg D., Witztum J.L. (1993) Effects of oleate-rich and linoleate-rich diets on the susceptibility of low density lipoprotein to oxidative modification in mildly hypercholesterolemic subjects. *The Journal of Clinical Investigation.* 91, 668-676.

Roche H.M., Zampelas A., Jackson K.G., Williams C.M., Gibney M.J. (1998) The effect of test meal monounsaturated fatty acid: saturated fatty acid ratio on postprandial lipid metabolism. *British Journal of Nutrition.* 79, 419–424.

Russell D.W., Schneider W.J., Yamamoto T., Luskey K.L., Brown M.S., Goldstein J.L. (1984) Domain map of the LDL receptor: sequence homology with the epidermal growth factor precursor. *Cell.* 37, 577–585

Salmerón J., Hu F.B., Manson J.E., Stampfer M.J., Colditz G.A., Rimm E.B., Willett W.C. (2001) Dietary fat intake and risk of type 2 diabetes in women. *The American Journal of Clinical Nurition.* 73, 1019–1026.

Schaefer E.J., Zech L.A., Jenkins L.L. (1982) Human apolipoprotein A-I and A-II metabolism. *Journal of Lipid Research.* 23, 850–62.

Schaefer E.J., Heaton W.H., Wetzel M.G., Brewer H.B. (1982) Plasma apolipoprotein A-I absence associated with marked reduction of high density lipoproteins and premature coronary heart disease. *Arteriosclerosis.* 2, 16–26.

Schaefer E.J., Foster D.A., Zech L.A., Brewer H.B., Levy R.I. (1983) The effect of estrogen administration on plasma lipoprotein metabolism in premenopausal females. J*ournal of Clinical Endocrinology & Metabolism.* 57, 262–70.

Schaefer E.J. (1984) The clinical, biochemical, and genetic features in familial disorders of high density lipoprotein deficiency. *Arteriosclerosis.* 4, 303–22.

Schaefer E.J., Ordovas J.M., Law S. (1985) Familial apolipoprotein A-I and C-III deficiency, variant II. *Journal of Lipid Research.* 26, 1089–101.

Schaefer E.J., Lichtenstein A.H., Lamon-Fava S., McNamara J.R., Ordovas J.M. (1995) Lipoproteins, nutrition, aging, and atherosclerosis. *The American Journal of Clinical Nurition.* 61, 726–40.

Schaefer E.J. (2002) Lipoproteins, nutrition, and heart disease. *The American Journal of Clinical Nurition.* 75, 191–212.

Schakel S.F., Buzzard I.M., Gebhardt S.E. (1997) Procedures for estimating nutrient values for food composition databases. *Journal of Food Composition and Analysis.* 10, 102–114.

Sevak L., McKeigue P.M., Marmot M.G. (1994) Relationship of hyperinsulinemia to dietary intake in South Asian and European men. *The American Journal of Clinical Nurition.* 59, 1069–1074.

Shah P.K., Kaul S., Nilsson J., Cercek B. (2001) Exploiting the vascular protective effects of high-density lipoprotein and its apolipoproteins: an idea whose time for testing is coming, part I. *Circulation.* 104, 2376-2383.

Siguel E.N., Chee K.W., Gong J., Schaefer E.J. (1987) Criteria for plasma essential fatty acid deficiency as assessed by capillary column gas liquid chromatography. *Clinical Chemistry.* 33, 1869–73.

Sorkin J.D., Andres R., Muller D.C., Baldwin H.L., Fleg J.L. (1992) Cholesterol as a risk factor for coronary heart disease in elderly men. The Baltimore Longitudinal Study of Aging. *Annals of Epidemiology.* 2, 59–67.

Stamler J., Wentworth D., Neaton J.D. (1986) Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222 primary screenees of the Multiple Risk Factor Intervention Trial (MRFIT). *The Journal of the American Medical Association.* 256, 2823–2828.

Stender S., Dyerberg J., Astrup A. (2006) High levels of trans fat in popular fast foods. *New England Journal of Medicine.* 354, 1650-1652.

Sudhof T.C., Goldstein J.L., Brown M.S., Russell D.W. (1985) The LDL receptor gene: a mosaic of exons shared with different proteins. *Science.* 228, 815–822.

Thomsen C., Rasmussen O., Lousen T., Holst J.J., Fenselau S., Schrezenmeir J., Hermansen K. (1999) Differential effects of saturated and monounsaturated fatty acids on postprandial lipemia and incretin responses in healthy subjects. *The American Journal of Clinical Nutrition.* 69, 1135–1143.

Tyko B., Maxfield F. R. (1982) Rapid acidification of endocytic vesicles containing alpha-2-macroglobulin. *Cell.* 28, 643–651

Urakaze M., Hamazaki T., Makuta M. (1987) Infusion of fish oil emulsion: effects on platelet aggregation and fatty acid composition in phospholipids of plasma, platelets, and red blood cell membranes in rabbits. *The American Journal of Clinical Nutrition.* 46, 936–40.

USDA/HHS (U.S. Department of Health and Human Services) (2000) Nutrition and Your Health: Dietary Guidelines for Americans, 5th ed. Home and Garden Bulletin No. 232. Washington, DC: U.S. Government Printing Office.

Valsta L.M., Jauhiainen M., Aro A. (1992) Effects of a monounsaturated rapeseed oil and a polyunsaturated sunflower oil diet on lipoprotein levels in humans. *Arteriosclerosis Thrombosis and Vascular Biology*. 12, 50–9.

van Erp-Baart M.A., Couet C., Cuadrado C., Kafatos A., Stanley J., van Poppel G. (1998) Trans fatty acids in bakery products from 14 European countries: The TRANSFAIR Study. *Journal of Food Composition and Analysis.* 11, 161–169.

van Poppel G., van Erp-Baart M.A., Leth T., Gevers E., Van Amelsvoort J., Lanzmann-Petithory D., Kafatos A., Aro A. (1998) Trans fatty acids in foods in Europe: The TRANSFAIR Study. *Journal of Food Composition and Analysis.* 11, 112–136.

Vessby B., Uusitupa M., Hermansen K., Riccardi G., Rivellese A.A., Tapsell L.C., Nälsén C., Berglund L., Louheranta A., Rasmussen B.M., Calvert G.D., Maffetone A., Pedersen E., Gustafsson I.B., Storlien L.H. (2001) Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women. *Diabetologia.* 44, 312–319.

Virtanen S.M., Feskens E.J.M., Räsänen L., Fidanza F., Tuomilehto J., Giampaoli S., Nissinen A., Kromhout D. (2000) Comparison of diets of diabetic and nondiabetic elderly men in Finland, The Netherlands and Italy. *European Journal of Clinical Nutrition.* 54, 181–186.

Ward K.D., Sparrow D., Vokonas P.S., Willett W.C., Landsberg L., Weiss S.T. (1994) The relationships of abdominal obesity, hyperinsulinemia and saturated fat intake to serum lipid levels: The Normative Aging Study. *International Journal of Obesity and Related Metabolic Disorders.* 18, 137–144.

Wardlaw G.M., Snook J.T. (1990) Effect of diets high in butter, corn oil, or high-oleic acid sunflower oil on serum lipids and apolipoproteins in men. *The American Journal of Clinical Nurition.* 51, 815–21.

Weggemans R.M., Zock P.L., Katan M.B. (2001) Dietary cholesterol from eggs increases the ratio of total cholesterol to high-density lipoprotein cholesterol in humans: A meta-analysis. *The American Journal of Clinical Nurition.* 73, 885–891.

Weggemans R.M., Zock P.L., Meyboom S., Funke H., Katan M.B. (2000) Apolipoprotein A4-1/2 polymorphism and response of serum lipids to dietary cholesterol in humans. *Journal of Lipid Research.* 41, 1623–1628.

Weijenberg M.P., Feskens E.J.M., Kromhout D. (1996) Total and high density lipoprotein cholesterol as risk factors for coronary heart disease in elderly men during 5 years of follow-up. The Zutphen Elderly Study. *American Journal of Epidemiology.* 143, 151–158.

Weinberg R.B., Geissinger B.W., Kasala K., Hockey K.J., Terry J.G., Easter L., Crouse J.R. (2000) Effect of apolipoprotein A-IV genotype and dietary fat on cholesterol absorption in humans. *Journal of Lipid Research.* 41, 2035–2041.

Welty F.K., Lichtenstein A.H., Barrett P.H.R, Dolnikowski G.G., Schaefer E.J. (1999) Human apolipoprotein (Apo) B-48 and Apo B-100 kinetics with stable isotopes. *Arteriosclerosis Thrombosis and Vascular Biology.* 19, 2966–74.

WHO (2006) WHO global infobase online. Available at: http://www.who.int/infobase/report.aspx?rid=112&ind=CHO. Accessed: 03.11.2010.

Yu S., Derr J., Etherton T.D., Kris-Etherton P.M. (1995) Plasma cholesterol-predictive equations demonstrate that stearic acid is neutral and monounsaturated fatty acids are hypocholesterolemic. *The American Journal of Clinical Nurition.* 61, 1129–1139.

Zock P.L., Katan M.B. (1992) Hydrogenation alternatives: Effects of trans fatty acids and stearic acid versus linoleic acid on serum lipids and lipoproteins in humans. *Journal of Lipid Research.* 33, 399–410.

Zock P.L., Katan M.B. (1992) Hydrogenation alternatives: effects of trans fatty acids and stearic acid versus linoleic acid on serum lipids and lipoproteins in humans. *Journal of Lipid Research. 33, 399–410.*

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