REVIEW OF LITERATURE
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Atherosclerosis, a degenerative process is associated with advancing age, mainly affecting larger arteries especially coronary and cerebrals. Numerous studies have implicated altered level of plasma lipoproteins in the pathogenesis of atherosclerosis. In particular elevated low density lipoprotein (LDL), diminished high density lipoprotein levels appear to be strong risk factor for the development of atherosclerosis.

Besides this many more factors like age, sex, stress, dietary habits, obesity, life style, hypertension, diabetes, family history of ischaemic heart disease (IHD) exert their influence on lipoprotein levels and development of atherosclerosis their own way. In above mentioned risk factors many of them are reversible e.g. smoking, dietary habit etc, while the influence of age, sex and genetic factors are irreversible.

CHANGE IN LIPID LIPOPROTEIN LEVEL
AFTER HIGH CHOLESTEROL DIET.

Previous studies have shown that effect of long term and short term feeding of diet rich in cholesterol has a variable response depending upon the individual variation. Dietary fat and cholesterol causes specific changes in specific lipoprotein in a variety of species (Mahley et al, 1978; Arora et al, 1986). These changes
have been associated with the development of atherosclerosis in experimental models (Mahley et al, 1979).

**CHANGE IN SERUM TOTAL CHOLESTEROL (STC)**

Cholesterol in normal human diet hardly bring any change in the serum cholesterol level (Ancelkeys and Anderson et al, 1956). But later it was proved beyond doubt that feeding cholesterol rich diet for 2-8 weeks raises serum total cholesterol in blood (Arora et al, 1986; Messinger et al, 1950; Conner et al, 1961 and Deborh Applebaum et al, 1979).

In 1940 Bruhn noticed that fat ingestion causes 20% rise in mean serum cholesterol level. On the contrary Nikkila and Korttinen (1962) observed a significant decrease in cholesterol level after 6 hour after a fat diet in healthy subjects.

The effect of high cholesterol fat load on post prandial cholesterol levels has also been studied by several workers in past, but insignificant difference has been found between postprandial and 10 to 14 hours fasting value (Albrink and Man, 1956; Pomeranze et al, 1954; Schilling et al, 1964). All these workers observed plasma cholesterol values upto 24 hours after test meal. The observation at 2 hourly interval after feeding cholesterol in dose of 0.5 gm/m² body surface area for 14 hours shows insignificant change in serum total cholesterol (Hanno Krauss, Pieter Groot, 1987).
M.C. Gaudet et al (1972) reported a drop of serum cholesterol level by 15% and 3.3% in adolescents subjects having initial serum cholesterol level 200 mg% or less respectively, after reducing the intake of cholesterol by 50%.

While in other studies no positive correlation could be established between cholesterol level and mean daily intake of energy, sugar, fat and cholesterol (Weidman et al, 1978). Lactovegetarians and non-vegetarians have been reported to have higher serum cholesterol than strict vegetarians (Sacks et al, 1975; Knuiman et al, 1982).

**CHANGE IN HIGH DENSITY LIPOPROTEIN**

Diet is an important modulator of the synthesis, secretion and concentration of serum lipoprotein. Conflicting reports have appeared on effect of dietary cholesterol on HDL levels.

Border et al (1964) reported increase level of HDL in rats fed cholesterol while Haft et al (1962) and Kritchevsky (1965) reported no change in HDL levels in cholesterol fed rats.

On the other hand Reiser et al (1966) and Howard et al (1968) reported decrease HDL in rats fed with high cholesterol diet. Narayanan (1971) demonstrated that HDL$_2$ decreased drastically about 50% in rats fed with high cholesterol diet. These results confirmed the earlier observations of Reiser et al (1966) that rate
serum HDL level was decreased irrespective of whether a saturated or unsaturated fat was used in diet supplemented with cholesterol. In short term feeding studies, marked reduction in dietary fat and isocaloric increase in carbohydrate diet resulted in decrease in HDL cholesterol in conjunction with elevation of serum triglyceride and VLDL. Studies of HDL composition have shown a decrease in ratio of apolipoprotein A-I and A-III and a decrease in HDL cholesterol to protein ratio (Schonfeld et al, 1976) consistent with a selective decrease in HDL₂ species (Blum et al, 1977).

There is evidence that substitution of large quantities of polyunsaturated fat for saturated fat in diet can result in decrease levels of HDL and proteins (Nichaman et al, 1967). An increase in P:3 ratio from 0.25:1 to 4:1 in diet fed to four normal subjects for five weeks resulted in decrease of HDL and apolipoprotein A-I concentration of 33 and 21 percent respectively, with an associated reduction in HDL₂: HDL₃ ratio (Shepherd et al, 1978). Other studies have however reported either no change (Lewis, 1978; Shore et al, 1981) or increase (Jackson and Glueck, 1980) in the level of HDL cholesterol with diet enriched in polyunsaturated fats.

High dietary intake of cholesterol in the form of three to six egg yolk per day, has been reported to produce increase in apolipoprotein E - containing HDL sub species in human (Mahley et al, 1978). This effect
was seen whether or not there was an increase in total plasma cholesterol. Despite the fact that HDL containing apolipoprotein E represented only a minor fraction to the total HDL, its presence was shown to account for an increase of 2.6 to 4 times the binding of HDL to LDL receptors of fibroblasts as compared to pretreatment HDL (Mahley et al, 1981). But this was not observed in another study (Applebaum et al, 1979). Recently it has been reported that level of HDL cholesterol and serum apolipoprotein A-I, but not apolipoprotein E increased with the feeding of diets high in both cholesterol and saturated fat (Tan et al, 1980).

A final consideration in evaluating the effects of dietary variables on HDL is that, while levels of HDL cholesterol and plasma apolipoprotein A-I are similar after overnight fast and the nonfasting state (Henderson et al, 1980), changes in levels and composition of HDL have been shown to occur acutely after meals containing fat. Cholesterol, phospholipid, and C-apolipoprotein levels in HDL subtypes increases and cholesterol in HDL decreases (Havel, 1973) Baggio et al, 1980) in conjunction with transfer of chylomicron lipids to HDL during the course of their catabolism. Recently it has been shown that HDL apolipoprotein A-I levels increased when fat was consumed in divided doses over a 10 hours period, but not when the same amount of fat was ingested as a single load (Kay et al, 1980).
Diet induced changes in LDL

Diet high in fat and cholesterol cause an elevation in LDL in most animals (Mahley, 1978). The response in man varies but in those subjects who have an elevation in plasma cholesterol, there is an elevation in plasma LDL levels. In 1979 Deborhapplebaum et al demonstrated significant rise of LDL level in human volunteers after feeding 5000 mg of egg yolk cholesterol/day for 30 days.

Age related difference in rise of LDL was demonstrated by Arora et al (1987). They found out that rise of serum total cholesterol after feeding high fat, high cholesterol breakfast for one week was much more pronounced in young (20-30 years) volunteers with major portion of rise being contributed by increased HDL. Contrary, in older age person the rise of serum total cholesterol was less marked with LDL contributing mainly in the increased levels.

Maudet et al (1981) demonstrated that there was significant fall in level of LDL in five volunteers 3 hours and 5 hours after taking butter diet. They attributed this fall due to defect in VLDL hydrolysis by serum lipases and due to metabolic blocking in liver or adipose tissue.

In addition to this the diet induced LDL are larger than LDL from the same species on low fat - low cholesterol diet. In a study performed by Rudel and co-workers (1979) on rhesus monkey showed that high
cholesterol diet induced LDL have molecular weight which are 1.5 fold larger than those of control LDL. Furthermore St. Clair and Leight (1973) reported that the diet induced, large LDL are capable of stimulating cholesteryl esterification and accumulation in smooth muscle cells to a greater extent than are normal LDL.

An additional alteration in the LDL, induced by the high cholesterol diets involve the apoprotein constituents. In normal LDL, the beta apoprotein is the major detectable apoprotein moiety, however in several species the LDL contain a variable amount of the E-apoprotein following cholesterol feeding (Mahley et al, 1977, Rudel et al, 1979).

**CHANGES IN SERUM TRIGLYCERIDE (STG)**
**AND VERY LOW DENSITY LIPOPROTEIN (VLDL)**

The level of serum triglyceride rises considerably after fat ingestion. Rise in the triglyceride level after fat ingestion has been reported after giving different amount of the fat load and measuring the levels at different time intervals (Nikkila and Konttinen, 1961; Denborough, 1963).

Angervall (1963) reported a significant correlation between fasting, 3½ hours and 7½ hours value of serum triglyceride postprandially.

Olefsky et al (1976) noted a biphasic plasma triglyceride curve with an initial peak occurring 1 to 3 hours after feeding and a secondary peak after 4 to 7
hours. The primary peak was accounted by increase in chylomicron levels in more than 98% cases, whereas secondary peak represented rise in very low density lipoprotein level in 82%.

Richard J. Havel (1957) concluded that increment in the concentration of triglycerides in the serum following ingestion of fat is entirely the result of an increase in their concentration in VLDL.

Excess production of VLDL and triglyceride is more often due to secondary abnormalities than to primary factors, perhaps the most common cause is high caloric intake associated with obesity, excess alcohol and excess carbohydrate. Increased levels are also found in obesity. Delayed clearance of triglyceride from the serum is noted in cases of ischaemic heart disease after high fat diet (Arora et al, 1987 and Brown et al, 1961).

**CHANGES IN VLDL REMNANTS (BETA-VLDL)**

Beta VLDL are the smaller particles than normal VLDL and contain more cholesterol. Both of these characteristically impart atherogenic potential to VLDL remnants.

Mistry et al (1977) reported that Beta VLDL can be induced by the cholesterol feeding in man. In addition to this preliminary studies from the Gladston foundation lab for cardiovascular disease indicate that certain individual respond to high fat high cholesterol diet by producing lipoprotein which are capable to delivering
cholesterol to macrophages. The beta VLDL may occur 
transiently as minor component of the human plasma 
fraction and after high fat diet and may cause repeated 
cholesterol deposition in cells of arterial wall over 
the years. The beta VLDL either chylomicron remnant or 
hepatic lipoprotein may represent the atherogenic parti-
cle postulated several years ago by Zilversmit.

FACTORS MODULATING PLASMA LIPIDS
AND LIPOPROTEINS IN HUMAN

A. AGE AND SEX

Significant relationship between sex and age 
of a person and his plasma lipid levels has been seen. 
Some workers have reported that the mean levels among 
females never exceed 85mg% while in men the mean level 
reaches its maximum in age group 40-59 and is 107 mg% 
(Schaefer and Nechemias, 1965). In other study females 
were found to have a markedly lower level (mean value 
130 mg/dl) than males (mean value 185 mg/dl).

In most population it has been demonstrated 
that women have higher level of HDL than men at all ages 
following puberty. A drop in HDL level seen in males at 
around the time of puberty (Beaglehole et al, 1980) has 
been related to the degree of sexual maturation 

Transient increase in HDL₂ have been reported 
at or near the time of ovulation(Barclay et al, 1965).
HDL level also changes with age. In male levels are stable until puberty and in adolescence, there is a decline followed by relatively stable levels in adulthood than plateau in older age. In females, there is a small linear increase in HDL from childhood to about 60 years after which no age effect is apparent (Heiss et al, 1980).

An age dependent increase of triglyceride levels only between 3rd and 4th decade has been reported in a cross sectional study of 500 working healthy Swiss males (Hyden, 1967; Dyerberg and Hjorne, 1972).

B. WEIGHT

Albrink et al (1962) assumed that the rise in triglyceride and cholesterol level with age might be due to age related weight gain. Increasing hypertriglyceridemia in weight gainers has been reported (Hyden, 1969).

C. DIURNAL AND SEASONAL VARIATION

Cholesterol and phospholipids show minimal diurnal variation, temporary increase are described as a consequence of what Kuo (196) termed "diurnal serum triglyceride level variation". A seasonal variation in serum triglyceride levels the value being higher in winter than in summer (Carlson and Lindstedt, 1968).
D. **OBESITY**

HDL levels are lower in obese individual than non obese (Wilson et al, 1972; Carlson et al, 1975 and Glueck et al). During the course of weight loss an increase in HDL concentration has been reported to occur in association with reduction in VLDL and total triglyceride concentration (Wilson et al, 1972). But in other studies HDL shows either no change or reduction (Widholm et al, 1978; Thompson, 1979; Howard, 1979).

E. **PHYSICAL ACTIVITY**

Accelerated rate of chylomicron removal after exercise and its accentuation after habituation to exercise has been observed (Krut et al, 1963). Definit reduction in triglyceride level after exercise has been reported by many investigators (Konttinen, 1963; Hollosey et al, 1964).

High levels of HDL are reported to be related with high level of endurance type exercise, including long distance runner, tennis player and soccer player (Wood et al, 1977; Lehtonen et al, 1978; Vodak et al, 1980) whereas a drop in HDL was found with caloric restriction in the absence of exercise (Weltman et al, 1980).

F. **SMOKING**

The effect of heavy cigarette smoking on postprandial triglyceridemia has been studied by many investigators. Decreased postprandial triglyceridemia during
smoking in the absorption phase has been reported (Konttinen and Rajasalmi, 1963) and has been speculated to be due to decrease absorption of fat from intestinal tract. One cigarette per hour caused the chylomicron count to rise in a group of young subjects but not in too elder subjects (Marder et al, 1952).

G. EFFECT OF ALCOHOLISM

A progressive rise in plasma triglyceride and an associated fall in free fatty acid (FFA) has been seen after alcohol administration (Jones et al, 1963). High concentration of STC, STC and phospholipids have been observed in patient with acute alcoholism (Losowsky et al, 1963). On contrary, Thompson et al (1979) could not find any effect of alcohol over plasma lipid levels.

Alcohol can increase fat mobilization from adipose tissue under some condition. More importantly alcohol can increase esterification and decrease oxidation of fatty acid in liver of experimental animals which should lead to increase hepatic triglyceride synthesis (Lieber, 1967).

Alcohol ingestion has been reported to raise level of HDL (Johanson et al, 1974; Belfrage et al, 1977). But the results of Glueck et al (1980) were contradictory to above statement.

In a large epidemiological study levels of HDL and amount of habitual alcohol intake in moderate range
have been independently correlated (Castelli et al, 1977).

H. EFFECT ON CHOLESTEROL LEVEL DUE TO MECHANICAL CAUSES

In addition there is considerable interlaboratory variation (Whitehead, Browsing and Gregory, 1973) particularly when manual methods are employed. Prolonged venous occlusion prior to the blood sampling increases cholesterol concentration because of haemoconcentration (Koerselaman, Lewis and Pilkington, 1961).

LIPID AND DIABETES MELLITUS

The main component of the hypertriglyceridemia in plasma of diabetics is very low density lipoprotein (VLDL) and rarely chylomicrons (Nik:ila, 1973 & 1974). VLDL can cause secondary hypercholesterolemia (Dunn et al, 1981).

TYPE-1 DIABETES (INSULIN DEPENDENT)

Uncontrolled diabetes with extremely high level of blood glucose is associated with the elevation of lipids levels. While the better blood glucose control lower the level of plasma lipids (Keiding et al, 1952). The observation supported by Woff and Salt in 35 juvenile diabetics (blood sugar >200 mg/dl) having high levels of cholesterol esterified F.A. and Beta-lipoproteins. Similar reports by New et al, while comparing diabetic with non diabetic either under or over the age of 30 years. However, Transman et al (196 ) did not confirm
these findings, with a higher range of normal cholesterol (150-392 mg/dl).

Lloyd (1970) strictly emphasized on diabetic control stating that "the findings of hyperlipidemia in a child with treated diabetes mellitus almost always indicates inadequate insulin control.

Acute insulin deficiency causes free fatty acid mobilization from adipose tissue and short lived secretion of VLDL and ketone bodies from liver (Balasse, 1972). Decreased activity of lipoprotein lipase enzyme (Fielding, 1972) due to insulin deficiency (Pykalisto, 1975) cause decreased clearance of triglyceride from plasma. Moreover acquired structural abnormalities of VLDL causes ineffective interaction in VLDL and lipoprotein lipase.

**TYPE-2 DIABETES (NIDDM)**

NIDDM is associated with alterations in plasma lipoprotein (Barach, 1952; Albrink, 1963 and Goldberg, 1981). There is mild to moderate degree of hypertriglyceridemia but without any significant reduction in plasma lipoprotein lipase activity.

Subtle abnormalities in post heparin lipolytic activity have been reported in untreated patients with type-2 diabetes and becoming normal after improved diabetic control (Brunelli, 1975).

High concentration of VLDL in NIDDM is most

LDL cholesterol level in NIDDM is a matter of controversy since higher levels were observed by few studies (Brillimoria, 1976; Howard, 1978; Taskivan, 1982) while the others deny it. Increased LDL production and impaired clearance in mild NIDDM and also decreased conversion of VLDL to LDL, reported by Kesselbah (1982 and 1983).

In NIDDM plasma HDL levels tends to decrease but reverts to normal with treatment (Calvert, 1978; Pause, 1978). But in IDDM HDL levels have been reported to be normal or increased (Nikkila, 1978).

The hypercholesterolemia in diabetes can occur because of:

a. Increased plasma VLDL level cause secondary increase in plasma cholesterol level since 20% of total lipid content of VLDL is cholesterol.

b. Diabetics affects the plasma LDL metabolism.

The exact mechanism is not clear but it has been proposed that:

(i) The increased synthesis of VLDL in diabetes causes increased LDL formation because VLDL is precursor for LDL.
(ii) Decreased catabolism of LDL in poorly controlled diabetic (Klitzman, 1982) due to glycosylation of plasma LDL (Klitzman, 1982) which alters the configuration of LDL, so that less interaction with specific receptors responsible for majority of LDL catabolism in normal persons (Brown, 1981).

**EFFECT OF ORAL HYPOGLYCEMIC AGENTS AND INSULIN ON PLASMA LIPID LEVEL**

While treating the both types of diabetics (type-1 and type-2), it was observed that both groups showed a fall in plasma lipid levels over the first month. Later only those diabetics who subsequently received only sulphonyl ureas showed continued improvement at one year.

A simultaneous fall in blood sugar and triglycercide on administration of sulphonyl urea (Morris et al, 1964; Holeman et al, 1978) is either due to triglyceride lowering property of sulphonyl ureas or there is another factor other than blood glucose levels affecting triglyceride values.

Insulin therapy in diabetics reduces free fatty acid and triglyceride concentrations but never equal or near normal value (Lewis et al, 1972).

**EFFECT OF DIET ON LIPID LEVEL IN DIABETICS**

A. High fat and low carbohydrate

In Rockefeller monograph (Alleu, 1919) "Lipemia is largely associated with the fat intake and with
According to Ervin (1919) the lipemia in diabetics will disappear with the elimination of fat from diet. Joslin (1921) suggested a relation between high protein fat diet and high degree of lipemia, he stated that with restricted diet, particularly of fat the blood fat rapidly falls. Bloor (1921) stated that there was deficiency of pancreatic hormone which is essential for the proper removal of the fat from the blood. The patients has a fat tolerance which can adjust itself according to the amount of fat ingested the mechanism for the utilization of fat might be expected to breakdown.

B. **Low fat and carbohydrate in diet**

The avoidance of low fat and high carbohydrate in diets of diabetic patients during the treatment, have been shown to lowering serum cholesterol, insulin requirements, improved glucose tolerance and reduced severity of vascular complications (Ellis, 1934; Rabinowitch, 1935; Singh, 1955, Kempner, 1958 and Van Eck, 1959).

However, hyperlipemia have been noted in non diabetics during administration of low fat, high carbohydrate diets.

The lipemic effect of such diet may be temporary one. In a study the reduction of dietary fat for long term showed that serum triglyceride levels returned to normal after several months (Autorix, 1961).
Elevated levels in essential hyperlipemia maintained on rice diets also returned towards control values after 3 months (Kao, 1959).

C. The Lipoproteins and CAD(IHD)

The relation between lipid lipoprotein and ischaemic heart disease has been studied in the depth in epidemiological studies and it is seen that lipids are only one of the several factors concerned with ischaemic heart disease (Lewrie, 1964).

Concentration of LDL cholesterol is directly related to and are predictive of the risk factor for CAD over a wide range (Gordon et al, 1981). Mortality rate from CAD in different communities are directly and linearly related with serum concentration of cholesterol and LDL cholesterol (Lewis et al, 1978). HDL cholesterol concentration are even more strongly predictive of the risk of CAD in most (Gordon et al, 1981; Goldbourt and Medalie, 1979) but not in all studies (Wilkund et al, 1980).

Increase in both degree and duration of lipemia in the patient with evidence of CAD has been reported by many workers (Waldow et al, 1954; Barrit, 1956; Bronte Stewart and Blackburn, 1950; Bouchier and Bronte Stewart, 1961).

Serum cholesterol level determination has been found unreliable with overt coronary heart disease
(Albrink et al, 1962), while triglyceride levels provide better differentiation (Albrink et al, 1961).

At young age (35-50 years) myocardial infarction is associated with higher triglyceride level while at higher age the opposite the case i.e. serum cholesterol more elevated than triglyceride (Carlson, 1960).

Type-2 and type-4 of hyperlipidemia has been seen to occur in equal proportions in coronary heart disease. In the study on post infarction lipid changes it was seen that serum FFA levels shown approximately $2\frac{1}{2}$ times increase than normal subjects within 8 hours of onset of pain and the level returning to normal on the second day. Beta lipoproteins used to fall within first 3-4 days with a corresponding fall in serum cholesterol levels. These levels rose again about 10th to 14th day but could not reach the normal levels before 2 months or more. VLDL rose within the first week, reached peak at 3 weeks and returned to normal by 6th to 8th weeks (Fredrickson, 1969).

The relationship of dietary fat and IHD remain an area of persistent controversy. The amount and type of fat fed in the diet with cholesterol is a determinant in the production of atherosclerosis (Hsia, 1959). The protein content of the cholesterol/fat diet is another limiting variable.

It is the circulating lipid complex that is in direct contact with the intima, no that it seems
likely that changes in the lipoproteins of plasma would be correlated best with the disease (Kritchevsky, 1964).

In epidemiologic studies, no population habitually subsisting on a diet low in saturated fat and cholesterol has been reported to have an appreciable amount of ischaemic heart disease (Bierman, 1979).

The mechanism by which the polyunsaturated fatty acids, and in particular linoleic acid, are hypocholesterolemic agents remains to be established.

Increase in the fecal steroids by polyunsaturated fat diets on alternatively, reduction in serum cholesterol by such diets attributable to transfer of the steroid to tissue pools especially muscle has been suggested as underlying mechanism (Findanza, 1976).

There is also a strong genetic influence in disease states. Reduce level of HDL cholesterol is found in adult first degree relative and prepubertal and pubertal children of patients with a history of acute myocardial infarction (Micheli et al, 1979; Pometta et al, 1979; Robertson et al, 1980). Recently evidence for autosomal dominant inheritance of low HDL levels has been reported in large kindred with a high prevalence of coronary disease (Verganić et al, 1981).

ATHEROSCLEROSIS

The possibility of atherosclerosis being a postprandial phenomenon was first proposed by Zilversmit
(1973). He hypothesized that chylomicron remnant or Beta VLDL may occur transiently as minor components of the human plasma fractions after diet high in fat and cholesterol is consumed. And this may cause repeated cholesterol deposition in cells in the arterial wall over the years, while the fasting cholesterol level may remain normal during the life time.

If atherogenesis is a postprandial phenomenon then premature CAD must be common in hyperchylomicronemic states. However, in familial lipoprotein lipase deficiency enormous quantities of chylomicrons accumulate in plasma, but accelerated atherosclerosis has not been reported (Fredrickson, et al, 1978).

ATHEROSCLEROSIS AND LIPID LIPOPROTEIN LEVELS

A. Serum Total Cholesterol (STC)

Elevated STC is a risk factor for coronary heart disease. At the level of 220 mg/dl the incidence of coronary artery disease (CAD) is nearly two fold as compared to level of 180 mg/dl (Kannel et al, 1971). Similarly patients with proved coronary heart disease have significantly higher cholesterol concentration than patients without CAD (Cohn et al, 1977).

B. Triglyceride

Several studies have shown that an elevation of plasma triglycerides is common in patients with CAD (Albrink et al, 1959; Hulley et al, 1980). Carlson
and Bottiger (1972) reported that rates of CAD rose linearly with increasing plasma triglycerides. However, there is currently great debate as to whether VLDL is directly operative factor in producing CAD, or if it is the association of increased LDL or decreased HDL level which are causative (Bilheimer, 1972).

C. Low Density Lipoprotein Cholesterol (LDL)

LDL cholesterol which constitutes about 75 per cent of the serum total cholesterol is more specifically associated with CAD than is total cholesterol. It has been known for many years that the reduction of elevated LDL in other primate species is followed by regression of arteriosclerotic lesions in coronary arteries in large vessel (St. Clair, 1983). We have now conclusive evidence in humans that reducing elevated LDL cholesterol will reduce the incidence of clinical events attributable to coronary arteriosclerosis (the lipid research clinics coronary primary prevention trial results, 1984).

D. High Density Lipoprotein (HDL) Cholesterol

HDL level has an inverse relationship with coronary artery disease (Gordon et al, 1977). The ability of HDL cholesterol to predict the developing of coronary atherosclerosis has been estimated to be four times greater than HDL cholesterol and eight times greater than serum total cholesterol (Gordon et al, 1977).
Each 10 mg/dl change in HDL cholesterol concentration is associated with 50% alteration in cardiovascular risk (Ernsteke, et al, 1984).

Subclasses of HDL can be fractioned by Zonal ultra centrifugation and include HDL_2 and HDL_3. Among these subgroups HDL_2 appears to have the strongest inverse relationship with CAD and accounts for different levels of HDL cholesterol between men and women (Gofman et al, 1954). The possible mechanism by which HDL cholesterol decreases atherosclerosis includes:

1. Reversal of cholesterol transport from the peripheral cells to the liver for removal from the body (Miller and Miller, 1975).

2. Inhibition of LDL cholesterol uptake by cells at the LDL receptor sites.