REVIEW OF LITERATURE
REVIEW OF LITERATURE

Hyperlipoproteinemia is considered to be one of the most important factor in development of atherosclerotic disorders. Numerous studies have implicated altered levels of plasma lipoproteins in pathogenesis of atherosclerosis. In particular, low level of high density lipoprotein, high level of low density lipoprotein and high level of serum total cholesterol appear to be high risk factors.

Atherosclerosis is a degenerative process associated with advancing years, mainly affecting larger arteries, particularly the coronary and cerebrials. The lesion of atherosclerosis passes through many phases - fatty streak, fibrous plaque and finally advanced lesion.

The changes in plasma lipoproteins after short term and long term feeding of cholesterol fat rich diet have been extensively studied in the past. Different types of experimental diets - crystalline cholesterol, egg cholesterol, butter, milk - cholesterol formula diets based on oil and protein and carbohydrate diets have been used to assess individuals response in plasma lipid profile (Connor et al, 1961; Deborah Applebaum-Bowden, 1970; Beveridge, 1971).

EFFECT OF FEEDING ON SERUM TOTAL CHOLESTEROL(STC)

Effect of long term and short term feeding of
diet rich in cholesterol has been extensively studied over the past 30 years. Dietary fat and cholesterol causes changes in specific lipoprotein in a variety of animal species (Mahley et al, 1977), quantitatively, a change in specific lipoprotein may be dramatic in one species than in another.

Ansellays and Anterson et al (1956) concluded that serum cholesterol level is essentially independent of cholesterol intake over the whole range of natural human diets. But Later on it was proved beyond doubt that feeding cholesterol rich diet for 2-8 weeks raises total serum cholesterol in blood (Arora et al, 1986; Messinger et al, 1950; Conner et al, 1961; Deborah Applebaum et al, 1979).

In an earlier report, Bruhn (1940) observed a 20% rise in mean cholesterol level after a fat load. Effect of high cholesterol fat load on postprandial cholesterol levels has also been studied in the past by several workers, but insignificant difference has been found between postprandial and 18-14 hours fasting values (Albrink and Man, 1956; Pomeranz et al, 1954 and Schilling et al, 1964).

Textured vegetable proteins lowered total serum cholesterol in hypercholesterolemic subjects with no change or slight elevation of HDL. Little effects were observed in normolipidemic subjects (Sirtori et al,
The replacement of animal protein with vegetable protein in the diet has been suggested to reduce the diet linked atherogenic (Carroll, 1982). However, sacks et al, (1983) found no appreciable correlation between total intake of protein, when consumed above minimum requirement and serum cholesterol level.

In one study, isocaloric replacement of starch with sucrose in mixed diet did not lead to changes in serum cholesterol (Mann and Truswell, 1972).

EFFECT OF FEEDING ON HIGH DENSITY LIPOPROTEIN (HDL)

Borden et al (1964) reported enhanced levels of HDL in rats fed cholesterol while Haff et al (1962) and Kricharsy (1965) reported no change in HDL levels in cholesterol fed rats.

There is evidence that substitution of large quantities of poly-unsaturated fat for saturated fat in diet can result in lower levels of HDL lipids and proteins (Nichaman et al, 1967). An increase in the P/S ratio from 0.25:1 to 4:1 in food diet fed to four normal subjects for five weeks resulted in reduction of HDL and apolipoproteins A-I concentration of 33 and 21% respectively, with an associated reduction in HDL2: HDL3 ratio (Shepherded et al, 1978). Other studies have however reported either no change (Lewis, 1978; Shore et al, 1981) or increase (Jackson and Glueck, 1980) in
levels of HDL with feeding of diets enriched in polyunsaturated fat.

High dietary intake of cholesterol, in the form of 3-6 egg yolk per day, has been reported to produce increase in apolipoprotein E-containing HDL sub species in human (Mahley et al, 1978). Tan et al (1974) showed that level of HDL and serum apolipoprotein A-I, but not apolipoprotein E increased with the feeding of diets high in both cholesterol and saturated fat.

Recently it has been shown that HDL apolipoprotein A-I levels increased when fat was consumed in divided doses over a period of 10 hours, but not when the same amount of fat was ingested as a single load (Kay et al, 1980).

**HDL AS A PREDICTOR OF CAD**

The ability of HDL to predict the development of coronary atherosclerosis has been estimated to be four times greater than total cholesterol. Each 10 mg/dl change in cholesterol concentration results in 50 percent alteration in cardiovascular risk (Yarr S, Goldbourt U, Even-Zohar et al, 1981). The ratio of total cholesterol to HDL cholesterol also is about as efficient as any other lipid profile in predicting the future development of CAD(Gordon T, Kannal WB, Castelli WP et al, 1981).
LOW DENSITY LIPOPROTEIN (LDL) CHANGES ON FREDING

Diet high in fat and cholesterol cause an elevation in LDL in most animals (Makley, 1970). The response in man varies, but in those subjects who have an elevation in plasma cholesterol, there is an elevation in plasma LDL levels. Deborah Applebaum et al (1979) demonstrated significant rise of LDL level in human volunteers after feeding 5000 mg of egg yolk cholesterol per day for 30 days.

Age related difference in rise of LDL was demonstrated by Arora and Gupta et al (1987). They found that rise of total serum cholesterol after feeding HCD 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 STC was less marked with LDL contribution, mainly in the increased levels.

Rund 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 tissues.

In addition to this, this has also been shown that diet induced LDL molecules have large molecular size than those on low fat cholesterol diet (Rudel et al., 1979). Cline and Leight (1979) have 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. Diet induced apoprotein fraction changes in LDL have also been reported (Nahley et al., 1977; Rudel et al., 1979).

CONCEPT OF LDL RECEPTOR IN CONTROL OF SERUM CHOLESTEROL

It is now considered that LDL receptors play a pivotal role in regulating the level of serum cholesterol (Kita et al., 1983). In rabbits, rats and hamsters more than half of the total LDL receptors are located in the liver. However, the precise distribution of these receptors in man is unknown.

Hepatic LDL receptors are suppressed whenever the liver's content of cholesterol increases or its demand for cholesterol is reduced. Thus receptor suppression occurs when a high cholesterol diet is consumed (Nai et al., 1981) or when bile acids are infused (Angelin et al., 1983). Conversely LDL receptors increase when hepatic cholesterol synthesis is blocked by drugs such as cholestyramine (Goldstein et al., 1982 and Wilhelmsen, et al., 1983), when bile acid binding resins are given (et al., 1983). Fasting has also been shown to suppress LDL receptor in rabbits (Goldstein, 1982). LDL uptake can be stimulated by thyroxine (Thompson, 1981) and by pharmacologic doses of estrogen (Winder, 1980).
All the changes in receptor activity alter the rate of uptake of LDL by the liver and cause reciprocal changes in plasma LDL levels. Whenever hepatic LDL receptors are suppressed, the plasma LDL level rises; conversely, whenever these receptors are induced, the plasma LDL levels fall. In familial hypercholesterolemia the basic defect is reduced number of LDL receptors. In normal person about 45% of the plasma LDL pool is removed from the plasma daily by the receptors, whereas in familial hypercholesterolemia heterozygotes it is about 15%. This receptor deficiency results in accumulation of LDL into the plasma, leading to raised level and premature atherosclerosis.

**FEEDING INDUCED CHANGES IN SERUM TRIGLYCERIDES (STG) AND VERY LOW DENSITY LIPOPROTEIN (VLDL)**

Rise in the triglyceride level after fat ingestion has been reported after giving different amounts of the fat load and measuring the blood levels at different time interval (Mikkila and Kinnunen, 1963; Denborough, 1963).

Clausen 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 level in more than 95% cases, whereas secondary peak represented rise in very low density lipoprotein (VLDL) level in 65%. 
HanusKrause et al (1967) did not reveal any significant changes in serum total cholesterol after a heavy fat cholesterol load, but found significant difference in triglyceride levels.

Arona and Roshanah et al (1987) put forward the concept of triglyceride tolerance test which showed significant difference in peak levels of TG in normal healthy patient of IDDM and that of diabetes.

Diet prior to the leading test meal, may be decisive under metabolic ward conditions, significant difference in fat tolerance has been reported in healthy subjects on an isocaloric diet, when the daily fat intake per kg of body weight was varied from 0.1-2 g (Hana el, 1987).

Test meal composition has also been shown to affect serum triglyceride level significantly. In human beings, glucose one hour and half an hour before as well as one and a half hour after a fat meal reduced or even eliminated the serum triglyceride rise (Albrink and Mon, 1956). Glucose addition to 111 I - labelled triolein caused a flatter triglyceride curve as compared to ingestion of the latter only (Barkowitz et al, 1989).

Long term studies on the effect of dietary protein on lipid level indicate that low protein intake is accompanied by a depression of serum lipids (Olson et al, 1957).
George C. Lin et al. (1983) incorporated 3 levels of dietary carbohydrate (40% and 60%) in the usual diet for 15 days in 8 patients suffering with endogenous hypertriglyceridemia. Fasting blood samples were drawn on days 11, 14, and 15 of each dietary period. In addition, samples were also drawn 3 hours before and after noon meal on days 14 and 15. They reported that low fat, high carbohydrate diet accentuates the metabolic risk for CAD that is already present in patients of endogenous hypertriglyceridemia. They also reported that rise in plasma triglyceride is mainly depends upon total calorie intake.

Arora and Kushwaha (1987) proposed a 'triglyceride tolerance test'. The workers gave a fat load and found a significant peak at 5 hour in healthy volunteers.

**CHOLESTEROL FAT TOLERANCE TEST**

The concept of such test is now now. Neuman (1967) studied the quantitative lipid changes in form of chylomicron count after giving a fat load. Brezovitz (1963) pointed out that radioactive fat tolerance is a better index for determining the functional state of lipid metabolism.

Silverman’s postulation of postprandial hyperlipidemia as a possible factor for pathogenesis of atherosclerosis aroused interest in determination of postprandial changes in lipid fraction after a meal rich in fat and cholesterol.
DIFFERENT FACTORS REGULATING FAT TOLERANCE

Age has been shown an important factor. Chylo-
micron count has been shown to rise more after a fat
load in subjects more than 50 years as compared to the
younger group (Becker et al, 1949). Hurstone et al
(1953) observed that the total fats persisted longer in
serum after fat loading in older subjects. Body weight
and the duration of lipemia were shown to be poorly
related (Barritt, 1956).

Miecon (1931) showed that at rest the lipid
level of normal subjects increased by 45% after 3 hours
of fat meal and the maximum was attained after 4 hours,
while at work these figures were 36% at 3 hours.

Smoking has also been shown to affect post-
prandial hyperlipemia. In habitual smoker, response to
a fat meal indicated a lower postprandial rise in serum
fat than to non-smoker (Konttinen and Rajasalmi, 1963).

Harder et al (1953) showed that one cigarette/hour caused
the chylo micron count to rise in a group of young
subjects but not in 2 elderly subjects.

Barritt et al (1956) could not relate
significantly between body weight and duration of
lipemia, however, it was shown that the fat tolerance
rose appreciably after weight reduction was enforced.
Reproducibility of fat tolerance has always been a controversial issue. While Norton (1980) and Coseo et al (1987) showed reproducibility of test over a period of six months, Brents Stewart and Blackburn (1988) found considerably variability in response to the same fat load.