INTRODUCTION

With advancing years certain changes are associated with many infectious diseases. The most prevalent degenerative change observed in the cardio-vascular system is atherosclerosis. A group of World Health Organisation defined atherosclerosis as a variable combination of changes of the intima of arteries consisting of accumulation of lipids, complex carbohydrates, blood and blood products, fibrous tissue and mal-deposits and associated with medical changes. It is now fairly generally accepted that there are both tissue or vascular factors and blood factors involved in the process of atheromatosis.

Wielen (1951) drew attention to the slowly developing increase in the thickness of arterial intima throughout the life. Male arterial intima appears to thicken faster than the arterial intima of females. He considered that the appearance of arterial lipid laden plaques was a natural consequence of the age dependent intimal thickening and his views have come to be regarded as "Senescence" theory of atherosclerosis.

There is evidence in man that arterial changes classified as atherosclerosis are more prevalent in some
parts of the world than in others. The disease is more prevalent in the privileged communities in which starvation is practically non-existent and conversely it is rare in countries afflicted by undernutrition. Now it is fairly known that the plasma lipids correlate with the nutritional status. But it is not fully established whether the increase in plasma lipid observed in populations exhibiting widespread atheroma is related to the disease. However, the elevation of the plasma lipids is one of the few metabolic abnormalities detected in this condition.

The fundamental problem in elucidating the pathogenesis of atherosclerosis is to identify dependent and independent variables operative within certain pathological limits.

Atherosclerosis is a metabolic disease involving altered metabolism of cholesterol, lipid, lipoprotein. Increasing level of circulating plasma cholesterol, lipid, lipoprotein constitutes the metabolic precursors for atherogenesis. The change in the cholesterol lipid metabolism has been attributed chiefly to the life span unbalanced diet, being rich in total fats, saturated fats, cholesterol and deficient in certain essential nutrients as vitamins, essential amino acids and essential fatty acids.

In 1852 Nekitansky considered that the thickening
of the intima was due to deposition of material derived from blood. This view was contended by Virchow (1956)\(^5\) who attributed the vascular lesions to a manifestation of inflammatory processes which were followed by fatty degeneration.

In 1934, Rosenthal while analysing the papers based on clinicopathological services made in different countries stated the following generalisation on the co-relation of atherosclerosis and life span dietary pattern. "In no race for which a high cholesterol intake in the form of butter, egg and milk fat are recorded is atherosclerosis absent." Another important conclusion arrived at in India and Egypt was that, atherosclerosis was apparently rare in poor classes, whose diet contains mostly cereals while on the other hand the disease is common among the well-to-do classes whose diet is rich in saturated fat and cholesterol.

It has been known for centuries that certain degenerative changes in arteries are associated with appearance of lipids in the lesions and Vogel (1847)\(^7\) discovered that cholesterol was constituent of atheromatous plaques.

Much epidemiological and laboratory research is being conducted on atherosclerosis and on its treatment and prevention by controlling the diet.
General survey conducted during the last two decades confirmed this conclusion that significant atherosclerosis is rare among the people over the life span whose diet is vegetarian and low in calories, total lipids, saturated fats and cholesterol while atherosclerotic heart disease is common amongst middle aged males whose dietary fats constitutes about 40% of the total calories.

There is a wide variations in the incidence of coronary heart disease among persons from different habits and mode of life from the same region. This difference mainly related to the serum cholesterol levels and dietary habits to people.

The inter-relationship among diet, plasma cholesterol level and atherogenesis is demonstrable for the peoples in the countries of economic development.

The relationship of dietary fats and serum cholesterol levels to the incidence of coronary heart disease at Agra has been analysed. It has been found that there is a relationship between age and coronary heart disease and also cholesterol levels. But the relationship between total amount of fat consumed and the incidence of coronary heart disease was insignificant.

Anderson et al. concluded that overnutrition with gain in body weight or an increased intake of saturated
fat in an isocaloric diet increases serum cholesterol. Restriction of energy intake leading to loss of weight, decreases it.

There is a considerable evidence that when diets are fed to human subjects such that the caloric intake exceeds the caloric requirement, the serum cholesterol level tends to rise. Conversely when the caloric intake is less than the caloric requirement, the serum cholesterol tends to decrease. These observations from the basis of the well-known experiments in which the serum cholesterol in certain obese subjects can be depressed by reducing diets.

In the experiments it was observed that plasma cholesterol level was lowered down by the isocaloric substitution of unsaturated vegetable or marine oil for saturated animal lipids in the diet. In the other experiment high caloric, high saturated fat, high cholesterol diets were supplemented with unsaturated vegetable oils which resulted in an increase in the total calories.

In some cases the diet was adjusted in such a way that there was no gain in weight. In such experiments South African Bantu showed a fall in the plasma cholesterol content. Similar observations were recorded even when high cholesterol fats (eggs) were added to the diet.

The aim of many investigations has been to find some
simple 'test' which would be indicative of atheromatous arterial involvement and then to apply this to clinically normal subjects to predict future clinical events.

The inter-relationship between dietary lipids and atherosclerosis was subjected to thorough clinical investigations during the last few years and in coronary heart disease, there was a significantly higher level of circulating serum cholesterol, lipids and β lipoproteins, while studying atherosclerosis cholesterol is the substance commonly estimated, but other substances such as β lipoprotein have been shown to vary sensitively which changes with the fat content of diet (Lloyd et al. 1962). As all the plasma cholesterol is carried as lipoprotein complex with α and β globulins, the plasma cholesterol was described in terms of the ratio of cholesterol bound to α lipoproteins to cholesterol bound to β lipoprotein. α/β lipoprotein ratio is of interest so far as it is reduced in subjects with the clinical coronary artery disease. But α/β lipoprotein ratio is no better as a predictor of atherosclerosis than the plasma cholesterol level. Other criteria included cholesterol-phospho-lipid ratio and the triglycerides.

The abundant evidence suggesting that atheromatous lesions are rich in both protein and lipid presents a major problem in attempts to reconcile all the variants of the
lipid.

The question regarding the exact role of various dietary components in hypercholesterolemia remains still unresolved. Divergent effects on the serum cholesterol concentration as a result of an alteration in the quality of dietary fat, type of sugar, bile acids, and thyroactive compounds have been reported. Among various dietary factors which have been implicated in the regulation of blood cholesterol concentration, the dietary fat has been studied most.

The search for the factors responsible for this fall in serum cholesterol level on feeding of the unsaturated vegetable oils form the subject of more recent studies. In the complete substitution experiments the observed fall in the serum cholesterol level could not be accounted for by the removal of dietary cholesterol as the addition of cholesterol to vegetable oil diet induced little or no renewed rise in that level.24-27, 34-38 Evidences were also obtained in other studies that the lowering of serum cholesterol level affected by the addition of unsaturated vegetable oils to the diet could not be attributed to the contents of phospholipids or other plant sterols of these oils.24,39

Reveridge et al. (1954) are of the view that the plant
sterols are at least partially responsible for such lowering of the serum cholesterol level as affected by the administration of corn oil.

It is quite natural to conclude from the above clinical findings that atherosclerosis is the resultant of the deficiency of essential fatty acids in human diet. But the fact that the usual American diets are not low in essential fatty acids, though the incidence of coronary disease is maximum.

It may be concluded that the role of unsaturated vegetable oils and EPA (essential fatty acids) in the lowering of cholesterol is not clear. Yet these clinico-pathological findings in parallel to the epidemiological findings have clearly manifested a close relationship between the level of plasma cholesterol and development of atherosclerosis on the one hand and between the nature of the diet and the level of plasma cholesterol on the other.

There have been many studies on dietary factors other than lipids and calories in serum cholesterol experiments. One of the factors implicated in the elevation of the plasma cholesterol level has been the ratio of calories derived from carbohydrate to calories derived from protein in the diet. Those studies are exceedingly difficult to access because, as a rule, they are of short duration and while it is possible to manipulate the plasma lipids by alterations to the protein content of the diet it is
difficult to assess the results unless it is known that the individuals have been in nitrogen balance at each stage of the experiment.

There is a great deal of evidence to support the hypothesis that in certain instances metabolic abnormalities which lead to the production of plasma hyperlipaemias are under genetic influences. \textsuperscript{41, 42} Plasma cholesterol levels are known to be elevated in xanthoma tuberosum and xanthomatendinosum. The genetic factors which influence the plasma lipids can be considered apart from the environmental or dietetic factors. Nevertheless, there is a marked inter-relationship between genetic and environmental factors because hereditary factors influence markedly the susceptibility of an individual in an unfavourable environment.

There is a considerable interest at the present time in possible preventive measures which may be instituted either to arrest the process of atheromatosis or to achieve regression of the lesions. Some of the few drugs were investigated which are responsible for the prevention of the increase in cholesterol.

Ostetrogena, when administered in excess to human males, the plasma cholesterol concentration is markedly reduced. \textsuperscript{43}
Thyroid, the effect of thyroid hormone on the plasma lipids has been known for many years. But this hormone is of limited value as a plasma cholesterol depressant. Nicotinic acid showed that it is effective in controlling the hypercholesterolaemia (dose - 1 gm to 9 gm.).

Sitosterol, which is present in grains, is 24 ethyl analogue of cholesterol. The presence of sitosterol in the diet interferes with the absorption of the dietary and biliary cholesterol, which is participating in the entero-hepatic circulation of cholesterol. Administration of sitosterol increases faecal excretion of cholesterol and reduces plasma cholesterol concentration if other factors remain unchanged.

Similarly, Triparanol, Phenyl acetic acid and Atromid are effective in lowering plasma cholesterol. But most of these drugs when administered at high dosages to man for a long period, produce side effects.

Some of the vitamins are also antiatherosclerotic in action. Ascorbic acid when fed with fats high in linolic acid reduces plasma cholesterol. The studies of Morrison (1948) suggested that chlorine might be effective in the control of hyper-cholesterolaemia as choline is capable of reducing liver lipids under certain conditions.

Rinehart et al. (1949, 1956) showed that it was
possible to induce in monkeys vascular changes by means of a diet deficient only in pyridoxine. These studies form the basis of various hypothesis that the human atherosclerotic lesion might be a consequence of a deficiency of pyridoxine.

Pyridoxine deficiency caused a small rise in the serum cholesterol concentration of rats fed on diet with or without cholesterol. Q 275 (Coenzyme Q) and high dose of vitamin D (Calciferol) had no effect on the serum cholesterol concentration but Calciferol in high doses caused greater deposition of cholesterol in the liver. 0.5% to 2.5% of nicotinic acid in the diet failed to reduce hyper-cholesteremia; actually it enhanced hypercholestremia and raised blood oxidised pyridine nucleotides.

If the concept is correct that some dietary factors are casually related to the production of arterial lesions, then it should be possible to influence the production of these lesions by manipulation of the amount of dietary factors ingested by a population on the basis of epidemiological studies cited previously the causative agent might be assumed to be some constituent of the lipid portion of the diet or a critical concentration of the dietary calories ingested as lipid.

Until 1910, all attempts to produce atherosclerosis
in experimental animals failed. During the years 1910-12 atherosclerosis could be successfully produced in rabbits by feeding animal tissues. By 1950, experimental atherosclerosis had been produced in chicks and rabbits which are more susceptible by simply feeding small amount of cholesterol and lipids over a long period. Lately, it became possible to induce atherosclerosis in rats and monkeys by feeding high cholesterol and high fat diets only. More recently, atherosclerosis can be induced by feeding diet containing 5% cholesterol, 2% sodium cholate, 40% butter fat and thiouracil to rats.

Stamler et al. (1957) have reported that saturated lard or hydrogenated vegetable fats were found to be equally effective as unsaturated vegetable oils such as cotton seed, linseed and corn oil in producing hypercholesterolaemia in experimented animals.

Animal experiments have shown that excess of both cholesterol and neutral fat was the prerequisite for atherosclerosis. The feeding of excess of cholesterol in absence of neutral fat or vice versa proved to be less atherogenic.

At a certain level of dietary cholesterol the feeding of neutral fats either of saturated or unsaturated vegetable oils or saturated animal fat increased atherosclerosis.
proportional to the amount of fat ingested. \(^{57}\) Exceptions to this conclusion of course, have been reported by other groups working with ground squirrels, geese and rabbits. \(^{58}\)

The incorporation of large amount of unsaturated vegetable oil in the high cholesterol diets of experimental animals neither caused the lowering of serum cholesterol level nor reduced the atherogenesis. It has also been demonstrated that a diet rich in vegetable oil, but free from cholesterol could produce atherogenesis in the rabbits and squirrels.

Thus, pathological findings and animal experimentations have shown the importance of the proportion of saturated and unsaturated, vegetable oils and cholesterol in the diet in controlling the level of serum cholesterol which is the cause of atherosclerosis.

Till 1956, little was known about the relative proportions and the compositions of various lipid groups in the blood and the atheromatous deposits.

Several groups of workers fed the rats with cholesterol and various oils or the combination of oils have led to general conclusion that non-essential unsaturated fatty acids promote hypercholesterolaemia while essential fatty acids and saturated acids counteract equally. The
change in the quality and amount of dietary fat and protein affects the blood cholesterol concentration in experimental animals and that it may affect the process of atherosclerosis. Thus it is the quality and not the quantity of the fat which appears to be more important.

Any alteration in the dietary level of fat or protein is made at the expense of the carbohydrate and it is assumed that change in carbohydrate does not affect cholesterol. However, it was reported that the serum cholesterol concentration of rats fed on a synthetic hypercholesteremic diet containing sucrose as the carbohydrate source was higher than that of comparable group fed on a diet containing starch as Carbohydrate. This observation focused attention on the role of carbohydrate in cholesterol metabolism. Absorption of cholesterol depends on the carbohydrate in diet. Sucrose and milk sugar produces high serum cholesterol.

From the above, it seems that dietary factors may have considerable effect on the metabolism and blood concentration cholesterol. The effects of fat and protein have been studied intensively. Less is known about carbohydrate. Recent studies indicate that carbohydrates in their various forms may be involved in atherosclerosis. The present study was undertaken to determine the effect of high carbo-
hydrate in presence of different fats on serum and liver cholesterol and whether this effect is modified by altering dietary conditions.
REFERENCES

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