DISCUSSION

One of the most startling facts that has to be faced is that fasting plasma cholesterol do not sufficiently represent an individual's risk for future CAD. Gregory et al (1983) reported that 40% of young patients of documented CAD, do not reveal raised fasting plasma cholesterol.

The manner in which an individual responds to single high cholesterol fat diet (HCFD) could possibly help in determining his chances of developing atherogenic process. Zilverenm (1973) proposed that atherogenesis may be a post prandial phenomenon.

Gemfibrozil has been said to reduce cardiovascular mortality but as fasting cholesterol does not reflect the true risk of CAD. So the drug should have some effect on post prandial lipid lipoprotein profile. As it is not feasible to give gemfibrozil for long periods in hope that it will alter favourably lipid-lipoprotein profile, so the effect of drug on post prandial behavior of the individual may be a good screening test to assess the effect of drug in long term. This has formed the basis of for the present work.

FASTING SERUM LIPOPROTEIN PROFILE:

In our study 6 subjects showed fasting STC level 200 mg% or more. Rest of the 16 subjects showed fasting STC level on day 1 less than 200 mg%.
4 out of 22 subjects showed a rise of STC and 18 subjects showed a fall of STC on day 7 as compared to fasting STC level on day 1. 13 out of 22 subjects showed a fall in fasting LDL on day 7 as compared to day 1, rest of 9 subjects showed a rise. 14 out of 22 subjects showed a fall of fasting HDL level on day 7 as compared to day 1, 4 subjects showed a rise and 4 showed no change in fasting HDL level on day 7 as compared to day 1.

Fasting STG level on day 7 showed a rise in 3 subjects and a fall in 17 subjects, while 2 subjects showed no change, as compared to fasting STG value on day 1. VLDL showed almost same pattern of changes as showed by STG.

We thought that these variations in fasting serum lipid-lipoprotein profile are due to day to day variability of lipid lipoprotein levels. These changes may also be contributed in part due to non-compliance of the subjects regarding the instructions to be followed during the study, at least in some subjects.

**POST PRANDIAL BEHAVIOR WITHOUT GEMFIBROZIL (DAY 1):**

According to pattern of rise and fall of LDL and HDL at 1 hr. post prandially we found that 12 subjects showed Type II behavior, (i.e. a rise of LDL and a fall or no change of HDL level at 1 hr.), 4 showed a Type I behavior (i.e. fall of LDL and a rise or no change of HDL at 1 hr.) and 6 subjects showed indeterminate behavior.

Explanation for fall in LDL at 1 hr. post prandially in Type I behavior is as follows: when high cholesterol fat diet
(HCFD) is given to the individual the LDL receptors got stimulated by some unidentified hormonal or neurogenic reflexes in anticipation to cholesterol load, that will enter in circulation. As a result the large amount of LDL from intravascular compartment shifts intracellularly, resulting into an acute fall in serum LDL and STC levels after 1 hr. the cholesterol level slowly increased after 3 hours as a result of the absorbed cholesterol and reverse intravascular movement of LDL, that has been entered in the tissues earlier.

The rise of LDL at 1 hr. post-prandially in Type II behavior can be explained by some inherent biochemical block in anticipating and assimilating cholesterol load by LDL receptors.

**POST PRANDIAL BEHAVIOR WITH GEMFIBROZIL (DAY 7):**

Out of 4 subjects, who showed Type I behavior on day 1, 2 changed their behavior to Type II and remaining 2 subjects showed blunting of Type I behavior (i.e. fall of LDL at 1 hr. post prandially decreased quantitatively) on day 1.

Out of 12 subjects, who showed Type II behavior on day 1, 4 subjects remained Type II on day 7 as well, 3 subjects changed their behavior to type I and 5 subjects showed blunting of Type II behavior (i.e. rise of LDL at 1 hr. post prandially decreased quantitatively) on day 1.

Out of 6 subjects who has showed their behavior to be indeterminate on day, 3 again showed indeterminate behavior on
day 7, but 3 subjects changed their behavior from indeterminate to Type II.

In subjects who has shown conversion of Type II behavior to Type I or who showed blunting of Type II behavior (i.e., tending towards Type I behavior) the possible explanation for LDL fall or quantitatively decreased rise of LDL may be as follows. As we know that in subjects showing Type II behavior there is an inherent biochemical block of LDL receptors, so the LDL rises postprandially. The Gemfibrozil seems to stimulate there blocked LDL receptors, as a result post prandial LDL level falls or the rise of post prandial LDL level decreases quantitatively. The second possible explanation is that Gemfibrozil increases lipoprotein lipase activity (Helsinki Heart study) thus decreasing post prandial LDL levels. It is difficult to explain these changes by increased hepatic VLDL turnover, which is well documented mechanism of action of Gemfibrozil, as this mechanism takes long time at least few weeks to produce appreciable changes in lipid lipoprotein profile.

In subjects who changed their behavior from Type I to Type II after gemfibrozil or who shown blunting of Type II behavior the drug might be blocking the LDL receptors by some unknown mechanism.

In this study we conclude that -

3 subjects who have showed type II behavior changed into type I behavior on day 7, and 5 subjects who were type II on day
i showed blunting of Type II behavior on day 7, thus Gemfibrozil must have got beneficial effect over these subjects.

2 subjects, who have showed Type I behavior on day 1 changed into Type II behavior on day 7 and 2 subjects who were Type I on day 1 showed blunting of Type I behavior. As subjects with Type I behavior are less prone for atherosclerosis and its complication, they do not need hypolipidemic agents, so Gemfibrozil should not be given to these subjects, as it might have some deleterious effect over these subjects.

3 subjects who showed indeterminate response on day 1 changed into Type II behavior on day 7, thus Gemfibrozil is not beneficial to these subjects or even may be harmful. And 3 subjects who were indeterminate on day 1, remain indeterminate on day 7, as well, so the long term effect of gemfibrozil in these subjects is difficult to predict. As our study consists of few number of subjects, further study with large number of subjects required to confirm our findings.