REVIEW OF LITERATURE
Atherosclerosis is the commonest cause of coronary artery disease, being responsible for more than 90% of cases (Blumgart et al., 1960). A minority of cases (8 percent) are because of coronary artery embolism, inflammatory diseases of coronary arteries like syphilis and congenital anomalous coronary artery lesions (Moritz et al., 1946).

Although any artery may be affected, the aorta, the coronary and the cerebral arteries are the prime targets of atherosclerosis.

In 1958 a study group of WHO defined atherosclerosis as a "Variable combination of changes of the intima of the arteries consisting of focal accumulation of lipids, complex carbohydrates, blood and blood products, fibrous tissue and calcium deposits and associated medial changes" (Cheng, 1974).

Although no agreement has been reached on the precise progression of various changes from the earliest recognisable lesions to the onset of clinically identifiable disease, the following histological abnormalities have been accepted as being present at one time or another in the development of atherosclerotic process (WHO technical Report series No. 143).

1. Patchy accumulation of lipid, mostly cholesterol and its esters but also phospholipids and triglycerides, either intracellularly (foam cells) or extracellularly
in the intima and inner media of affected arteries.

2. Fibroplasia, largely confined to subendothelial portion of the intima, in the form of mucopolysaccharides, reticulin, collagen fibres and hyalinization.

3. Fibrin-like film attached to the intimal surface or covered by endothelium.

4. Accumulation of complex carbohydrates.

5. Calcification in fine or coarse granules.

6. Cholesterol crystals and fine, granular, amorphous glycoprotein material.

7. Medial changes such as lipid infiltration, disintegration of smooth muscle fibres, disruption of elastic fibres, cellular infiltration, around vasovasorum and mucoprotein accumulation.

8. Secondary changes such as ulceration, thrombosis, or haemorrhage.

AETIOPATHOPHYSIOLOGY

Ischaemia refers to lack of oxygenation due to inadequate perfusion. Ischaemic heart disease (IHD) is a condition of diverse etiologies. One factor is common in all conditions i.e., disturbance of cardiac function due to imbalance between oxygen supply and demand.

Ischaemic heart disease was defined by a WHO group in 1955 as "Cardiac disability acute or chronic arising from reduction or arrest of blood supply to the myocardium in association with disease process in the coronary arterial system", (WHO Tech. Report, 1977).
The most common cause of ischaemia is atherosclerotic disease of epicardial coronary arteries, which by reducing lumen of these vessels cause absolute decrease in cross sectional area of a epicardial vessel by approximately 75% percent. A maximal increase in flow to meet increased myocardial demand being not possible. When luminal area is reduced by more than 80 percent, blood flow at rest may be reduced and minor further reduction of stenotic orifice can cause dramatic limitations of coronary flow and severe myocardial ischaemia.

There is disagreement amongst cardiac pathologists concerning the frequency and significance of coronary arterial thrombosis in patients with acute myocardial infarction. Baroldi (1965) found arteriosclerotic narrowing of coronary arteries without recent thrombosis in 53 percent of cases. In patients who died of acute coronary episode suddenly or within 6 hours of initiation of symptoms almost all of these patients had extramural CAHD, but only 10 percent had coronary thrombosis. As a result of these observations Roberts concluded that fresh coronary thrombosis was usually the result and not the cause of myocardial infarction (Roberts, 1972).

Myocardial infarction has been reported in young adults whose coronary arteriogram showed no abnormality (Khan et al, 1974). A possibility is occlusion of artery at its origin which might be missed by arteriography (Glancy, 1971).
Besides atherosclerosis, coronary blood flow can also be limited by arterial emboli (Wenger, 1958) syphilis and inflammation (Moritz, 1946). Cheitlin et al (1975) listed 44 different diseases that may cause myocardial infarction. Myocardial infarction in infants and children is more often related to coronary artery embolism, arteritis or congenitally anomalous vessels than to degenerative disease (Sor, 1969).

**PATHOLOGY**

Within the first 12-18 hours after the onset of coronary occlusion which leads to infarction, gross changes in the myocardium may not be visible. Recognizable histologic changes are delayed for 5-6 hours and then myocardial fibres appear eosinophilic with fainter cross striations. With new techniques histologic changes may become recognizable within a few hours (Li64, 1978). Fatty infiltration may take place and after 24 hours polymorphonuclear infiltration begins (Waller et al, 1956). After 24-48 hours myocardium grossly appears pale or yellow possibly with haemorrhagic areas. Fibrosis begins after 3rd or 4th week and a healed scar is present as a rule by 6 weeks reaching maximum density by the end of 2nd month.

**CORONARY ATHEROSCLEROTIC HEART DISEASE (CAHD)**

The concept of "risk factor" first appeared in an early Framingham study report (Kannel et al, 1961). A risk factor for CAHD is a characteristic of a person.
(Demographic, psychological, anatomic or physiologic) that increases the likelihood (risk) of that person developing some manifestations of cardiovascular disease (Yannel, 1984). The risk factor is not only statistically associated with cardiovascular disease, but as a result of meeting several criteria, it is also considered to be causally related to the disease (Susser, 1973).

Risk factors can be divided into 3 groups.

A. Non modifiable risk factors.
B. Modifiable risk factors.
C. Probable risk factors.

Non Modifiable Risk Factors

Non modifiable risk factors are age, sex and family history of premature CAHD. These are powerful predictors of MCAD, but these are not alterable. It may be more important to intervene on modifiable risk factors in males or those with a strong family history.

Modifiable Risk Factors

A. Major

1. Elevated serum lipid levels (cholesterol and triglycerides).
2. Habitual diet high in total calories, total fats, saturated fats, cholesterol, refined carbohydrates and salt.
4. Smoking.
5. Carbohydrate intolerance.
6. Obesity.

B. Minor
1. Oral contraceptives.
2. Sedentary living habits.
3. Personality type.
4. Psychosocial tension.

C. Possible factors influencing the development of coronary atherosclerosis or its complications.
2. Alcohol intake.
5. Urban birthplace, residence.
6. Social over crowding.
7. Heavy body frame.
8. Income and living standard.
9. Blood group A.
10. Decreased physical fitness.
11. Hypoxia, carbon monoxide.
12. Carbonyl haemoglobin.
13. Alpha radioactivity in water.
14. Decreased stool roughage.
15. Deficiency - vitamin C or E, calcium, magnesium, chromium, manganese, vanadium, lithium or fluoride.
16. Relative or absolute deficiency of copper.
17. Lack of pectin in diet.
18. Abnormal methionine metabolism.
19. Milk antibodies.
20. Immune reaction.
21. Virus infection.
22. Short stature.
23. Respiratory impairment.
24. Decreased vital capacity.
25. Tachycardia at rest.
26. Abnormal ECG at rest or during exercise.
27. Abnormal cold pressure test.
28. Coagulation disorders.
29. Sticky platelets.
30. Elevated haematocrit.
31. Elevated erythrocyte sedimentation rate.
32. Leukocyte count.
33. Axillary hair index.
34. Increased ear canal hair.
35. High levels of circulating insulin.
36. Hyperuricemia.
37. Hypothyroidism (latent).
38. Hyperestrogenemia.
40. Level of education.
41. Birth order.
42. Age of father at birth.
43. Climate.
44. Residence of low altitude.
Age has a dominant influence on the development of clinically significant atherosclerosis. Clinically overt atherosclerosis, as evidenced by death rates from ischaemic heart disease, rises with each decade up to age 85 years. So there is a close relationship between age and severity of atherosclerosis (Mc Gill, 1978 and Strong, 1978). Other factors such as mode of life, hypomnentia or concomitant wasting diseases, however, can significantly retard the atherogenic process or minimize its invasiveness. This argues in favour of the concept that a relation to age although frequent, is not necessarily involved (Moriyama, 1971). Myocardial infarction is a disease predominantly of the middle aged and the elderly, between 50 and 60 years. The western patients are nearer or over 60 while in India population Kinnare (1982) and Bhusharnath et al, (1985) found most of the patients between 40-70 years with an average age of 53 years, 30 percent of the patients belonging to age group 50-60 years.

SEX

It is universally accepted that men are more prone to clinical manifestations of coronary atherosclerosis than women of child bearing age. After menopause, there is rapid narrowing of the sex difference in the incidence of
aneurina pectoris or myocardial infarction and this approaches
to equality at about 75 years (Kay, 1970). Of the many
reasons presented for sex difference in susceptibility to
atherosclerosis, a possible protective effect of
oestrogen, differences in blood lipids and haematocrit,
reduced risk of cigarette smoking (Bentsen, 1973) and more
sheltered way of life are proposed. However, there is no
conclusive evidence for any of these. Agarwal et al (1978)
observed myocardial infarction in 6.5 percent female and
93.5 percent male patients and Wasir et al (1985) in
10 percent female and 90 percent male patients thus showing
dominance of the disease in males.

FAMILY HISTORY OF PREMATURE CORONARY
ATHEROSCLEROTIC HEART DISEASE

It has been seen that certain groups have a
predisposition for premature coronary atherosclerotic
heart disease. It has been confirmed that individuals
with either parents or siblings affected by the disease
prior to age 50 have a greater risk of coronary athero-
sclerosis at younger age. In certain cases the relative
risk may be as high as 5 times (Fredrickson, 1972). This
may represent the clustering of many risk factors within
families rather than a unique genetic predisposition to
atherosclerosis. In particular hyperlipidemia (genetic
or diet induced), hypertension and diabetes, all tend to
familial. Family history of CAHD was present in 26 percent
of 175 cases (Masir et al., 1985). Chinnah et al (1979) found positive family history in 26 percent of his 100 cases and Gupta et al (1987) in 31 percent cases.

Geogry et al (1983) observed that family history of CAHD was more significant in younger patients of acute myocardial infarction (≦40 years of age) than in older patients. In patients below 40 years he found that the family history was positive in about 65 percent cases in comparison to 32 percent patients above 40 years of age.

MAJOR MODIFIABLE RISK FACTORS

HYPERLIPIDEMIA

There is an overwhelming evidence that hyperlipidemia is associated with increased incidence of premature ischaemic heart disease (IND). All types of hyperlipoproteinaemias including hypertriglyceridaemia and hyperlipoproteinaemia have been correlated with severity of atherosclerosis and the incidence of IND.

The importance of hypercholesterolaemia is associated with age. The Framingham study showed that in men and women 35 to 44 years of age, serum cholesterol levels of 265 mg/100 ml or over were associated with a five times higher risk of developing coronary artery disease than were levels below 220 mg/100 ml. This study also showed that cholesterol levels in males below age 40 were closely related to the future development of IND. This relation was much less pronounced in older individuals. Low density lipoprotein (LDL) was independently
related to the risk of CAHD for both men and women (Kannel, 1976). In contrast to this high density lipoprotein (HDL) was inversely related to the risk (Castelli, 1977).

Patients with high VLDL (very low density lipoprotein) who come from families with familial combined hyperlipidemia appear to be at same increased risk as those members of these families with elevated LDL levels. In contrast, patients with comparably elevated VLDL levels who came from families with pure monogenic familial hypertriglyceridemia do not appear to have a increased risk. In addition, high VLDL may increase the risk of premature atherosclerosis when combined with other risk factors for coronary artery disease such as diabetes, hypertension and patients on chronic haemodialysis. Waks et al (1985) observed hypercholesterolemia in 37 percent of his 165 cases of acute myocardial infarction. In study of Chinnah et al (1979) out of 100 patients below 40 years 23 percent had high cholesterol, while Gupta et al (1987) found in 19 percent of 40 cases.

**HYPERTENSION**

Hypertension is a risk factor of prime importance and established association with coronary atherosclerosis (Frais, 1969). Higher the blood pressure, greater is the risk of coronary atherosclerotic heart disease (Alexander, 1975; Kolata, et al., 1976). In the Framingham study, the incidence of IHD in men aged 45 to 62 years with blood
pressure exceeding 160/95 was more than five times than in normotensive men (BP 140/90 or less) (Kannel, 1979).

In the US National Co-operative polling project Research group (1978) which generated data for 10 years period from approximately 7500 men, the risk of IND in individuals with diastolic BP greater than 105 mm Hg was four times than individuals with diastolic BP 84 mm Hg or less.

The fact that predominantly systolic hypertension in the elderly is innocuous is not true. In Framingham study isolated systolic hypertension has been shown to be associated with increased risk of coronary heart disease. There is no indication even in elderly that cardiovascular risk is more closely linked to diastolic than to systolic pressure (Kannel, 1980).

The risk of atherosclerosis appears to be diminished by therapeutic reduction of blood pressure. Recent studies have shown that reduction of diastolic levels that had been greater than 105 mm Hg significantly reduces the incidence of IND, strokes and congestive heart failure in men. Even when the with diastolic blood pressures between 90 to 105 mm Hg are similarly maintained on adequate treatment, the incidence of some of these complications may be reduced (Edwin, 1987).

In a study of 100 cases below 40 years of age Chinnah et al (1979) found hypertension in 20 percent cases. In another study of 40 cases by Gupta et al (1987) 15 percent cases were found hypertensive.
DIABETES

Framingham study (Kannel et al., 1979) showed that for all age groups in both sexes, the incidence of cardiovascular diseases is more in diabetics than among nondiabetics. There is at least a two fold increase in the incidence of myocardial infarction in diabetic men as compared to nondiabetic men. For diabetic women the incidence was almost three times than non diabetic women. The approximately two fold increase in the incidence of hypertension among diabetics, particularly in adult females, may increase the risk further. Moreover, it is also frequently associated with obesity and in females with low HDL cholesterol. Both these factors will further enhance the risk. Thus it is difficult to isolate diabetes mellitus as a single risk factor, since it is well recognized that obesity, hypertension, hyperlipidemia are also frequently present in diabetic patients (Epstein, 1967).

In women the triad of obesity, diabetes and low HDL cholesterol carries an especially high risk for CAD (Gordon et al., 1977).

Bansal (1959) found history of diabetes mellitus in 10.3 percent cases in a series of 108 cases while Vytillingham (1964) reported an incidence of 20 percent in 700 cases. Wasir et al (1983) in a study of 165 young myocardial infarction patients found diabetes in 15 percent cases.
et al (1971) showed progressive and comparatively
synergistic effect of the risk factors (hypertension,
cigarette smoking, over weight, elevated cholesterol etc.)
In a study of 200 cases, Agrawal et al (1979) found
15 percent patients without any coronary risk factors,
33 percent with single and 52 percent with two or more
risk factors. In another study of 165 cases, Wasir et
al (1985) observed that 36 percent of young myocardial
infarction patients had no modifiable risk factors. This
was in sharp contrast to the 18 percent prevalence of
absent risk factor in the older myocardial infarction
group. In whole of the group, 22 percent patients had no
coronary risk factor. Out of all the patients with
recognized risk factors, 47 percent had one, 37 percent
had two, 12 percent had three and only 4 percent had more
than three coronary risk factors.

EPIDEMIOLOGY

The first pre-mortem diagnosis of coronary
thrombosis was made by Aidan Hamner (1878). Clinical
correlation and post mortem features of myocardial
infarction were first described by Herrick (1912).

In USA there has been significant decline in
CVD mortality recently. CHD mortality climbed through
the 1950s, plateaued in the 1960s and then declined
sharply in 1970s and this trend is continuing (Havlock
et al, 1979; Cooper et al, 1970). This trend is for all
Diet

Role of diet in development of CAD remained debatable many years but now most authorities agree that a diet rich in total calories, total and saturated fats, cholesterol, refined sugar and salt is a major coronary risk factor. Although still there are many skeptics (Mann, 1977) but it is thought that there is a direct relationship between diet, hyperlipidemia and the development of CAD. This is supported by following facts summarized by Glueck (1978).

1. Dietary cholesterol intake 0-600 mg/day is closely related to plasma cholesterol levels and dietary saturated plasma fatty acids elevate the serum cholesterol levels, whereas polyunsaturated fatty acids reduce them (Hegsted, 1965 and Rifkin, 1977).

2. Low cholesterol, low saturated fat and high polyunsaturated fat therapeutic diets reproducibly lower plasma cholesterol levels by 10 to 20 percent. (National Diet Heart Study Group, 1968).

3. Populations with sharply lowered dietary cholesterol and saturated fatty acid intake have lower plasma cholesterol levels and reduced CAD incidence (Simek, et al, 1974).
4. Immigrants from populations having low plasma cholesterol to ones in which it is high, develop cholesterol levels comparable to their host populations. This fact is supported by the study of Japanese emigrants. The gradient for the crucial three variables (Dietary saturated fat, blood lipids and IHD) increased from indigenous Japanese to migrant Japanese to native Caucasians (Key's, 1970).

5. Due to campaigns by various organisations, cholesterol intake in the American population has declined since 1970 and the polyunsaturated/saturated ratio in the dietary fat has increased. Concurrently there has been a definite lowering trend in serum cholesterol levels of adult Americans between 1971 to 1974 as compared to levels during 1960 to 1962. (U.S. National Centre for vital and Health Statistics 1977). In the same time period a significant downward trend (20 percent) in IHD mortality occurred among persons 36 to 74 years of age in USA (Wacker, 1977).
SMOKING

Cigarette smoking is one of the most potent risk factors for atherosclerosis. The surgeon General Report (1964) has first established association between cigarette smoking and IHD. In general, the risk of CAHD is 2-6 times more in smokers than non-smokers (Aronow, 1973 and Astrup, 1973).

The effect of cigarette smoking is more closely related to the number of cigarettes smoked per day than to the duration of the habit (Kannel, 1981).

It has also been shown that those who quit smoking have only half the risk of myocardial infarction than those who continue to smoke. However, the major influence of smoking is upon incidence of sudden death. Those who stop smoking show a prompt decline in risk and may reach the risk level of non-smokers as early as after one year of abstention (Edwin, 1987). The benefit of quitting cigarette smoking do not extend beyond age 65 years for heart attacks (Gordon et al, 1974).

At autopsy the degree of aortic and coronary atherosclerosis was found to be greater in smokers than non-smokers (Strong, 1979).

OBESITY

Obesity has for long been considered as a significant independent coronary risk factor (Stamler, 1967; Hubert, 1985). Obese individuals are more prone to develop hyperlipidemia, systemic hypertension and
diabetes mellitus (Gordon et al, 1977 and 1979). It has also been noted that weight loss is also accompanied by a corresponding reduction in the level of the major atherogenic risk factors (Ashley, 1974). The risk of CAHD in obesity is more obvious because of its association with other risk factors like hypertension, diabetes and hyperlipidemia.

Banerjea (1958) observed that obesity did not have a significant effect on the incidence of IMH. Gregory et al (1983) found obesity in 58 percent of 165 young cases. Nasir et al (1987) found obesity in 15 percent of 300 cases.

**MINOR MODIFIABLE RISK FACTORS**

**ORAL CONTRACEPTIVES**

It has been seen that women receiving oral contraceptives have significantly higher risk of CAHD than non users (Beral, 1976). Mann et al (1977) reported 2.8 times increased risk of death from myocardial infarction in women 30-39 years and 4.7 times in women 40 to 44 years, who use oral contraceptives.

**SEDENTARY LIVING**

Physical activity may be important because it not only reduces risk of CAHD but also improves efficiency of cardiovascular and respiratory system and improves muscle tone. Epidemiological evidence supports an association between physical inactivity and increased

In the Framingham study the overall mortality, cardiovascular mortality and CAD mortality were all inversely related to the level of physical activity (Paffenbarger, 1977; Kennel et al, 1979). However, this effect was rather modest as compared to other risk factors examined but did persist even when these were taken into account (Kennel, 1970).

PERSONALITY TYPE

The Framingham study showed that Type A women (with competitiveness, impatience, potential for hostility, exaggerated sense of time urgency) developed CAD in general and angina in particular twice as common as type B women. Type A Framingham working women had the same risk as type A house wives (Haynes, et al, 1980).

Men who exhibited type A behaviour (work overload, suppressed hostility and frequent job change) were found to be at increased risk of CAD especially in the 55–64 years age range (Morris et al, 1969; Rosenman et al, 1973).

PSYCHOSOCIAL TENSION

Framingham study showed that social and psychosocial tension, anxiety, suppressed hostility are common in women who suffer from CAD than women of the same age who remained free of CAD (Haynes, 1980). Some observations were made by Syme (1975).
EXCESSIVE COFFEE INTAKE

Coffee was once incriminated as a risk factor (Kannel, 1977). However Framingham study showed no association between coffee intake and coronary attacks when cigarette smoking is adequately taken into account (Damber et al, 1974).

MULTIPLE RISK PROFILES

It is acknowledged that CAD results from a variety of factors, though none has been found to be strictly deterministic. The risk associated with any major risk factor varies according to co-existent constellation of other risk factors. For this reason and because a constellation of risk factors provides substantially better risk prediction than any single factor, multivariate risk assessment is recommended (Gordon, 1982).

Large number of prospective epidemiologic studies show that coronary event in an individual with two predisposing risk factors was not simple sum of two individual risk factors but in fact the risk is much higher. For example, cigarette smoking is associated with 3-5 fold increase in relative coronary risk and a cholesterol level above 275 mg percent with a 3-5 fold greater risk than a cholesterol level lower than 225 mg percent. When these two risk factors are present in same individual, however, the coronary risk becomes 14 to 16 times (instead of 6-9 times) greater than in an individual free from these risk factors (Brand et al, 1976). Stamler (1967) and Kannel
age groups and for both the sexes. Similar trends are also reported from Australia and Finland.

This decline is attributed to more awareness in public about the health implications of overnutrition, cholesterol values in blood and its consumption, obesity (3.4 percent decline for men and 5.2 percent for women), increased physical activity, effective control of hypertension and declining trend of smoking (Stamler, 1981).

Ischaemic heart disease is believed to be on increase in India as in other developing countries (Modu, 1984), related possibly to the increasing prevalence of coronary risk factors as a result of changing life styles. Clinical studies had estimated that IND contributes 10–20 percent of all cases of heart diseases in Indian hospitals (Banerjee, 1964). Population based surveys have been rare, the one in Chandigarh (Sarvotham, 1968) showed prevalence rate of 66/1000 males and 63.7/1000 in females in the urban population while low figures of 1 percent have been mentioned in low income suburban population (Berry, 1976).

The incidence of myocardial infarction on the other hand was shown to be 1.29/1000 in Rohtak town population (Gupta, 1978) and in 52–63 percent of hospitalized cases of IND (Banerjee, 1970 and Naik, 1968).

PROGROMAL SYMPTOMS

Many patients with acute myocardial infarction have a history of previous angina pectoris. In a study, Francis et al (1963) found no previous history of angina
pectoris in 52 percent patients with first attack of acute myocardial infarction.

Patients with known CAD having pattern of stable angina pectoris usually exhibit increased duration and/or frequency of pain or start developing rest angina days or weeks prior to infarction which may be a warning signal of impending attack. One study described prodromal symptoms in 65 of 100 patients. Fifty nine out of these 65 patients had pain as prodromal symptoms. These symptoms began during a period of 2 months to as little as 4 hours before infarction (Soloman et al, 1969).

PRECIPITATING FACTORS

In most patients of myocardial infarction, the onset of infarction cannot be related to unusual effort. However, there is disagreement about whether physical effort can be blamed as a precipitating factor in some instances. Master et al (1941) found that the incidence of acute myocardial infarction following unusual effort was not out of proportion to the percentage of the 24 hour day spent in such effort. Yater and associates (1948) suggested that in some instances physical exertion could have precipitated the attack in the patients with underlying CAD.

CLINICAL FEATURES

Symptoms of myocardial infarction are quite variable. In the mildest form it may go unrecognised and be disclosed subsequently only by ECG. At the other end
of the spectrum there may be sudden death presumably due to ventricular fibrillation or asystole.

CHEST PAIN

The pain is the most common presenting complaint in patients with myocardial infarction. It may, however, occur without any pain (Roseman, 1954 and Lindberg, 1960). In one study of patients with acute myocardial infarction 10 percent had no pain and 10 percent had very slight or atypical pain (Stokes, 1969). In another study, 25 percent of patients with acute myocardial infarction aged 30–62, did not have any pain (Kannel et al, 1970).

Evans and Suffer (1956) found that atrial fibrillation and hypertension were common in patients with painless infarction. They also reported syncope as the initial symptom in 4 out of 70 patients with painless infarction. Painless infarction is more common in diabetics, elderly and the seriously ill patients (Braunwald, 1987).

Pain of acute myocardial infarction is similar in quality and location to that of angina pectoris but is often more severe and prolonged. Pain may persist from half an hour to a day or so. Pain is seldom of longer duration unless there is some complication e.g. pericarditis or intermittent attacks of recurrent ischaemia.

Pericardial friction rub is found in 6–10 per cent cases of acute myocardial infarction after first few days of infarction, usually on the 3rd or 3rd day (Stevens, 1953). A pericardial friction rub is ordinarily absent
in first 24 hours (Hoff, 1962).

Fever often occurs after first 24 hours and the temperature usually does not exceed the normal by 2 to 3°F. Fever usually lasts for a few days at a maximum of about a week. In one study fever was found in 150 out of 160 patients with anterior infarction. The maximum morning temperature was 39°C in 99 percent cases (Lofmark et al., 1976).

Derangement of ventricular function in patients with acute myocardial infarction may be manifested by development of diminished and low pitched first heart sound (Adolph et al., 1970), ventricular filling or S3 gallop sound, atrial gallop sound (S4) and paradoxical splitting of 2nd sound (Harvey, 1969; Coh., 1974). There may be prolongation of atypical systolic impulse (late systolic bulge) or an ectopic systolic impulse at peri-apical area during first few days and then may resolve (Haikal, 1971; Hurst, 1972). The development of apical systolic murmur may be due to papillary muscle dysfunction.

LABORATORY INVESTIGATIONS

Non-specific reaction to myocardial injury is associated with polymorphonuclear leukocytosis which appears within a few hours after the onset of chest pain, persists for 3-7 days and often reaches a level of 12000 to 15000 leukocytes/mm³. The ESR rises slowly, peaking during the 1st week and sometimes remains elevated for 1-2 weeks.
There is increased urinary catecholamine 
excretion which may be induced by acute infarction, pain 
arrhythmia or heart failure. Plasma hydrocortisone, 
growth hormone and urinary catecholamines are increased 
during first few days. There is also impaired glucose 
tolerance during this period. This impaired glucose 
tolerance is related to increased catecholamines and 
growth hormone levels (Lehovits et al, 1969).

Within an hour after acute myocardial infarction 
plasma free fatty acid level often increases significantly. 
Although there is moderate variation in individual patient, 
the plasma cholesterol level, which reflects predominantly 
LDL cholesterol tends to decrease slowly for few weeks 
after acute myocardial infarction, whereas plasma trigly-
ceride level tends to be moderately elevated for a few 
weeks following a brief decrease (Fredrickson, 1969).

Their levels on first day are close to the 
levels attained 3 months later (Pyle et al, 1971).

**SERUM ENZYMES**

Enzymes are released in large quantities into 
blood from necrotic heart muscle following myocardial 
infarction. The rate of liberation of specific enzymes 
after infarction differs from each other. The enzymes 
which are usually of diagnostic significance are SGOT 
CPK and LDH. The serum glutamic oxalacetic acid (SGOT) 
begin to rise above normal value (3-40 units/l) within 
6-12 hours after infarction, reaching a maximum within
1-3 days and remaining elevated usually till 4th and may be upto 8th day. Increase above 40 units is found in more than 97 percent of myocardial infarction (Agress, 1960). It is not very specific enzyme because it is also found in skeletal muscle, liver and RBC and damage to these tissues may also liberate this enzyme. Thus in congestive heart failure, shock and hepatitis, this enzyme will be elevated.

CPK is found in heart, brain, and skeletal muscles but not in lungs and liver. Damage to these tissues liberate this enzyme in blood. It can be elevated by strenuous exercise, chronic alcoholism, convulsions, pulmonary disease, cardioversion, cerebrovascular disease and intramuscular injection.

In clinical practice, CPK determination is of little value when the patient with chest pain is receiving intramuscular injections because its level may increase 5-20 times (Meltzer, 1970; Shaft, 1970). The CPK has three isoenzymes namely BB, MB and MM. The CPK-MM isoenzyme has been reported to be both sensitive and specific in myocardial infarction (Robert, 1973; Wagner, 1973). When more than 2 percent of total CPK is CPK-MM, it is abnormal. Positive responses were not found in cases of CHF, cardiac arrhythmias, unstable angina, pulmonary embolism, and cardioversion. CPK-MM may appear as early as 4-6 hours after the onset of infarction and reaches peak values at 18-24 hours, at the same time as total CPK.
activity returns to normal at 48-72 hours (Rapaport, 1977). In myocardial infarction CPK-MB should exceed 3 percent of total CPK, when total CPK exceeds 100 units per litre.

In myocardial infarction, the level of LDH rises during first day, peaks at 3-4 days and returns to normal in 14 days. There are five isoenzymes of LDH, LDH is specific for heart. Its value rises before the rise of total LDH and may rise when there is no rise in total LDH. Increased LDH_1 is a more sensitive indicator of myocardial infarction than total LDH, being raised in more than 95 percent of cases.

Raised serum myoglobin values were found in all 32 cases of acute myocardial infarction studied within 12 hours after onset of chest pain (Meidlin et al, 1978). Serum myoglobin values might reflect the size of myocardial infarction (Kogen, 1975). Myoglobinuria exceeding 5 mg percent was found in all cases of acute myocardial infarction studied. Myoglobinuria often preceded the rise in serum cardiac enzyme levels and was a more sensitive indicator of cardiac muscle necrosis (Bernstein, 1973).

Serum nickel values rose in 72 percent of patients with acute myocardial infarction studied 12-36 hours after its onset. The mechanism of its rise is not known (Sunderman, 1978).
E.C.G.

The ECG is of paramount importance in recognition of myocardial infarction especially when the history is atypical or when the patient is so ill that he is unable to give a proper history (Wilson et al, 1944; Myers, 1949).

However, there are limitations of ECG recognition of myocardial infarction. While the ECG is seldom normal following acute myocardial infarction, the diagnostic changes are present in only 60 percent cases of acute myocardial infarction (Zins and Cosby, 1950). In another study changes were diagnostic in 82 percent but only in 27 percent when there was an already healed infarct (Sullivan et al, 1978).

The earliest changes are hyperacute T wave changes indicating myocardial ischaemia while injury pattern evolution of transmural infarction is an elevation of ST segment in leads facing the infarct area and pathologic Q waves denote necrosis.

In anteroseptal infarction - Q, ST, T wave changes appear in lead $V_1 - V_4$.

Anterolateral infarction $I, aV_4, V_5, V_6$.

Extensive anterior wall $I, aVE, V_1-V_6$.

Inferior wall $II, III, aVF$.

True posterior MI - Prominent R wave depressed ST segment and peaked T wave appear in $V_1, V_2, V_3$.

Rt ventricular infarction is recognised by ST elevation in $V_{4R}, V_{5R}, V_{6R}$.
Usually for the first few hours or a day or so after chest pain there are only ST and/or T changes and only after then pathological Q waves appear (Mather, 1965) so the serial ECGs are very important for diagnosis of myocardial infarction.

ST segment remains elevated for several days to as long as 1-2 weeks then it settles down in an uncomplicated infarction.

Pathologic Q wave may increase in size for several days or weeks. Later it remains stationary or decrease in size, perhaps due to scarring and decreased size of infarcted area. In an appreciable percent of cases the ECG, returns to normal or nondiagnostic pattern over years following myocardial infarction. Levine (1951) found ECG changes of old infarction in 20 percent cases, Kasegosted (1966) in 34 percent cases and Young (1970) in 35 percent cases only.

Right ventricular infarction is almost never an isolated finding and usually is associated with inferior and/or true posterior infarction and almost never occurs with anterior wall infarction (Robert, 1978).

Typical pain of myocardial infarction is deep and visceral the quality being heaviness, squeezing, acting (Ross et al, 1966). The other presentation can be in the form of tightness, pulling, constriction, burning sensation, bursting discomfort or stabbing. Pain and discomfort are most often present over middle and lower sternum or left precordium. However, it is not uncommon for the distress
to be centered elsewhere. Besides retrosternal and precordial regions, it may be located only in left upper arm, or radiate down the entire left upper extremity, at back over the interscapular region, lower jaw, neck, upper abdomen or both upper limbs. Pain below umbilicus has been described to be noncoronary.

Pain is usually associated with nausea, vomiting, sweating, weakness, giddiness, anxiety, breathlessness and palpitation. Other less common presentation of myocardial infarction with or without pain are sudden onset breathlessness, sudden loss of consciousness, confusional state, sensation of profound weakness, unexplained profuse perspiration the appearance of arrhythmia or merely an unexplained drop in arterial blood pressure. The urge to defecate may be an early symptom of acute myocardial infarction (Schroeder et al, 1976). This may lead to "bed pan death".

**PHYSICAL FINDINGS**

The majority of patients demonstrate a considerably high blood pressure during pain even though patient is normotensive in past.

It is also seen that most of the patients develop a gradual decline in blood pressure during first few days following myocardial infarction (Rothlitt et al, 1975). In 112 patients with acute myocardial infarction and 96 with cardiac ischaemia, serial BP readings were
made for 72 hours. During 1st hour after hospital admission 31.7 percent had a BP of 160/100 mm Hg or higher and by 6th hour, without specific antihypertensive therapy only 6.3 percent had BP in this range (Gibson, 1978).

Most patients seen within 30 minutes of chest pain have an abnormal heart rate and blood pressure (Webb et al, 1972). Sympathetic overactivity as manifested by sinus tachycardia with or without transient hypertension, is more common in patients with anterior infarction. The genesis and significance of sympathetic overactivity in patients with acute myocardial infarction is unknown. In experimental myocardial infarction, sinus tachycardia has been shown to have a possible adverse effect on the ischaemic myocardium and stimulation of sympathetic nerves lowers the ventricular fibrillation threshold (Norris et al, 1972).

Sinus tachycardia in myocardial infarction may also occur due to fever, anxiety, pericarditis, volume depletion, pulmonary embolism and cardioaccelerator drugs. However, persistent sinus tachycardia, is an ominous sign because it is commonly associated with severe left ventricular dysfunction. In some cases it may precede other findings of left ventricular dysfunction (Norris et al, 1972).

Sinus bradycardia with a heart rate of 40-60 beats/min. is sometimes present, especially when there is seen within first hour or two of the even (Romhilt,
1973 and Pentridge, 1974). Various mechanisms have been proposed to explain the early bradycardias: stimulation of the vagal neuroreceptors in the region of coronary sinus and atrioventricular node, ischaemia of the sinoatrial and atrioventricular nodes and interference with cholinesterase activity by the ischaemic process. Bradycardias are not only more frequent but also are more serious at the very onset of myocardial infarction, because arterial hypotension is found in the majority of patients with bradycardia and blood pressure is below 80 mm Hg in nearly half of these patients (Pentridge et al, 1974).

The importance of bradycardia in the genesis of serious ventricular tachyarrhythmias, including ventricular fibrillation becomes apparent when an increasing the heart rate which had earlier showed down, ventricular ectopics are abolished (Warren et al, 1976).