CHAPTER I

REVIEW OF LITERATURE.
CHAPTER II

REVIEW OF LITERATURE

SOME BASIC CONSIDERATIONS

CARDIAC TISSUES:

The myocardium is the most important structure of the heart. Because its contraction causes the blood to flow. It should be realised that only part of the cardiac walls consists of muscle fibres and that within the muscle fibres the contractile substance is limited to the fibrils. About half of the heart's weight is made of non-contractile material such as the Sarcolemma in the muscle fibres, connective tissue in the heart skeleton, Tendones and valves, and finally blood vessels and Lymphatics and nerve fibres. All these elements are inter­oven with the muscle fibres or closely connected to them. During Cardiac contraction or relaxation they are deformed and resists to some degree to shortening or lengthening of the myofibrils. Little is known about the mechanical effects of the coronary vessels upon the function of the ventricles. They appear heavily engorged with blood in the live organ. Five to ten percent of the cardiac output passes through the coronary system. A significant mass of beating heart consists of circulating blood, contained within the anatomical bounds of the epicardium.
CORONARY CIRCULATION:

Blood supply to the heart comes from coronary arteries and also directly from the blood within the cavity of the heart. Coronary arteries are the branches of the aorta. They are the right and the left. The anatomic patterns are classified as right coronary artery preponderant or left coronary artery depending upon which artery crosses it. The crux is that region of the posterior surface of the heart where all four chambers and the interatrial and the interventricular septa meet (Anderson 1964).

COLLATERAL CIRCULATION:

Anastomotic communication of up to 40 micra diameter exist between coronary vessels in normal heart. This is of little functional importance, but these may dilate up to 200 micra at the time of need (Frimetal et al 1947).

In such hearts a coronary artery arises from the aorta to supply the pulmonary corus. It is seldom occluded and it may serve as a source of collateral circulation.

The basic vein connect coronary vessels to the heart chamber. Normally it carries a small but significant blood flow. These may also rise up to the occasion at the time of need and maintain a substantial circulation.
FEW WORDS OF PECULIARITY OF CORONARY ARTERY:

Coronary arteries have thicker internal coat compared with the similar calibre arteries of the body. These are muscular type of arteries with elastic fibres distributed among the muscle fibres of the media. There is no well defined external elastic layer. These arteries run apart of their course with the substance of the myocardium and compression of this part during systolic may lead to natural strain on the proximal epicardial segment.

COMMON SITES OF OCCLUSION AND CONSEQUENT INFARCTION, IF OCCURS:

Commonest is the anterior descending branch of the left coronary artery (Crawford 1961). Next in frequency is the right coronary artery and next is left circumplex branch. The infarction, when occurs, is naturally in the distribution of supply of these branches, often modified by collaterals. It is easy to imagine that a sudden occlusion will give little time for the collateral channels to develop, whereas in gradual occlusion there is a fair chance of coronary collateral circulation to develop. It is not dependent on individual's age as was formerly believed. Although the usual consequences of coronary occlusion is acute myocardial infarction, there are exceptions; patients who die, say within hours of coronary
occlusion may not reveal infarction, as there is no time for necrosis to develop. Conversely narrowed coronary vessels may precipitate acute myocardial infarction.

WHAT IS MYOCARDIAL INFARCTION:

Myocardial infarction is usually the result of occlusion of one or more coronary arteries. However, repeated experience has shown that this is by no means always true. Many theories have been suggested to account for the occurrence of myocardial infarction and sudden death when neither acute occlusion nor recent haemorrhage in subintimal spaces of the coronary arterial system can be found. It is recognised that the balance between adequate and inadequate blood flow in a patient having disease of the coronary arteries is a delicate one since increased metabolic demands by the myocardium may place the patient in negative balance. Thus acute coronary insufficiency may be precipitated in the absence of acute occlusive lesions of the coronary arteries. However, the circumstances which imitate acute insufficiency by increasing the energy demands on the myocardium may not be obvious or recognizable clinically.

Patients with prolonged episode of pain and equivocal evidence of myocardial infarction may
experience one of the following clinical courses:

1. Sudden death;
2. Recovery without persistent ischaemia;
3. Recovery after development of infarction;
4. Death after development of infarction.
ENZYMES (IN GENERAL):

Enzymes are of supreme importance in biology. Life depends on a complex network of chemical reactions brought about by the specific enzymes, and any modification of the enzyme pattern may have far-reaching consequences for living organism. On the other hand, enzymes, as catalysts, are receiving increasing attention from physical chemists. The mechanism of action of enzymes is in itself one of the most fascinating field of scientific investigation.

Enzymology has become a large rapidly developing subjects. It is connected with many sciences, especially biochemistry, physical chemistry, bacteriology and microbiology, genetics, botany and agriculture, pharmacology and toxicology, pathology, physiology, medicine and chemical engineering.

The beginning of the subject "Enzymology" can be traced back to the early nineteenth century, but the great developments have come during the last forty years. The first clear recognition of an enzyme was made by Payen and Persoz in 1833 when they found that an alcohol precipitate of malt extract contained a thermolabile substance which converted starch into sugar.
Towards the end of nineteenth century, increasing knowledge of the structural organic chemistry or substances of biological interest made it possible to study the range of action or 'specificity' of enzymes. It is to Emil Fischer (1894) who brought the idea of enzyme specificity and of the close steric relationship between enzyme and substrate.

The main interest during the early days of the subject was centred on the enzymes of digestion and fermentation; the importance of the intra-cellular enzymes was recognised much later. In fact the purification of intra-cellular enzymes started not before 1937. Since that date the emphasis has entirely changed, and the enormous increase in the number of known enzymes has been largely due to the discovery of new intra-cellular enzymes. The increased knowledge of the enzymes of living matter has brought the increased understanding of the mechanism of many of the most fundamental vital process, especially of the metabolic process which lead to the production and utilization of energy, on which life depends.

Enzyme Kinetics, which has undergone great development since the classical work of Henri and Michaelis early in the century, has now reached an
advanced stage and is being actively pursued, with the object of elucidating the mode of catalysis by enzymes. The mechanism of enzyme catalysis is also being studied by more direct methods, including especially the use of isotopes. Many different lines of study are converging to give the beginnings of a picture of the intimate mechanism of enzyme action, which is one of the most fascinating problems of the present time.

Perhaps the most satisfactory definition of enzyme is: a protein with catalytic properties due to its power of specific activation. The word protein, which rules out such non-enzymatic catalysts as glutathione and other co-enzymes, is a generalization from the fact that all the enzymes which have been obtained in the pure state have proved to be proteins, and enzymes generally, whether isolated or not possess properties characteristic of proteins e.g. thermolability. The second half of the definition rules out such non-enzymatic proteins as cytochrome which indeed is a catalytic protein, but by virtue of its action as a carrier and not by activating any other substance. Such proteins may be compared with other co-enzymes which function as biological.
catalysts only when themselves activated by specific enzymes. The substance on which an enzyme acts and which is activated by the enzyme is turned the "Substrate" of the enzyme. Activation is a phenomenon, which takes place by the formation of a specific activated complex which involves changes of both kinetic and potential energy.

The facts of specificity show that the substrate combines with a particular part or site in the enzyme, and this is known as the 'active centre'.

It is frequently found that the addition of substance which do not take part in the reaction diminishes its velocity. This substances are known as inhibitor.

Finally, it must never be forgotten that enzymes derive their greatest importance from the fact that life itself is intimately bound up with enzyme catalysis. Changes in the enzyme activities of body fluids during disease are of diagnostic and prognostic value. Many of the diagnostically important enzymes occur intracellularly and they are frequently associated with particular subcellular particle. Glutamate dehydrogenase and isocitrate dehydrogenase
are found mainly in the mitochondria, while acetyl cholinesterase, alkaline phosphatase and glucose-6-phosphotase occur principally in the microsomes. In a normal subject the circulating enzyme levels are kept within limits by a number of mechanisms. Release of enzymes by the tissues are balanced by excretion into bile or in urine or by inactivation. During disease, the plasma enzyme levels may rise very considerably. Virus or bacterial incubation causes the damage to cells, thereby altering membrane permeability and consequent release of enzyme to the extra-cellular fluid. Since enzymes are not evenly distributed throughout the body, elevation of blood levels of certain enzymes may provide valuable information concerning the nature of the lesion under investigation. Sometimes a diseased process may lead to a diminution of the circulating enzyme activity. For example, in some liver diseases protein production is impaired and these leads to a diminution of plasma pseudo cholinesterase activity (Willkinson 1962).
MECHANISM OF ENZYME LEAKAGE (IN GENERAL):

Most of the workers dealing with the abnormal elevation of enzymes in myocardial infarction, in muscular dystrophy or any other similar conditions of muscles could not specifically propose the mechanism of the intracellular enzyme leakage through the membrane resulting in increased serum level. So assumptions in this respect are many.

Pearce et al (1964) suggested that the intracellular enzymes are liberated in excess in the serum as a result of local inflammation or ischaemic necrosis due to some pathological conditions present in the muscle. They emphasised on the increased permeability of the cell membrane, which is dependent upon some other conditions in the neighbourhood of the tissue cells concerned. This is also held by Thomson et al (1960), Thompson et al (1959) and Hughes (1963).

Saito et al (1963) and Griag et al (1963) stated that increased serum level of creatine phosphokinase in hypothyroid was found to be reversed by appropriate treatment by thyroxine and they found that thyroxine has a direct inhibitory effect on the
activity of Serum Creatine Phosphokinase and their findings did not correlate with the hypothesis of increased membrane permeability.

Zierler (1957) with experiment on rat diaphragm noted that the diffusion of aldolase took place from the muscle fibres and this was greatly enhanced by glucose lack, anoxia and high potassium concentration. All these factors have in common effect upon cellular metabolism. The permeability properties of membrane is dependent upon this metabolic activity and chemical potential energy responsible for this metabolic alteration is believed to be due to afflux to potassium ions and influx of sodium ion in cells. Fowler et al (1962) observed that a number of enzymes (two transaminases, aldolase and two dehydrogenases) levels in skin are abnormally elevated after strenuous exercises. Their findings in respect of leakages of these enzymes are quite in agreement with those of Zierler (1957). Dawson (1966), while conceding with the observation of Zierler (1957) further stated that three factors seemed to influence the degree of elevation of serum enzymes after tissue damage - the rate of release of enzyme from the tissue, the rate of clearance from
the serum and normal level, presumably contributed by normal wear and tear of cells.

Pellegino and Bibbiani (1964) suggested that the increase in permeability of all membrane depends upon general response to some "noxious stimuli" such as injury, X-ray irradiation to tissue cells. They considered glucose - lack, anoxia, increased potassium concentration in serum are of accessory factors in enhancing the permeability of the cell membrane. This concept of increased permeability are well corroborative with that of Dowben and Zackerman (1963) who narrated this permeability is an effect of certain kinds of injuries (X-ray irradiation etc.) and disturbances in metabolism in cells.

**ENZYMES IN MYOCARDIAL INFARCTION:**

Transient elevation of several serum enzymes are observed during days following an episode of Myocardial Infarction. A brief outline of important of them are discussed here.

La Due et al (1954) first reported the increased serum glutamic oxaloacetic transaminase (SGOT) activity in acute myocardial infarction. He found elevated values of serum oxaloacetic transaminase (SGOT)
level in 74 out of 75 patients and the peak rises were proportional to the size of infarction.

Nydick et al (1955) produced a series of graded infarcts by partial occlusion of the coronary arteries of dogs. Muscle in the infarcted zones was found to contain appreciably less glutamic oxaloacetic transaminase than surrounding myocardium and there was a rough parallel between the amount of heart muscle infarcted and the rise in serum glutamic transaminase (SGOT). The duration of the elevation of the serum glutamic transaminase (SGOT) was also proportional to the extent of tissue damage.

Rudolph et al (1955), Steinbergh et al (1955), Merrill et al (1955), La-Due and Wroblewski (1955), etc. reported on both clinical and experimental studies that the serum glutamic oxaloacetic transaminase activities begin to rise in 4 to 6 hours, reaches its peak in 18 to 36 hours and return to normal in 4-6 days.

Chinsky et al (1956), Agress et al (1956), Kattus et al (1956), Merrill et al (1956), etc. have the same observation as reported by the 1955 group of workers.

Ordell (1956) examined the value of
serial parallel determinations of three enzymes, serum glutamic oxaloacetic transaminase, serum Lactate dehydrogenase (SLD), serum malate dehydrogenase (SMD) and found that the serum malate dehydrogenase activity was maximal in 16-20 hours after infarction; SGOT and SLD reached peak values in 20-34 hours and 30-40 hours after occlusion respectively.

White (1956) preferred serum Lactate Dehydrogenase (SLD) to glutamic oxaloacetic transaminase (SGOT as an aid to the diagnosis of myocardial infarction, because of the relative ease of its determination and of the longer duration of its elevation above normal range.

White (1956), Volk et al (1956), Bing et al (1956) studied extensively increased aldolase activity in myocardial infarction.

La-Due (1957) concluded after study of 300 patients with acute myocardial infarction that the peak rise of serum glutamic oxaloacetic transaminase (SGOT) activity to 250 units or above was always a grave prognostic sign. Sinha, B.C. (1958) studied serum Lactate dehydrogenase (SLD) activity
in myocardial infarction in West Bengal. Agress (1959) has reviewed the extensive literature on this subject and has reported that of 1,255 cases of proven myocardial infarction in which the serum glutamic oxaloacetic transaminase (SGOT) was determined, not fewer than 96.9% exhibited positive correlation. The small number of cardiac patients who are reported to have raised serum glutamic oxaloacetic transaminase (SGOT) activities without apparent infarction are considered by Agress to have had small infarction. In many of the series reviewed, cases were included only when the diagnosis were unequivocal and in consequence a higher proportion showed raised enzyme levels than would have been expected had all the cases been unselected.

Howell and Smith (1959) observed raised serum glutamic pyruvic transaminase (SGPT) level in 23 patients out of 28 of acute myocardial infarction.

Freeman et al (1959) found variable elevation of serum lactate dehydrogenase (LD) in contrast to the regular increase in the serum glutamic oxaloacetic transaminase (SGOT) in this condition.

Wilkinson and Pryse-Davies (1960) observed
in a daily serial determination of serum glutamic transaminase (SGOT) activity in a relatively mild cases of myocardial infarction, the electrocardiogram supported the diagnosis, but in some cases, he found it was difficult to interpret because of the changes due to previous infarction and digitalis therapy.

Wroblewski et al (1960) and Wieme (1959), studied the electrophoresis of serum lactic dehydrogenase (SLD) enzyme in normal adults that it consists of principally of five isoenzymes. They are anodic isoenzymes (L.D.1 and L.D.2) or fast moving isoenzymes, cathodic isoenzyme (L.D.4) and L.D.5) or slow moving isoenzyme and isoenzyme of intermediate mobility (L.D.3). In cardiac muscle the enzyme is of the first type whereas in liver and skeletal muscle LD4 and LD5 predominate. Fast moving isoenzymes rose predominantly in myocardial infarction and even in pericarditis and persisted longer than the total serum lactic dehydrogenase activity.

Elliott and Wilkinson (1961) observed normal serum lactic dehydrogenase (SLD) activities in a number of confirmed cases. But serum lactate dehydrogenase (SLD) and serum alpha hydroxy butyrate
dehydrogenase (SHBD) ratio is frequently below the normal range, indicating that heart tissue is probably making an abnormal contribution to the circulating enzyme level. 

Agostoni et al (1965) reported increased level (between 4-160 units) of gamma glutamyl transpeptidase activity in myocardial infarction (normal range 19.8 ± 3.9F units).

In the first 4 days the serum level of Gamma-Glutamyl transpeptidase remain, however, normal. The enzyme activity increased from the 5th day, reached the maximum level at about the tenth day and did not return to normal range until after 30 days.

Warburton et al (1965) and Smith (1964) established the typical serum creatinine phosphokinase (SCPK) pattern in 20 recently developed cases of myocardial infarction and found out that serum creatinine phosphokinase (SCPK) remained raised for about 4½ days, which was the longest period of increase recorded. In proved myocardial infarction serum creatinine phosphokinase was raised to between 6 and 20 times the upper normal level.

Griffiths (1966) demonstrated in a study of 79 patients suffering from myocardial infarction,
the serum creatinine phosphokinase (SCPK) follows a similar course as serum glutamic oxaloacetic transaminase (SGOT). Serum creatinine phosphokinase (SCPK) rises early in the illness, reaches a peak by the second day and is usually normal by the 6th or 7th day. Serum creatinine phosphokinase (SCPK) activity is raised in 96% of cases of myocardial infarction.

Oka (1954), Moore et al. (1960) reported that pseudo cholinesterase in plasma decreases in myocardial infarction. Detail about this enzyme is given in Chapter IV. Basu, Chatterjee and Ganguly (1970) proposed the prognostic importance of this enzyme in myocardial infarction. So it was found worthwhile to study the plasma pseudo cholinesterase in myocardial infarction in tropical climate like West Bengal in the present study.
ASCORBIC ACID METABOLISM IN MYOCARDIAL INFARCTION

STRESS AND MYOCARDIAL INFARCTION:

The epidemiology of stress is exceedingly complex. Response to individual to the environment seems to be much more critical than the events overtly taking place in the environment. Hence it is difficult to assess the degree of stress in a particular individual when he is reacting to a "life situation" with which he is confronted. For these and other reasons the behavior of stressful situation like myocardial infarction is difficult to assess and it varies from individual to individual depending on various factors - atherosclerosis, serum lipid content, obesity, emotional situation etc. It has been reported that student display a transient elevation of the serum cholesterol level immediately prior to important examination.

There is some evidence that a certain type of "personality profile" is associated with predisposition to coronary heart disease and that patient with such a profile secrete significantly more epinephrine and nor-epinephrine than control subjects (Katz, 1958). So the coronary prone individual have been found to have higher serum cholesterol and increased urinary excretion of vanillyl Mandelic acid.
Myocardial Infarction is a stressful condition, both physical and emotional stress play in this condition. Like physical stress emotional stress elevate serum cholesterol levels and shorten the blood clotting time transiently. In this stressful situation, body homeostasis is greatly influenced. It may operate by disturbing endocrine balance e.g. via Pituitary adrenal stimulation and catecholamine release (Friedman et al, 1959), thereby influencing blood pressure, cholesterol metabolism, coagulation and fibrinolytic activity. There is every probability that the transient hyperglycaemia, which occurs in myocardial infarction may operate in the above manner or by some unknown mechanism including an action via the nervous system.

INCIDENCE OF HYPERGLYCAEMIA IN ACUTE MYOCARDIAL INFARCTION


Vytilingam (1966), Datey et al (1967), Lal et al (1967), observed hyperglycaemia in established cases of myocardial infarction (after acute infarction) in different parts of the world.

Lal et al (1968) reported abnormal glucose tolerance curve after acute myocardial infarction in higher income group patients. He studied 120 cases and found that with the passage of time the incidence of hyperglycaemia curve falls and that of normal curve rises. The incidence of hyperglycaemic curve was much higher 66.03% in patient above 50 years of age as compared to 38.7% in patients with age below 50 years in their series. It is quite possible that to the stress of acute myocardial infarction the elderly patients react more than the younger age group as far as the development of hyperglycaemia is concerned.

Datey et al (1967) also reported a higher incidence of hyperglycaemia (81.5%) in the infarction patients above 50 years as compared to those below 50 years 60.0%.

Eckerstrom (1951), Sowton (1962) also reported abnormal glucose tolerance curve in 74% and 73% cases respectively after myocardial infarction.

Gruickshank (1931) first suggested that the arteriosclerotic changes in the pancreas are responsible for this transient hyperglycaemic condition after acute
myocardial infarction. Sowton (1962) felt that myocardial infarction precipitated latent diabetes. Vallance Owen et al (1963) reported the presence of insulin antagonism in patients with cardiac infarction. But Raab et al (1936) thought that the stress of accompanying pain etc. resulted in increased adrenocortical activity and disturbances of the hypothalamus. Mathur et al (1968), who observed 76.5% of diabetic glucose tolerance in myocardial infarction cases as compared to normal controls (16%) matched for age and sex, suggested the probable reason for such a finding may be that the acute physical and psychological stress which may follow an episode of acute myocardial infarction may excite the adrenopituitary axis and this disturb the glucose tolerance probably to a greater extent in those who are predisposed to diabetes. The other mechanism may be the irritation of vegetative nervous system. The resultant hypothalamic disturbance leads to temporary hyperglycaemia.

ASCORBIC ACID METABOLISM

Burns et al (1951) carried out metabolic study of ascorbic acid in guineapigs after fortifying the ascorbic acid with radioactivity (c^{14}) and respiratory CO_{2} and urinary oxalic acid were determined. Conversion of ascorbic acid to CO_{2} and urinary oxalic
acid were found to have the usual phenomenon, the effect of the former being noted as prominent.

ABT et al (1963) studied the metabolism of ascorbic acid in human. They stated that the major portion of the acid excreted within first few hours following ingestion, through expired air and urine. Each molecule of C\(^{14}\)O\(_2\) in the expired air represents a molecule of the radioactive ascorbic acid administered. The excretion of the same in urine represents intact ascorbic acid as well as degradation products. Metabolic study was also carried out by Atkins et al (1964) in normal adult male subjects after applying single physiological does of ascorbic acid - 1-C\(^{13}\). The end product of ascorbic acid through urine and respiration were studied. It was reported that the exalate formation and urinary excretion of ascorbic acid accounted for about half of the total ascorbic acid turnover and other half being converted to respiratory CO\(_2\) from carbon atom 1. Bellman and Burns (1958) used canbonyl-labelled - L. ascorbic acid, to study the metabolic effects in man and guineapigs and stated that decarboxylation is presumably the first step in the complete oxidation of carbon chain to CO\(_2\). In human, they practically did not observe oxidation of the carboxylcarbon of L. ascorbic acid to CO\(_2\).
whereas in guineapig the reverse reaction was noted and 70% of the carboxyl labelled - L. ascorbic acid (C\textsuperscript{14}) was found to have been converted into CO\textsubscript{2}.

From this they put forward a hypothesis that the metabolic rate (by way of carboxylation of L. ascorbic acid) of ascorbic acid is comparatively slower in human biological system than that of the guineapigs. Baker et al (1965) held the conversion of L. ascorbic acid to CO\textsubscript{2} in human biologic system is not the usual sequence of metabolism of ascorbic acid. The production of CO\textsubscript{2} observed by some workers was probably due to impurities in the materials used.

Damron et al (1952) stated that spontaneous conversion of injected ascorbic acid to dehydro- ascorbic acid and diketogulonic acid occurs in vitro at physiological pH ranges. The same authors demonstrated metabolic paths of the three compounds - ascorbic acid, dehydro ascorbic acid and diketogulonic acid in "tissue recovery experiment" in guineapigs. Of these, ascorbic acid is most stable, dehydro is moderately so, and diketogulonic acid rapidly disappears from the system; dehydroform of the acid possessing the property of spontaneous conversion to ascorbic acid. To represent the same this may be said down as:

Ascorbic acid $\xrightarrow{\text{Dehydroascorbic acid}}$ Diketogulonic acid.
The diabetogenic effect of dehydroascorbic acid (DHA) and diketogulonic acid (DKA) are known for a long time. Patterson (1950) offered the explanation that they act by destroying the sulphydryl groups of enzymes essential to normal carbohydrate utilization. Evidently sulphydryl and disulphide groups are quite important in carbohydrate metabolism.

Martinez (1951) has shown that the sulphydryl content of blood and tissues falls in depencreatized animals and that pretreatment with sulphydryl compounds decreases the severity of the resultant diabetes. This hypothesis is developed by the animal experiment.

Rally et al (1948) studied the effect of administered insulin on blood ascorbic acid levels in dog and reported that insulin administration caused a prompt fall in whole blood and plasma levels of ascorbic acid and a decreased urinary excretion. The level in the buffy coat rose slightly, not nearly enough; however, to account for the lowered plasma level. It was concluded that ascorbic acid shifted to intravascular tissue as a result of insulin administration, possibly to tissues where the vitamin and the hormone are concerned together with
It is a fact that Vitamin C is increased in scorbutic guineapigs with consequent hyperglycaemia (Sigal, 1936; Nair, 1941; Giroud, 1941; Banerjee et al, 1947, 1958) in scorbutic monkeys (Banerjee et al, 1957), in human subjects with low ascorbic acid level (Hjorth, 1940; Sechar, 1942).

Intravenous injection of dehydro ascorbic acid (DHA) in rat leads to chronic hyperglycaemia and glycosuria. Cysteine and glutathione, if injected intravenously just before the injection of dehydro ascorbic acid (DHA); can prevent this diabetogenic action. Substances which are diabetogenic which also cause diminution in the insulin content of the pancreas, also lower the glutathione content of the tissues. In human diabetes also, glutathione content of blood and pancreas is low. It is known that glutathione combines with dehydro ascorbic acid (DHA) and thereby prevents the diabetogenic action of this substance. Increased dehydroascorbic acid (DHA) present in the tissues of scorbutic guineapigs might combine with glutathione of the tissues and thereby cause a fall in the available glutathione concentration in the Beta cells of the pancreas. The protective role of glutathione on the sulphydryl enzymes in the beta cells is the further
jeopardized, which result in the death of the beta
cells and administered secretion of insulin
(Banerjee, Deb and Belavady, 1952).

Ketone bodies such as acetoacetate and
beta hydroxy butyrate cause marked disturbances in
carbohydrate metabolism with depletion of reduced
 glutathione (GSH) and onset of diabetes. The develop-
ment of hyperglycaemia caused by acetoacetate was
aggravated in scorbutic guineapigs. That ascorbic
acid is highly beneficial in checking ketolysis
and that the administration of Ketone bodies caused
depletion of ascorbic acid, show a close relationship
between each other. The rate of reducing compounds
such as GSH in the oxidation of ascorbic acid to
dehydro ascorbic acid is known. The hydrolysed glucose
cyclo-acetate (GCAL) which is a reducing compound
converts dehydro ascorbic acid to ascorbic acid. Like
GSH, which is converting dehydro ascorbic acid to
ascorbic acid. Glucose cycloacetoacetate which is
a precusion of L-ascorbic acid in rats, depressed
liver Ketogenesis in normal as well as hyperthyroid rats
(Nath et al, 1968).

Nath et al (1968) proposed that the possi-
bility of disturbances in the process of reconversion
of dehydroascorbic acid to ascorbic acid and subsequent
increase in the concern of the former in the blood and tissue, before it can be further broken down to diketogulonic acid etc. Dehydro ascorbic acid has also been reported to be diabetogenic acting synergistically with alloxan to produce diabetes. Increased amounts of dehydro ascorbic acid and diketogulonic acid in the liver hemogenate of rats injected with ketone bodies conform this view.

Ganguly S.K. and Ghosh B.P. (1969) studied the percentage of plasma dehydroascorbic acid and diketogulonic acid combined in total ascorbic acid in normal human subjects and diabetic patients of different grade. Among normal subjects, whose blood sugar range was 80 to 120 mgs/100 ml. plasma, mean value of dehydro ascorbic acid and diketogulonic acid combined percentage was 59.8% (S.D. ± 5.9, range 45.4 to 70.0). Mean percentage values of dehydro ascorbic acid and diketogulonic acid combined were 74.6% (S.D. ± 9.4, range 66 to 90) in diabetic patients with blood sugar range 121 to 150 mgs/100 ml. plasma, 84% (S.D. ± 7, range 75 to 100) in patients with blood sugar range 151 to 250 mgs./100 ml. in severe diabetic group of patients with blood sugar about 250 mgs./100 ml. plasma. On the other hand, the total ascorbic acid content in hyperglycaemic state was found to decrease to some
There is a definite correlation between blood dehydro ascorbic acid diketogulonic acid content combined and blood sugar. The higher is the sugar level in blood, the greater is the percentage of dehydro ascorbic acid and diketo gulonic acid content combined in total ascorbic acid.