Discussion
DISCUSSION

The human body contains blood, phlegm, yellow bile, and black bile. These are the things that make up its constitution and cause its pains and health. Health is primarily a state in which these constituent substances are in the correct proportion to each other, both in strength and quantity, and are well mixed - Hippocratic treatise.

The Hippocratics postulated that diseases arise because of humoural imbalances. Imbalances arise from natural causes such as heredity, regimen (diet and other behaviour), and climate. Different kinds of imbalances produce different diseases with symptoms and development that were acutely observed by the Hippocratics. The course of a disease was affected by the development of a particular humour, producing crises that signalled basic changes in patient outcome.

Health is not an absolute quantity but a concept whose standards are continually changing in different lands with the acquisition of knowledge and the establishment of cultural objectives. Disease is a reaction for the worse between individual man and the stresses, strains, and other adverse factors of his surroundings, the response being conditioned by the genetic make-up of the individual. The human body, a miracle of mechanical perfection is composed of an infinite number of cells that collect to form definite tissues that later group into organs. The infinitely complex and delicate structure of the organ may be damaged by a variety of influences. The cellular damage can be regarded as the fingerprints of disease.

From time immemorial, extensive study has been carried out about the importance of the blood groups in various diseases, for example, persons with group 'O' are susceptible to duodenal ulcer and rheumatoid arthritis, patients with blood group 'A' who take oral contraceptives are more prone for Thrombo-embolic disorders, and persons with group 'B' are more vulnerable to infection by small pox virus which contains an 'A' group antigen like substance (Sathiavakesan et. al., 1984). McConnell (1980) and
Rotter (1983) reported an association between peptic ulcer and several indirect genetic markers such as blood group association. Johnson et al., (1964) and Lowan (1973) reported that individuals with blood group ‘O’ are at an increased risk of developing antral gastric ulcer, and combined duodenal and gastric ulcer. The blood group profile of healthy population in North Kerala and that of the patients show that people with blood group A have a differential susceptibility to gastric carcinoma. In the present study, blood group ‘O’ predominated other groups with regard to lesions in the esophagus, stomach, small and large intestines, liver and the group with cancerous lesions. Blood group ‘A’ was predominant in non-cancerous lesions of the pancreas.

The liver plays an important role in the regulation of many aspects of carbohydrate, lipid and protein metabolism, as a result of which there is bi-directional passage across the hepatocyte surface membrane of substances such as glucose, aminoacids, glycerol, free fatty acids and vitamins. Carbohydrate is mainly stored in the liver as glycogen and regulation of hepatic glycogenolysis is largely responsible for the maintenance of normal blood glucose concentrations. Glucose can also be produced by gluconeogenesis within the liver by hydrolysis of fats and proteins and by the metabolism of fatty acids, glycerol and amino acids. Synthesis of triglycerides from glycerol and fatty acids, and of protein – which include both cell structural protein and enzymes from amino acids also occurs within the liver cell. Ammonia produced in the intestine from the interaction of enteric organisms with urea and aminoacids, and delivered to the liver through the portal vein and to a lesser extent ammonia derived from protein metabolism in peripheral tissues, is converted largely to urea by the Kreb’s-Henseleit cycle within the liver cell (Holldorf et al., 1970). The hepatocyte is responsible for the synthesis and release into the hepatic sinusoid of a number of proteins, which are exported including most of the major plasma proteins and lipoproteins. Certain endogenous products of metabolism such as bilirubin and many hormones, and exogenous substances such as
drugs, organic anions and toxins in the circulation are extracted from the plasma by the hepatocyte (liver cell). In contrast to the excretory function of the kidney, that of the liver deals largely with protein bound materials in the circulation. The substances that are insoluble in water are rendered water soluble within the hepatocyte either by the metabolic transformation to more polar products or by conjugation with radicals. These conjugates are subsequently secreted into bile or urine (Anthony and Berk, 1979).

The liver cell is especially liable to injury because of its function of taking up and dealing with many metabolites, toxic substances, drugs and poisons. The vast number of chemicals used industrially and pharmacologically provide an ever increasing hazard to the liver, particularly as it has been shown that certain chemicals are harmless to most individuals, but can cause extensive liver damage in individuals with a special susceptibility as, yet unpredictable. The liver also receives blood draining the gastrointestinal tract, and is exposed to poisons and toxins absorbed from the gut. A succinct account of hepatotoxic chemicals has been provided by Weinbren (1966). Their effects include liver cell injury and necrosis, inflammatory changes and cholestasis (stagnation of bile).

The pancreas is a mixed exocrine and endocrine organ. The exocrine portion consists of numerous dark-staining acini composed of tubular and spherical masses of cells that are the subunits of the lobule. The golgi structures in these lobules house secretory granules that are a group of 12 to 15 different enzymes. The endocrine portion consists of islets of Langerhans, which contain specialized cells that secrete insulin and glucagon - the hormones responsible for glucose homeostasis.

The liver has a large reserve capacity for the synthesis of urea, which is the main product arising from hepatic extraction and metabolism of ammonia. This process may be impaired in acute or chronic hepatocellular diseases. Apart from the mild and
moderate elevations in urea and creatinine in subjects with liver disease in the present study, the strikingly elevated levels of urea in subjects with cirrhosis (elevated to 197 mg/dL with corresponding increase in creatinine to 4 mg/dL in a subject), in subjects with hepatitis (a subject with malarial hepatitis recorded 157 mg/dL urea and 5.1 mg/dL creatinine and a subject with alcoholic hepatitis recorded 104 mg/dL urea and 3.8 mg/dL creatinine) may be due to the hepatic insufficiency and the corresponding increase in creatinine level in these patients with high urea concentrations may be due to complications heading to renal failure associated with hepatic failure as indicated by Anthony and Berk (1979). In addition, gastrointestinal haemorrhage which occurs in patients with cirrhosis complicating with portal hypertension may be a factor that tends to increase blood urea concentration as observed by Dawson (1965) who has also suggested an increase in blood urea levels during conditions of severe prolonged cholestasis which may have occurred in some of the patients with stones in the bile duct which in turn may have been formed due to increased bilirubin. In patients with cancer of the liver, bile duct and ampulla of Vater, the strictures or cancerous growth would have caused cholestasis. Dehydration and high protein intake are also supposed to increase blood urea concentration in hepatic diseases according to Dawson (1965). In subjects with pancreatitis, blood urea nitrogen may be significantly increased owing to prerenal azotemia and possibly even to acute renal injury according to Peter Banks (1998). In the present study, however there were no significant alterations in the urea levels in patients with pancreatitis.

The disturbances of glucose homeostasis in hepatocellular disease are associated with changes in the serum concentration of hormones which play an important role in the regulation of glucose metabolism, such as insulin, glucagon and growth hormone. The increased blood glucose level observed in subjects with liver disease, more specifically cryptogenic and other types of non-viral cirrhosis in the present study, have
also been reported earlier by Megyesi et al. (1967) and may be the consequence of hepatogenous diabetes. There has also been a phase of hyperbilirubinaemia in the subjects of the present study with liver disease and increased serum alkaline phosphatase (SALP) levels, which may have also contributed to the hyperglycaemic condition. This condition has been postulated by Anthony and Berk (1979). Moderate to severe hyperglycaemic levels were observed in subjects with acute and chronic pancreatitis (to a higher level in acute phase of pancreatitis) in the present study. This may be associated with increased levels of serum glucagon. An increase in the serum glucose level in chronic pancreatitis occurs when more than 80% of the pancreas has been destroyed. The increased level of blood glucose in pancreatic cancer in the present study may be due to the tumourogenesis involving the islet cells in the pancreas. Few subjects with liver disease displayed blood glucose concentrations as low as 36 mg/dL. This severe hypoglycaemic condition might be the consequence of massive hepatic necrosis that occurs during fulminant hepatitis and acute liver failure. Condition such as the above has been reported by Alvira and Forman (1974). Samson et al. (1967) reported that the hypoglycaemia in fulminant hepatic failure might be due to a large measure of impaired glucose release.

The association of jaundice and of change in the colour of the urine and faeces in relation to disease of the liver dates to antiquity (Watson, 1976) and tests involving the measurement of direct reacting and total bilirubin concentration in plasma can provide a great deal of information about the status of the hepatobiliary system. Bilirubin is the normal metabolic end product of a series of enzymatic reactions by which the haem moiety of haemoglobin and other haem proteins is catabolised. Most of the bilirubin produced normally results from catabolism of haemoglobin of mature red blood cells by reticulo-endothelial cells of the spleen, liver and bone marrow and is present in trace amounts of true conjugated (direct) bilirubin as determined by elaborate isotopic
techniques by Brodersen in 1974. Hepatic parenchymal cells catabolise circulating free haemoglobin if any. Unconjugated (indirect) bilirubin formed at the peripheral sites is transported to the liver complexed to albumin. In the microsomes of the liver cell, the unconjugated bilirubin later bound to ligandin or Z protein (organic anion binding proteins) is conjugated with mono or di-glucoronides (polar molecules) catalysed by UDP-glucoronyl transferase, to form water soluble conjugated (direct) bilirubin which is followed by rapid removal of conjugated bilirubin into bile (Anthony and Berk 1979).

In the present study, the bilirubin levels were markedly elevated in subjects with hepatitis induced by hepatotrophic viruses and drugs. Moderate elevations were noted in acute phases of hepatitis and malarial hepatitis. Mild elevations were observed in conditions of alcoholic and tuberculous hepatitis, cirrhosis and pancreatitis. Bilirubin levels were on the higher side in hepatitis when compared to cirrhosis in this study. These elevations may have resulted from an increase in bilirubin production or a reduction in the hepatic clearance of bilirubin. The elevated indirect bilirubin in conditions of hyperbilirubinaemia might be due to the inefficient delivery of bilirubin to the liver cell due to the poorly distributed hepatic blood flow in necrotic conditions, or defects in the mechanisms of hepatocellular uptake, intracellular binding or conjugation with polar molecules. The transport of direct bilirubin from the hepatocyte to the bile canaliculus appears to be extremely sensitive to various types of liver injury (Anthony and Berk, 1979). The elevated serum concentration of direct bilirubin may have resulted from ineffective excretion of the same in bile. This condition would have warranted the elevated bilirubin concentrations in conditions of cancers of the ampulla of Vater and bile duct as obstruction to the flow of bile in the biliary tract occurs in this situation. Elevations in bilirubin levels in pancreatic cancer might be due to the cancerous process involving the head of the pancreas adjacent to the bile duct leading to bile duct obstruction. Whereas in the conditions of hepatobiliary disease with no
obstruction to the bile flow, metabolic disorders involving a rate of bilirubin production exceeding its excretion might be the cause of increased direct bilirubin. In the present study there were no observations of isolated increase in the indirect bilirubin fraction which is the result of hepatic and/or haematologic cause. The alterations in direct bilirubin levels in this study specifically indicate hepatobiliary dysfunction. Findings as above have been documented by Berk et al. (1974). In patients where biliary excretion is reduced, a more modest degree of haemolysis – which commonly accompanies many forms of hepatobiliary disease may be responsible for the elevation of direct and indirect bilirubin concentration in the serum (Anthony and Berk, 1979).

The liver plays a crucial role in haemostasis. All of the major coagulation (clotting) factors (except factor VIII) are synthesized in the hepatocytes. Prothrombin is the clotting factor II and the prothrombin time (PT) test is one which tests the extrinsic coagulation pathway and depends on factors I, II, V, VII and X. Two phenomena associated with hepatobiliary disease are said to markedly affect the plasma concentration of liver cell-synthesized clotting factors viz., severity of a hepatocellular lesion and the degree of bile stasis (Anthony and Berk, 1979). Prolongation of the prothrombin time as observed in the present study with conditions of hepatitis and cirrhosis might have occurred due to the extensive hepatic parenchymal disease and hepatocellular dysfunction. Hepatocellular necrosis secondary to hypoxaemia may be associated with marked prolongation of PT (Anthony and Berk, 1979). In a few patients the prothrombin time exceeded 60 seconds and this reflects the degree to which the synthesis of clotting factors is depressed and this can be regarded as an index of hepatocellular insufficiency as defined by Roberts and Cederbaum (1972). Elevated PT in subjects with hepatitis 'B' virus and drug induced liver injury as observed in this study have also been reported by Robert Scheig (1996) who stated that a prolonged PT in liver disease indicates that the liver disorder is a chronic one and the elevated PT in acute hepatitis indicates that the
condition may lead to fulminant hepatitis. Prolonged PT may precede clinical
deterioration and has been related to the development of coma in acute hepatocellular
disease (Colombi, 1970; Hillenbrand et al., 1974).

Most of the enzymes, which are commonly measured in the sera of patients with
hepatobiliary diseases, fall into two large groups based on the usual significance of a
raised serum activity. In one group, increased activities predominantly reflect lesions
affecting the parenchymal liver cell (hepatocyte); in the other, they predominantly reflect
the lesions affecting the biliary tract (Anthony and Berk, 1979). The enzymes – Serum
Glutamic Oxaloacetic Transaminase (SGOT) also known as serum aspartic aminotransferase
(AST), and the Serum Glutamic Pyruvate Transaminase (SGPT) also known as serum
alanine aminotransferase (ALT) are located primarily in the cell sap of the hepatocyte.
These enzymes catalyse the following reaction;

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\begin{align*}
\text{L-Aspartate} + \alpha-\text{oxoglutarate} & \leftrightarrow \text{oxoglutarate} + \text{L-glutamate} \\
\text{L-Alanine} + \alpha-\text{oxoglutarate} & \leftrightarrow \text{Pyruvate} + \text{L-glutamate}
\end{align*}
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Most of the volume of SGOT and SGPT is found in the hepatocytes (Zimmerman
and Seeff, 1970). When the liver cell is injured, these proteins leak through the liver cell
membrane into the circulation and the serum levels will rise. The amount of enzyme
normally present in the circulation presumably is caused by the wear and tear, and
breakdown of cells throughout the body. The half-life of these enzymes in circulation is
very short, therefore serum levels give virtually a day-to-day reflection of the hepatocyte
injury (Robert Scheig, 1996). SGOT and SGPT are the most important markers of
hepatocellular injury. The highest serum levels of these enzymes are encountered in
patients with viral, toxin-induced, and ischemic hepatitis. Smaller elevations (<300 IU/L)
are observed in alcoholic hepatitis (Reichling and Kaplan, 1988). The AST-to-ALT ratio
in serum is also a useful indicator in the differential diagnosis of hepatocellular injury.
states. According to Anthony and Berk (1979), a raised activity of SGOT usually implies recent or continuing damage to the liver and a raised activity of SGPT suggests that there is probably a hepatic lesion.

In this study, the levels of SGOT and SGPT were elevated in subjects with hepatitis and cirrhosis, the striking elevation being almost 20 times the normal with regard to SGOT and 25 times the normal with regard to SGPT in subjects with hepatitis. Markedly elevated levels (> 1000 IU/L) were more specifically observed in subjects with hepatitis 'B' virus and hepatitis 'A' and 'E' virus induced hepatitis. The other groups showed a moderate or otherwise mild elevation of the enzymes. The striking elevation in the level of enzymes in viral hepatitis suggests that extensive liver cell injury or death has occurred. According to Clermont and Chalmers (1967), in acute viral hepatitis, the SGPT activity usually rises more rapidly and reaches a higher value than that of SGOT and remains abnormal for a longer time, and values of both enzymes tend to be higher in hepatitic conditions with hyperbilirubinaemia. The same was the finding in the present study too. In many instances of this study, the level of SGPT was greater than SGOT, which is suggestive of hepatocellular injury (Robert Scheig, 1996). It is assumed that marked elevation of serum aminotransferases (SGOT & SGPT) in acute hepatic syndrome may be due to increased release of intracellular enzymes (Wilkinson, 1970).

In certain types of liver disease, there was a mild elevation in both SGOT and SGPT levels and the SGOT level was higher than the SGPT. In subjects of this study with alcoholic hepatitis and cirrhosis, the SGOT activity was higher and moderately elevated than SGPT as observed by Zimmerman and Seeff (1970). Wilkinson (1970), Zimmerman and Seeff (1970) and Skrede et al. (1973) have suggested that if any hepatic lesion is associated with appreciable liver cell necrosis, the increased release of mitochondrial enzymes from cells may result in a relatively greater increase in SGOT.
than SGPT activity due to the increased contribution of the mitochondrial isoenzyme of SGOT. Mossberg and Ross (1963) have indicated elevated values of transaminases in association with the large bile duct obstruction. In the present study, the moderate elevations of these enzymes in cancers of the bile duct and gall bladder and mild elevations in cancers of the liver, ampulla of Vater and pancreas may be due to the obstruction of the bile canaliculi (in the case of liver cancer) and of the bile duct (in other cancers mentioned above) by the cancerous processes. Moderate elevations of activities, according to Neale et al. (1966), may also be due to primary biliary cirrhosis, drugs, cirrhosis, alcoholic hepatitis, cancer of the liver, acute pancreatitis, intrahepatic and extrahepatic infections associated with disturbed hepatic function. In patients with hepatic tumours, the serum SGOT activity is usually increased, the degree of increase being a rough index of the mass of the tumour (Anthony and Berk, 1979).

In contrast to hepatocellular injury which invariably results in elevations in SGOT and SGPT levels, cholestatic injury typically causes a fourfold or greater elevation of the serum Alkaline Phosphatase (SALP) which is an enzyme that liberates inorganic phosphate from a variety of organic orthophosphate esters. It is derived largely from the liver, bone, intestine and placenta. SALP activity can be demonstrated in the brush border epithelium of the bile duct and sinusoidal surface of hepatocytes and the activity of SALP in hepatobiliary disease reflects the degree of bile stasis rather than hepatocellular necrosis (Kaplan, 1972). SALP is produced by the biliary tract at the level of canaliculi in the liver to the mucosa of the gall bladder and the bile ducts. In the present study, the SALP levels were moderately or mildly elevated, not only in conditions of bile stasis but in almost all conditions of liver disease. Ritt et al. (1969) have indicated that the SALP tends raised in cases of massive hepatic necrosis due to leakage of preformed enzyme from the hepatocytes. Kaplan and Righetti (1970) and Anthony and Berk (1979), have indicated that moderate or marked elevations of SALP
activity occur in conditions of complete bile duct obstruction as has occurred in cases of
certain groups of this study with cancer of the pancreas, bile duct, ampulla of Vater and
gall bladder, and in viral hepatitis. The elevated levels of SALP in other cancers in this
study can be supported by the fact that this enzyme and a variant isoenzyme produced by
some malignant neoplasms may contribute to an increased activity of this enzyme
(Kaplan, 1972; Warnes, 1972; Robert Scheig, 1996; Richard Moseley, 1996).

The levels of liver enzymes were found to be higher in hepatitis than in cirrhosis
and in cases of viral hepatitis than in non-viral hepatitis in the present study. Mild
elevations of activity are usually found in patients with predominantly hepatocellular
lesions such as viral hepatitis or cirrhosis. In intrahepatic cholestasis, the SALP may be
as high as 20 times the upper limit of normal. In inactive cirrhosis, the activity of the
enzyme is mildly increased. But in patients with alcoholic cirrhosis, marked elevations
occur due to severe fatty change causing intrahepatic cholestasis. Large nodules of
regeneration in macronodular cirrhosis may cause more bile duct compression than
smaller ones in micronodular cirrhosis which is responsible for higher activities of SALP
in patients with macronodular cirrhosis (Anthony and Berk, 1979). The cause of
elevation of SALP includes space occupying lesions in the liver such as granulomata as
observed by Bodvall (1973) and may be the cause of enzyme alteration in the present
study with regard to tuberculous and malarial hepatitis.

Levels of SGOT, SGPT and SALP may be abnormal in pancreatitis according to
Peter Banks (1998) who expressed that these values are higher in patients whose
pancreatitis is caused by biliary tract disease than in alcoholic pancreatitis. Presumably,
the presence of calculi in the common bile duct is the most important factor that accounts
for this difference. On occasion, pancreatic inflammation may encroach on the distal
common bile duct in acute pancreatitis, causing an element of obstruction.
In normal subjects, the serum amylase so measured is derived from a number of sources. Among healthy individuals the pancreas and salivary glands account for almost all measurable amylase in serum. Increases in total serum amylase reflect leakage of pancreatic isoamylase from the inflamed pancreas and pancreatic necrosis. This first reaches the circulation through venous routes, and later through lymphatics and by absorption from the peritoneum (Goldberg et al., 1975). Serum amylase is increased in at least 75% of cases of acute pancreatitis on the initial day of symptoms and remains elevated in most patients for 5 to 10 days. The serum amylase level is not increased in all episodes. For example, during exacerbation of chronic alcoholic pancreatitis, the serum amylase value may remain in the normal range, presumably because substantial prior damage to the gland reduces enzymes available to be released. In pancreatitis associated with hypertriglycerideremia, total serum amylase levels may also remain normal. This effect is attributable to an inhibitor associated with triglyceride elevations (Peter Banks, 1998).

In most instances of acute pancreatitis, total serum amylase activity is greater than three times the upper limit of normal (as observed in the present study), whereas in the majority of instances in which there is serum amylase increase, occur in the absence of acute pancreatitis, the increase being less than three times the upper limit of normal. However, in some instances, acute pancreatitis can be documented with less than three times the increase in total serum amylase activity. In the present study, an increase in serum bilirubin was observed in subjects with pancreatitis and pancreatic cancer. Liver function tests may be abnormal if there has been compression of the intrapancreatic portion of the common bile duct by fibrosis of the head of the pancreas. In this circumstance, alkaline phosphatase is usually increased, and on occasion the serum bilirubin value is also increased (Peter Banks, 1998).

Proteins produced by the liver cell are synthesized on polyribosomes bound to the rough endoplasmic reticulum, from which they are discharged into the plasma. Changes
in the concentration of an individual protein in the plasma may be due to an altered rate of either synthesis or catabolism of the protein. Many plasma proteins, including albumin and prothrombin are synthesized by the parenchymal liver cells. In hepatocellular diseases, there is often a tendency for the concentrations of these proteins in plasma to fall (Anthony and Berk, 1979), as has occurred in the present study in conditions of cirrhosis. It is usually assumed that a diminished synthetic rate of these proteins by the liver is a major factor that contributes to this phenomenon (Tavill, 1972).

Albumin is synthesized by the liver cell and is the protein secreted by this cell in the largest quantity (Rothschild et al., 1973). In patients with chronic hepatocellular disease, particularly cirrhosis from any cause, serum albumin tends to be subnormal and this can be commonly attributed to a low synthetic rate of this protein (Hasch et al., 1967; Robert Scheig, 1996). An increased plasma volume as encountered in subjects with cirrhosis often contributes to hypoalbuminaemia according to Lieberman and Reynolds (1967) as a consequence of which the intravascular albumin pool tends to be relatively less abnormal than the serum albumin concentration and may even be in the normal range (Dykes, 1968). In chronic disease, the albumin concentration falls and that of globulin rises. The fall in albumin level may predominate in advanced hepatocellular disease resulting in a decrease in the total protein concentration, whereas the increase in the level of globulin may predominate in some patients with chronic active hepatitis [usually in those positive for hepatitis B surface antigen (HbsAg⁺)] resulting in an increase in the total plasma protein concentration. Several liver produced plasma proteins are acute phase proteins, the serum concentrations of which tend to rise in response to certain phenomena associated with tissue injury such as inflammation (Koj, 1974) which may be the reason for the mild increase in protein levels in certain types of hepatitis and pancreatitis in the present study. An acute phase response may contribute to well maintained, or increased, serum concentrations of these proteins in hepatobiliary diseases.
The reason for appreciably normal levels of total protein and albumin levels in most conditions of hepatobiliary disease in the present study might be due to the reason suggested by Cohen et al. (1961) that the normal half-life period for survival of albumin in the circulation is about 18 days, and thus if synthesis of the same were suddenly to cease, it would take a few weeks for an appreciable fall in the absence of abnormal losses or increased catabolism.

The finding of a low serum albumin concentration during an illness as observed in some subjects with malarial hepatitis would raise the possibility that the patient is suffering from either an acute exacerbation of a pre-existing chronic hepatic lesion or co-existent acute and chronic hepatocellular lesions as suggested by Anthony and Berk (1979).

The study of the blood has a long history. Humankind probably always has been interested in the study of blood because it is likely that even primitive peoples realized that loss of blood, if sufficiently great, was associated with death.

Anaemia is a manifestation of disease and is not a disease in itself. It may be a subtle sign of chronic renal insufficiency, of malignancy, or of chronic infection that has not otherwise declared itself (Wintrobe, 1999). Anaemic condition was observed in almost all experimental groups of this study, particularly with reference to malarial hepatitis.

Alterations in the number of circulating leucocytes and in the relative proportions of various leucocyte types are long-recognized measures of the reaction of the host to disease processes and noxious agents. In many instances, these alterations provide insight into the nature of the pathologic process, and may be seen in association with both acute infections and also many chronic ailments (Brown, 1905; Reznikoff, 1932; Wintrobe, 1939). In many acute infections, the blood neutrophil concentration increases. Rapidly growing neoplasms may cause neutrophilia, presumably as a result of necrosis within areas that
have outgrown their blood supply. A role for tumour necrosis factor alpha (TNF alpha) is suggested by the finding that infusion of TNF alpha is associated with leucocytosis (Lenk et al., 1989). When the liver, gastrointestinal tract, or bone marrow is involved, the counts may be especially high. Also, some tumours may contain and release hematopoietic growth factors, such as granulocyte-macrophage colony stimulating factor (Sawyers et al., 1992), which increase leucocyte production with resultant leucocytosis. In contrast to pyogenic infections, leucopenia and neutropenia are commonly associated with some bacterial and viral infections (James and John, 1999). Leucocytosis was observed in cases of pancreatitis and certain cancerous conditions in the present study. According to Peter Banks (1998), the white blood cell count is frequently increased in acute pancreatitis and may be markedly increased in the presence of severe pancreatic injury and the white blood cell count is usually normal in the absence of significant active inflammation of the pancreatitis.

The advent of contemporary era of cancer cytogenetics can be dated to 1960 when Nowell and Hungerford reported the first specific chromosome anomaly in human tumour, the Philadelphia chromosome in chronic myelogenous leukaemia. Since 1960, a remarkable sequence of specific chromosomal rearrangements and non-random changes in chromosome number have been recognised (Sandberg, 1980). It is now widely accepted that cancer results from the accumulation of mutations in the genes that directly control cell birth or cell death. But the mechanisms through which these mutations are generated are the subject of continuing debate. It has been argued that an underlying genetic instability is absolutely required for the generation of multiple mutations that underlie cancer (Loeb, 1991; Hartwell, 1992). The instability exists at two distinct levels; in a small subset of tumours, the instability is observed at the nucleotide level and results in base substitutions or deletions or insertions of a few nucleotides. In most other cancers, the instability is observed at the chromosome level, resulting in losses and gains of whole chromosomes or large portions of chromosomes (Christoph et al., 1998).
According to Gerald (1977), malignant neoplasms of the gastrointestinal tract and accessory organs had accounted for approximately 25% of all cancers and 28% of cancer deaths. The major sites of involvement included the esophagus, stomach, large intestine and pancreas. During that time, at least nine distinct varieties of hereditary gastrointestinal (GI) cancers were identified. In some others, the genetic element involved was also recognised. Each cancer is influenced by a different gene and several are associated with extra-alimentary manifestations.

In Mumbai, esophageal cancer predominates other GI cancers, but Poona showed increased risk for stomach cancer, with females having high rates of esophageal cancer. Data from cancer hospitals in India indicate that the major GI cancer seen in these hospitals is esophageal cancer. Gastric cancer has a high frequency ratio at Chennai and Hyderabad (Gangadharan, 1980).

In the present study, the most frequent site of cancer occurrence was the esophagus. High rates of esophageal cancer were reported in India, Singapore, Jamaica, parts of eastern and southern Africa and Brittany by Gerald (1977). Wu and Ruan (1981) in their cytogenetic study on peripheral blood cells of esophageal cancer and epithelial dysplasia patients showed that incidence of both numerical and structural chromosome aberrations were higher in disease groups than in the control group. Chromosomal gain of 1, 2, 3, 8, 16, 17 and 20 and loss of chromosome Y in cell lines were noted in a cytogenetic study on four human esophageal cancer cell lines by Xiao et al. (1998). Other frequent changes were partial deletion of 1p, translocation of 2q and amplification of 5p, 8q and 13q, and deletion of 17p suggesting non-random chromosome aberration may play an important role in the pathogenesis of human esophageal cancer. Numerous chromosome imbalances involving chromosomes 1q, 3p, 3q, 4p, 4q, 5p, 7p, 8p, 8q, 9q, 11q, 13q, 14q, 18p, 18q, 20p, 20q, Xp and Xq were observed in esophageal squamous
cell carcinoma by Atiphan et al. (2000). In the present study, subjects with esophageal cancer displayed karyotypes such as addition of the whole chromosome 13, 8q+ and 11q-. Another subject with a mosaic karyotype with 8p- also presented with esophageal cancer. These findings corroborate with the findings of the above mentioned researchers. Two subjects with esophageal cancer showing translocation (1q-; 13q+) was also observed. The manifestation of esophageal cancer in these subjects may be due to the participation of these chromosomes in the process of aberration as these chromosomes are involved in the development of cancer as observed by Atiphan et al. (2000).

A study by Beuzen et al. (2000) confirmed the high frequency of chromosomal numerical aberrations in esophageal and gastric adenocarcinomas, and alterations such as loss of Y chromosome, monosomy, trisomy and tetrasomy were frequently observed in adenocarcinomas. These alterations occurred early during the neoplastic transformation of Barrett’s mucosa. Comparative genomic hybridisation studies on lymphomas of the gastrointestinal tract revealed that gains of chromosomal material were more frequent than losses (Thomas Barth et al., 1998) and the most frequent aberrations were over representations of all or parts of chromosome 12 and 11, of 1q, parts of chromosome 2, 8 and 9. Gains of parts of chromosomes 3, 5 and 16 were also observed. The most frequent deletions involved chromosome 2q, 6q and 13q.

There are striking geographic fluctuations in the incidence of cancer of the stomach. Although substantial environmental components are suggested, the precise factors remain elusive (Gerald, 1977). In the present study, cancer of the stomach was the fourth in occurrence. In a majority of gastric cancers, no specific pattern has been identified and a multifactorial mechanism such as the interaction of multiple genes and environmental factors has been suggested. Van Grieken et al. (2000) have justified that a complex of chromosomal aberrations are involved in gastric cancer, and their pattern
does not depend on the bacterial species *Helicobacter pylori* status or strain, nor on the histological type of the tumour. Chromosomal aberrations observed by them were frequent gains of chromosomes 8q and 13q, predominant losses on chromosomes 2q, 9p, 12q, 14q, 15q, 16p, 16q, 17p, 17q, 19p, 19q and 22q, common regions of overlap were 2q11-14, 8q23, 9p21, 12q24, 13q21-22, 14q24 and 15q11-15. Deletion of the long arm of chromosome 7 has been related to loss of tumour suppressor genes which may constitute a primary step of carcinogenesis in many kinds of malignancies. Banerjee *et al.* (1997) reported of the non-random loss of chromosome 3 while Katayama *et al.* (2000) reported deletion of 7p in gastric lymphoma. Corroborating to the above studies, subjects with gastric cancer in the present study presented with aberrations involving chromosomes 9 with inversion, chromosome 7 with deleted short arm and translocations causing deletion of short arm of chromosome 7 and gain of long arm of chromosome 16. These aberrations might have played a major part in the development of cancer in these patients.

The incidence of colorectal cancer shows a wide geographic variation and India along with other Asian and African countries has a low incidence (Deo *et al.*, 2001). Most patients present with advanced disease. In this study, colon cancer was the third in occurrence among cancers of the GI tract. Although epidemiological studies indicate that environmental factors play a dominant causative role in carcinoma of the colon, there is significant evidence of a genetic component.

Allelic deletions of tumour suppressor genes or chromosomal fragments are frequently observed (Chang *et al.*, 1994). Chromosomal abnormalities have been reported in colorectal carcinomas for more than a decade, and recent evidence has shown that allelic losses, particularly at chromosome locations 5q, 17p, and 18q, play major roles in the genesis of large bowel tumours (Nishio *et al.*, 1991; Laurent *et al.*, 1992; Grandjouan, 1996). Tumour-suppressor genes, which normally function to suppress tumour development, are
frequently inactivated in colorectal neoplasms by mutation or allelic deletion, thereby promoting tumourigenesis. The loss of function of tumour-suppressor genes located on chromosomes 5q, 18q, and 17p is critical for colorectal tumourigenesis. A deletion within chromosome 5 in patients with familial adenomatous polyposis (FAP) led to the identification of the APC gene on the long arm of this chromosome (5q21). A tumour suppressor gene, termed DCC (deleted in colon cancer), is located on chromosome 18q (Fearon et al., 1990) and its proposed normal function is to promote proper cell-cell adhesion. Loss of this gene's function seems to play a role in later stages of the adenoma-carcinoma sequence, because allelic deletion of this locus occurs in only 11% to 13% of small tubular or tubulovillous adenomas but in 47% of adenomas with foci of cancer and in 73% of frank colon cancers (Kinzler and Vogelstein, 1996). In the present study, a subject with cancer of the large intestine displayed the chromosomal aberration 5q-, which is an important site of location of tumour suppressor genes, and this may be the reason for the manifestation of cancer in the subject.

Karyotype analysis by Koji Sasajima et al. (1993) in a patient with rectal cancer accompanied by multiple polyps in the GI tract showed 46,XX, inv(3) [p12.2q25.3]. This condition was noted in two subjects presenting with colon cancer in the present study suggesting that the development of carcinoma of the rectum results from the allelic loss in chromosome 3p. Takagi et al. (2000) have suggested that the PPP2R1B gene is one of the true targets at 11q23, and its inactivation is involved in the development of all types of colorectal cancers. The existence of different aneuploidization routes correlated with specific chromosome aberrations were suggested by Di Vinci et al. (1999) and intratumour homogeneity of deletions in 1p appeared to be an early occurrence of strong selection. The authors also suggest that tumours with monosomies and in particular monosomies and trisomies for the same chromosome support aneuploidization and chromosome instability during the colorectal tumour progression based on loss of
symmetry during chromosome segregation. Despite considerable inter-individual variations, increased chromosome breakage and rearrangement in addition to sex chromosome aneuploidy may be the signs of chromosome instability in the predisposition to colorectal cancer (Richard et al., 1994).

More is known about the DNA lesions that underlie the microscopic changes of malignancy in the colon than about other digestive tract cancers. This is because inherited predispositions to colonic cancer have provided the basis for research strategies referred to as "reverse genetics." Reverse genetics is based upon the co-segregation of two or more clinically evident diseases to one region of an inherited chromosome in affected families. It has led to the identification of new genes that are responsible for the inheritance of the diseases (germ-line mutations). However, the same genetic lesions occur at random in normal people (somatic mutations) and are part of the genetic sequence leading to the development of the more common sporadic type of colonic cancer. The somatic, acquired lesions that impair (inactivate or activate) the normal functions of these genes are under investigation in other digestive tract cancers and premalignancies (Grandjouan, 1996).

So far, five genes have been identified as targets for germ-line mutations that are responsible for inherited colonic cancer. Adenomatous Polyposis Coli (APC) gene, localized on the long arm of chromosome 5 (5q21) and its germ-line mutations cause familial adenomatous polyposis coli (FAP), an autosomal dominant inherited disease characterized by the development of up to thousands of colonic adenomas and associated with other extracolonic lesions. Hereditary nonpolyposis colorectal cancer (HNPCC) is another group of inherited autosomal dominant conditions. Four genes are implicated in HNPCC and belong to a family of genes that encode proteins responsible for DNA-mismatch repair. These genes are referred to as hMSH2 (human homologue of a
bacterial mutS gene) located on 2p16, and human homologues of bacterial mutL genes - hMLH1 located on 3p 21-23 (which may be the reason for the presentation of cancer in a subject with 3p' in a patient with cancer of the colon in the present study), hPMS1 on 2q31-33 and hPMS2 on 7p22. (Fishel et al., 1993; Leach et al., 1993; Bronner et al., 1994; Nicolaides et al., 1994; Papadopoulos et al., 1994).

Although there is a strong genetic component to the well-defined hereditary polyposis and nonpolyposis colon cancer syndromes, which exhibit a mendelian pattern of inheritance, about 95% of common (sporadic) adenomas or carcinomas arise in persons who do not have these syndromes (Steven and Young, 1998).

Cancer of the liver stood fifth in the frequency ranking of cancers in the present study, and in those related to hepatobiliary system, liver cancer was the first followed by cancers of the bile duct and gall bladder. Comparative genomic hybridisation studies by Kusano et al. (1999) on hepatocellular cancer revealed common sites of increase in DNA copy number to be 1q and 8q. Frequent decreases in copy number were observed at 4q, 8p, 10q, 13q, 16q and 17p. Amplification in 11q13, gain of 8q24 and 10q, and loss of 13q13-14 were the other findings of their study. Cytogenetic analysis of HCC cell lines and primary HCC tissues by Shiou-Hwei et al. (1994) have shown that chromosomal region 1p35 - 36 to be the region most commonly affected. The authors also observed frequent genetic alterations at the distal part of chromosome 1p, with a common region mapped to 1p35-36, which is also the region with frequent loss of heterozygosity in colorectal cancers. Loss of heterozygosity at chromosomes 4q, 11p, 13q, 16q and 17p was frequently demonstrated in hepatocellular carcinoma by Wang and Rojer (1988), Tsuda et al. (1990) and Fujimori et al. (1991). In the present study, two subjects with cancer of the liver presented with deletion of the long arm of chromosome 4. In support of the above finding, loss of 4q12-21 and other aberrations such as chromosomal losses...
in 1p34-36, 5q13-21, 6q13-16, 8p21-23, 13q, 16q and 17p13, and gains were noted in 1q, 6p, 8q, 11q13, 14q12 and 17q12 in a study by Sakakura et al. (1999) involving hepatocellular cancer.

A genomic hybridisation study by Rijken et al (1999) revealed a gain in 11 chromosomal arms and loss of 9 chromosomal arms, in whole or in part involving bile duct cancers. The most frequently lost chromosomal regions were 6q, 7q, 8p, 10p, 12p, 12q, 17p, 18q and 22q. The most frequently gained regions were 2q, 6p, 7p, 8q, 11q, 12p, 13q, 17q, 19q, 20q and Xp.

Missense mutations of the p53 tumour suppressor gene have been identified in gallbladder cancers. Between 90% and 95% of such tumours demonstrate abnormal p53 (on 17p13) expression on immunohistochemical staining using monoclonal or polyclonal antibodies (Wee et al., 1994; Diamantis et al., 1995). A possible genetic basis for some bile duct cancers is suggested by the finding of point mutations at codon 12 of the c-Ki-ras gene (on 12p12.1) in some 20% of patients. Furthermore, as many as 70% of these tumours expressed abnormal p53 immunopositivity, distal bile duct cancers being more likely positive than proximal cancers (Diamantis et al.,1995).

Shiraishi et al. (2001) performed a comparison of DNA copy number changes involving tumours arising from the liver, bile duct and pancreas and their study revealed that some genomic alterations were common to tumours of all three organs as they are in close proximity to each other, while some alterations were preferential in certain types of tumour. Gains of 1q and 8q and losses of 8p and 17p were common to all tumours. In contrast, 13q14 and 16q losses were detected exclusively in hepatocellular cancers. The incidence of 17q21 gain and 5q loss was higher in bile duct cancer. Pancreatic cancers exhibited higher incidence of 5q14-q23 gain and 19p loss. 20q+ was the...
chromosomal aberration observed in a subject of the present study involving cancer in the bile duct. Gains of 7p, 7q, 12p and 20q and losses of 3p, 6q, 9p and 18q were frequent in both bile duct and pancreatic cancers as observed by Shirashi et al.(2001).

With exception of cancers associated with idiopathic hereditary pancreatitis, familial aggregations are not considered characteristic of tumours of the pancreas (Gerald, 1977). In pancreatic cancers, similar to bile duct cancers, the most frequently lost chromosomal regions were 6q, 7q, 8p, 10p, 12p, 12q, 17p, 18q and 22q. The most frequently gained regions were 2q, 6p, 7p, 8q, 11q, 12p, 13q, 17q, 19q, 20q and Xp (Rijken et al., 1999). This suggests that carcinomas of the bile duct and pancreas share a number of genetic changes. In pancreatic tumours analysed by Schleger et al. (2000), chromosome 18 was preferably altered and losses were found at 8p, 10q, 13q and 18q. Commonly gained regions were located on 3q and 8q. High copy number amplifications of the chromosomal regions 5p, 8q22-ter, 12p12-cen, 19q12-13.2 and 20q were identified. Hyperploidy and chromosomal imbalances, predominantly affecting chromosome 8 were a constant finding in the study of Zoger et al. (1998). Sato et al. (2002) suggested that the increased level of chromosomal instability of chromosome 8 might play a critical role in the development of aggressive tumour phenotype during pancreatic cancer progression.

The application of strategies aimed at identifying genetic alterations occurring at the transcriptional and chromosomal level in pancreatic cancer have led to the identification of more than 500 genes with differential expression in pancreatic cancer. A number of chromosomal regions containing putative tumour suppressor genes or oncogenes were also identified (Wallrapp et al., 1999). A high copy number of 6q was detected in a study by Wallrapp et al. (1997) directed to identify chromosomal aberrations in pancreatic cancer. Their study also revealed amplification of the gene c-myb in advanced tumours indicating a possible correlation to tumour progression and aggressive tumour phenotypes.
Cancer of the duodenal region, particularly, those involving the ampulla of Vater contributed a great deal in the present study.

South Indian food dishes, comprising several deep fried items have been proved to be mutagenic. Polycyclic aromatic hydrocarbons (PAHs) such as benzo(a)pyrene, chrysene and dibenzanthracene, which are potent and proven carcinogens have been identified and quantified in several of the commonly consumed South Indian food dishes and food components. Most of the pyrolysed items contained PAHs in appreciable quantities Sivaswamy et al. (1991).

Premalignant lesions in the gastrointestinal tract are of two types; those characterized by the presence of dysplastic mucosa and those without dysplasia. Premalignant lesions without dysplasia have only a slightly increased risk of progression to carcinoma. They include lesions such as juvenile or Peutz-Jegher polyps which have epithelium that is essentially normal. Nondysplastic mucosa is seen in inflammatory bowel disease and in Barrett’s esophagus, both of which are premalignant conditions. Nondysplastic premalignant lesions or mucosae invariably become dysplastic before becoming invasive. These contrast with lesions characterized by the presence of dysplastic mucosa, such as adenomas and squamous dysplasia, which have a much higher likelihood of developing invasive cancer (Riddell and Path, 1996). Lanspa et al. (1992) have evidenced that flat adenomas may be a marker for some types of hereditary nonpolyposis colon cancer (HNPCC).

It is assumed that all cancers would go through stages of increasing dysplasia prior to invasion, starting with mild dysplasia through moderate and severe to carcinoma in situ. In some carcinomas, only mild or low-grade dysplasia may be present with direct invasion from this grade of dysplastic epithelium (Riddell and Path, 1996). Dysplasia is an unequivocally neoplastic proliferation essentially equivalent to an adenoma, which
may not only be a marker or precursor of carcinoma, but may itself be malignant and associated with direct invasion into the underlying tissue (Riddell et al. 1983). The same terminology may also be used in non-colitic dysplasia of the large bowel and in dysplasia found elsewhere in the gastrointestinal tract, including Barret's Esophagus (Riddell and Path, 1996).

Peter Riegman et al. (2001) observed losses of specific regions on 5q, 9p, 17p, 18q and Y in cases of Barret's esophagus with varying grades of dysplasia. In the invasive cancers, additional losses at specific regions of 3p, 4p, 4q, 8p, 13q, 14q, 16q and 22q as well as gains regions in 3q, 8q, 12p, 15q and 20q were detected. The identification of 12 patients with Barret’s esophagus in this study, with two among these expressing chromosome aberrations such as 4p− and 18q+ that are characteristic of those aberrations observed in cases of Barret’s esophagus by various authors, raises concern about the increased frequency of manifestation of this precancerous condition in the population of this part of the country. p53 gene mutations in Barret's esophagus have been shown to be useful markers of progression to high-grade dysplasia by Younes et al. (1993) where p53 abnormalities occur before the development of aneuploidy (cellular DNA content abnormalities).

When DNA is measured, the epithelium from biopsies indefinite for dysplasia is often aneuploid, and in ulcerative colitis, it may carry a risk of carcinoma similar to that seen in low-grade dysplasia (Bernstein et al., 1994). One study of colitic dysplastic and cancerous lesions examined loss of heterozygosity. p53 was affected in 47%, the retinoblastoma (Rb) gene had been deleted in one-third; the APC and adjacent mutated in colon cancer (MCC) gene were also deleted in one-third. In those heterozygous at two or more loci, loss of heterozygosity of p53, Rb, and/or the APC/MCC locus was found in one-half (Greenwald et al. 1992).
Microsatellite instability is also present in tumours which were detected in esophageal cancers, gastric cancers and colorectal cancers (Tomita et al., 1999) and they presumably play a role in the pathogenesis of dysplasia and cancers in colitis (Suzuki et al., 1994). If there is a lesion in the DNA mismatch repair mechanism within the cell caused by inactivation of one of these genes, the unrepaired damage in the microsatellite loci is readily seen. In effect, they act as markers of the underlying genetic defect. Colonic tumours arising in HNPCC show this microsatellite instability, compared with normal cells (Grandjouan, 1996).

Fragile sites (points at which the chromosome is liable to break) are a frontier in human genetics and have drawn attention for their apparent association with the origin of chromosome rearrangements in cancer. A statistical analysis was done by Grant and Frederick (1985) to determine the significance of association between fragile sites and cancer breakpoints and this study resulted in a highly significant statistical association. 44 fragile sites were identified and evidence is gathering. Certain fragile sites at cancer breakpoints appear to involve oncogenes. An extension of the present research study will elucidate the possibility of significance of fragile sites and cancer chromosome breakpoints.

Certain benign tumours are marked by chromosome rearrangements. The mixed tumour of the parotid gland, for example, has a characteristic t(3;8) translocation (Mark et al., 1980; 1982) and secondary rearrangements involving chromosome 12. Another benign tumour with a consistent chromosomal change is one the menigioma of the central nervous system. Monosomy 22 is commonly seen in meningiomas and deletions of the long arm of chromosome 22 may also be seen. The dividing line between benign and malignant neoplasms is often a fine one on a clinical level. Since benign tumours can have chromosome abnormalities that are reminiscent of those in cancer cells, it seems appropriate to include benign tumours in the consideration of chromosome changes in cancer (Zankl and Zang, 1872; Mark et al., 1982).
Genetic alterations are common in Ulcerative Colitis (UC) variably affecting \( k-ras \), \( p53 \), the adenomatous polyposis coli (APC) genes, and microsatellite instability in an accumulative (though not necessarily sequential) manner (Kern, 1994). To date, these suggest that colitic carcinomas express different mutations to noncolitic carcinomas. \( c-Ki-Ras \) seems less involved in dysplasia and cancer in UC than in noncolitic neoplasia (Brumer \textit{et al.}, 1990; Meltzer \textit{et al.}, 1990; Bell \textit{et al.}, 1991; Brumer \textit{et al.}, 1991; Chaubert \textit{et al.}, 1994), but \( Src \) has also been found to be elevated in dysplasia (Cartwright \textit{et al.}, 1994). A correlation between high \( c-myc \) expression and dysplasia have been suspected by Pavelic \textit{et al.} (1992).

Several hereditary conditions are characterised by polyps of the GI tract, differing in incidence, associated pathology, malignant potential and expressivity. Virtually any polyp can develop dysplasia in time. In hyperplastic polyps, these have been called "dysplastic hyperplastic polyps," "mixed polyps," and "serrated adenomas." (Riddell and Path, 1996). Other benign polyps (e.g., hyperplastic polyps in the stomach, juvenile polyps and in conditions of Peutz-Jegher's syndrome) can undergo dysplasia (Lewin \textit{et al.}, 1992). Perhaps the most compelling evidence that colon carcinomas arise from previous adenomas is the observation that cancer cells in a malignant polyp share the identical pattern of molecular alterations as the neighbouring adenoma cells but they acquire additional mutations that are presumably critical for malignant behaviour (Baker \textit{et al.}, 1990). In the present study, polyps in the colon were the most encountered than polyps in other parts of the gastrointestinal tract.

Several subjects with benign lesions in the present study displayed chromosomal aberrations characteristic of cancerous lesions. The aberrations observed in patients with Barrett’s esophagus are discussed above, those with antral gastritis presented with chromosomal aberrations \( 9p^- \) and \( 14q^- \) and a patient with gastric ulcer showed
12q* (aberrations characteristic of cancer of the stomach). Two subjects with polyps in the large intestine displayed inversion of chromosome 3 which is one of the characteristic aberration in colorectal cancer. A subject with cirrhosis of the liver exhibited chromosomal translocation involving the long arm chromosome 13 and three patients with chronic pancreatitis presented with translocations involving chromosomal arms 5q, 8q and 12p which are characteristic aberrations in the corresponding cancerous lesions involving the respective digestive structures. These aberrations might be markers suggesting possible underlying malignant process. It was interesting to note the chromosomal aberration 5p- in three patients with ulcerative colitis suggestive of a possible precancerous condition when noting the loss of the short arm of chromosome 5 during translocation in a patient with cancer of the colon. Similarly, the mosaic karyotype 46,XX / 45.XO was observed in a patient with barrett’s esophagus and in a patient with esophageal cancer suggesting the possible role of the missing chromosome in the suppression of dysplasia in female subjects.

Many chromosomal aberrations have been identified in the present study. The identified altered chromosomal regions may harbour tumour suppressor genes or oncogenes which are involved in the multistep process of carcinogenesis or disease pathology. These data may provide evidence for the occurrence of characteristic genomic alterations which are of biological relevance for the genesis of digestive system cancers. Hope this study will enable oneself to appreciate the importance of biochemical alterations and chromosomal aberrations in benign and cancerous lesions of the digestive system. In addition, the medical fraternity can use this information to advance in the anticipation and early recognition of the disease, and can discuss problems arising from genetic factors with patients and will help direct clinical screening, prevention trials and prophylactic surgery.
The measurement of DNA content of epithelial nuclei by flow cytometry or image analysis will be the most promising result, particularly in predicting which patients with benign lesions or predisposing conditions will develop neoplasia. With the development of newer techniques, it will be possible in the future, to screen populations and to identify those with a genetic risk for cancer. It may be possible to give a measurable risk as to the likelihood of the future development of cancer. Furthermore, the presence of genetic defects in exfoliated cells may lead to the identification of occult cancers. Although a number of these concepts are already being applied in the research field, our knowledge and technology is in its infancy. There is, however, the potential for the development of true markers of cancer or pre-cancer.

Thus the adoption of molecular genetics will eventually unravel the sequence of molecular events, invisible at microscopic and functional levels, that lead to the development of Gastrointestinal cancer. Recognition of the true nature of these tumours permits early detection and treatment as well as cancer prevention through the use of genetic counseling. Cancer prevention may be categorized as primary or secondary. Primary prevention concerns the ability to identify genetic, biologic, and environmental factors that are etiologic or pathogenetic and to alter their effects on tumour development. The goal of secondary prevention is to identify existing pre-neoplastic and early neoplastic lesions, symptomatic and asymptomatic, and to treat them thoroughly and expeditiously. The assumption is that early detection improves prognosis.

Chromosomal alterations in subjects with cancer and benign lesions are numerous and include a growing number of translocations and inversions as well as deletions and duplications. Certain sites of chromosomal rearrangement or damage may involve oncogenes. Certain non-cancerous lesions may predispose to the chromosomal rearrangements characteristic of cancer cells. To understand more fully the events of
chromosomal abnormalities and rearrangements in the cancerous and non-cancerous lesions of the digestive system, it will be important to discover more cancer chromosome rearrangements, map the genes lost and rearranged. Molecular cytogenetic studies will provide more precision. As for now the present research study has to some extent elucidated several chromosomal aberrations and the intriguing possibility of the relationship between the chromosomal aberrations observed in benign lesions and malignant lesions.