REVIEW OF LITERATURE
Malabsorption is a comprehensive term which includes both defective hydrolysis of large molecules and ineffective uptake of breakdown products of these molecules in the small intestine.

Normal digestion and absorption can be divided into three sequential stages.

1. Intraluminal stages.
2. Intestinal stage.
3. Lymphatic transport stage.

PATHOPHYSIOLOGIC MECHANISMS

A pathophysiologic classification of different causes of impaired digestion and absorption and disease associated with these defects are summarised in table 1.

INTRALUMINAL STAGE

Impaired hydrolysis and solubilization of nutrients in the small intestinal lumen.

IMPAIRED FAT ABSORPTION

Because pancreatic lipase and colipase are necessary for triglyceride hydrolysis in the duodenum, disorders that cause pancreatic enzyme deficiency lead to fat malabsorption. Pancreatic enzymes are inactivated by a low luminal pH (as occur in the Zollinger Ellison syndrome) with consequent malabsorption of fat. The products of triglyceride hydrolysis namely fatty acid and
<table>
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<tr>
<th>Affected mechanism</th>
<th>Pathophysiology</th>
<th>Associated diseases</th>
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<tbody>
<tr>
<td>I. INTRALUMINAL STAGE</td>
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<tr>
<td>b. Solubilization (Fat)</td>
<td>Distruption of the enterohepatic circulation of bile.</td>
<td>Biliary tract obstruction, terminal ileal resection or disease small bowel bacteria over growth, cholestasiatic liver disease.</td>
</tr>
<tr>
<td>a. Availability of ingested nutrients</td>
<td>Decreased CCK-PZ release</td>
<td>Extensive small intestinal obstruction.</td>
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<td>b. Deficiency of intrinsic factor for promoting B₁₂ absorption. Uptake of Vit. B₁₂ by intestinal Bacteria tape worms, Binding by Oxalates of fatty acids or phytates.</td>
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<td>Percocisous anemia.</td>
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<td>II. INTESTINAL STAGE</td>
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<tr>
<td>b. Epithelial cell transport (fat protein)</td>
<td>Loss of normal epithelial cells</td>
<td>Crohn's disease, celiac disease, Sarcoidosis tropical sprue, radiation enteritis, intestinal ischemia, whipple's disease, ilial resection, eosinophilic gastroenteritis colchicine, neomycin.</td>
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<tr>
<td>IV. UNEXPLAINED (MULTIPLE)</td>
<td>Lymphatic duct obstruction.</td>
<td>Lymphangiestasia, lymphoma, tuberculosis, carcinoid.</td>
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<tr>
<td></td>
<td></td>
<td>Diabetes mellitus, giardiasis, insufficiency hyperthyroidism Hypogammaglobulinemia.</td>
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monoglycerides are solubilized by bile salts to form micelles and are then absorbed in the small intestine. Disorder that interrupt the enterohepatic circulation of bile salts lead to impaired micelle formation and fat absorption.

**IMPAIRED PROTEIN ABSORPTION**

Although protein hydrolysis begin in the stomach through the action of pepsin, it mainly occurs in small intestine, catalyzed by pancreatic proteases. Deficiency of pancreatic proteases (trypsin, chymotrypsin and carboxypeptidase A and B) results in impaired hydrolysis of polypeptide. Therefore, chronic pancreatitis and pancreatic resection can lead to protein malnutrition. Pancreatic proteases are also important for vitamin \( B_{12} \) absorption. These enzymes release vitamin \( B_{12} \) from R proteins, prior to binding with intrinsic factor. In profound pancreatic insufficiency, normal release of the vitamin from R proteins does not occur, so the amount of vitamin available for binding to intrinsic factor for absorption is decreased.

**IMPAIRED CARBOHYDRATE ABSORPTION**

Most diseases that cause carbohydrate malabsorption do so by affecting the intestinal stage of digestion and absorption. However, because pancreatic amylase catalyzes the hydrolysis of starch to oligosaccharides some carbohydrate malabsorption is seen in pancreatic insufficiency.
DECREASED AVAILABILITY OF INGESTED NUTRIENTS AND COFACTORS FOR ABSORPTION

Vitamin B₁₂ malabsorption can result from intrinsic factor deficiency (following gastrectomy or antibody formation directed against gastric parietal cells or intrinsic factor in pernicious anaemia). A rare inherited disorder results in the production of an abnormal intrinsic factor by gastric parietal cells, which is unable to bind vitamin B₁₂ in the intestinal lumen (Yand et al, 1985; Levine et al, 1985) and the absorption of vitamin is therefore impaired. In addition bacteria in the small intestine lumen of patients with blind loops syndrome can bind vitamin B₁₂. Vitamin B₁₂ deficiency also occurs in patients infected with the fish tapeworm, diphyllobothrium latum, because the worm completes with the host for dietary vitamin B₁₂.

Certain dietary constituents can bind nutrients in the intestinal lumen, which then become unavailable for absorption. For example, excessive dietary oxalate binds calcium with the consequent formation of calcium oxalate. Similarly, long chain fatty acids bind calcium (in fat malabsorption) and a high dietary phytate content binds iron.
INTESTINAL STAGE

Abnormalities of Small Intestinal Mucosa

Impaired Epithelial Cell Digestion:

Oligosaccharides are hydrolysed to monosaccharides by specific enzymes, located in the brush border membrane of intestinal epithelial cells and the monosaccharides are then transported across the cells. When specific brush border enzymes are deficient the non-absorbed oligosaccharide are metabolised by colonic bacteria to di and trisaccharides. Carbon dioxide and hydrogen with consequent abdominal distension and flatulence. Although a number of disaccharidase deficiencies have been described, the most common is lactase deficiency, which may be either congenital or acquired. Lactase is required for hydrolysis of lactose to glucose and galactose, which are then transported across the enterocyte by a sodium dependent active transport mechanism. Congenital lactose deficiency present in infancy and is rare. Acquired lactase deficiency may be either a primary decrease in the amount of the enzyme in the mucosa or may occur when there is abnormality or destruction of small intestinal cells as seen in celiac disease, acute infections enteritis, Crohn's disease tropical sprue or radiation enteritis.

IMPAIRED EPITHELIAL CELL TRANSPORT

Transport of Multiple Nutrients

A number of disease cause significant loss of intestinal surface area resulting in malabsorption of
all major dietary constituents. Conditions in which intestinal epithelial surface area is reduced or remaining epithelial cells are abnormal include celiac disease, tropical sprue, collagenous sprue, radiation enteritis, Whipple's disease, eosinophilic gastroenteritis and intestinal ischemia. Extensive surgical resection of the small intestine also reduces the epithelial surface area available for absorption. Colchicine inhibits cell division and reduces the number of cells available for absorption and neomycin produces blunting of the small intestinal villi through an unknown mechanism leading to steatorrhea. In all these disorders due to drugs steatorrhea is typically mild (6 to 15 gm of fecal fat/day) and patients have decreased D-xylose absorption test.

**TRANSPORT OF CARBOHYDRATE**

Specific defects in the absorption of carbohydrate are usually caused by mucosal enzymes deficiencies. However, there is a rare, recessively inherited disorder in which carrier mediated transport of glucose and galactose in the intestinal epithelial cells membrane is impaired. This present clinically as a watery diarrhoea in infant shortly after births.

**Transport of Amino Acids**

There are also rare recessively inherited defects in amino acids transport. Hartnup disease is characterised by impaired transport of neutral amino acids (phenyl -
alaline and tryptophan) by intestinal and renal epithelial cells. Patients have pellagra like dermatitis due primarily to a deficiency of tryptophan (a precursor of nicotinamide). Although protein malnutrition is not seen because dipeptide absorption is normal. Similarly, patients with cystinuria although unable to transport dibasic amino acid (Cystine, lysine and arginine) have few symptoms of protein malabsorption. Patients with these disorders may have diarrhoea, attributed to bacterial metabolism of the excess amino acids in the intestine. They also have aminoaciduria with the formation of renal calculi in cystinuria.

TRANSPORT OF FATS

Micelles consisting of the product of triglycerides hydrolysis (monoglyceride, free fatty acids and glycerol) phospholipids, cholesterol and bile salts are transported from the intestinal lumen across the apical membrane of small intestinal epithelial cells. Disaggregation of micelles occurs during the transport process, diglycerides and triglycerides are resynthesized in the cells and subsequently chylomicrons are formed from triglycerides, phospholipids, cholesterol, and apoproteins. In the rare inherited disorders abetalipoproteinemia, chylomicrons formation is impaired due to absence of apolipoprotein B. Fat malabsorption results and fat accumulation within
epithelial cells because its export across the basolateral membrane is inhibited.

**OTHER INHERITED TRANSPORT DEFECTS**

Vitamin $B_{12}$ deficiency is occasionally due to impaired intestinal transport. The vitamin $B_{12}$ intrinsic factor complex can bind to ileal cells, but transacross the cells does not occur (Burman et al, 1985). In congenital folate deficiency folic acid transport is impaired as a result of a rare specific intestine cell transport defect.

**LYMPHATIC TRANSPORT**

Impaired transport of nutrients from the small intestine. Disease that cause lymphatic obstruction can lead to fat malabsorption and a protein losing enteropathy. In intestinal lymphangiestasia, the subepithelial lymphatic are dilated and functionally obstructed. Consequently, removal of chylomicrons in the lymph is abnormally slow in this condition. In infiltrating disease of the small intestine (for example, tuberculosis enteritis, intestinal lymphoma, and whipple's disease). Mononuclear leucocytes may compress lymphatic vessels in the small intestinal wall and retard chylomicron removal. In addition, enlargement of regional lymphonodes (as in tuberculosis, lymphoma, metastatic carcinoma and metastatic carcinoid disease) may produce lymphatic obstruction and fat malabsorption.
UNCLEAR MECHANISM

A number of diseases are associated with malabsorption, but the pathophysiologic reason for the impaired absorption is unclear. Normal enterocyte function may be impaired in amyloidosis and giardiasis (Deka et al, 1982). A significant impairment of absorption of fat and D-xulose was seen in the rat with experimental giardiasis. Familial amyloidosis with polyneuropathy, steatorrhoea was found 58% and impaired D-xylose absorption in 52%.

The main reason for the gastro intestinal dysfunction is a disruption of the gut autonomic nervous system rather than a barrier to absorption of nutrients across the intestinal wall (Steen and Ek, 1984). Malabsorption is common in patients with acquired immune deficiency syndrome (AIDS), some of whom have intestinal Kaposi's sarcoma or infection with mycobacterium avium intracellular, but in some no obvious etiology for diarrhoea and impaired absorption can be found (Scott et al, 1985, Allison and Bornman, 1983). Mild, but not severe, exocrine pancreatic insufficiency may occur in acquired immune deficiency syndrome however, fat malabsorption is more commonly associated with a small intestinal cause (Kapembwa et al, 1990). Kinetics of D-xylose absorption in patients with human immunodeficiency virus enteropathy, Ka (an absorptive rate constant) was reduced out of proportion to the minor histologic changes present in the duodenal biopsy specimens (Flit, D. Ehrenpreis et al, 1991).
Hypcholesterolemia has been noted to occur in the acquired immunodeficiency syndrome and has been associated with the malnutrition and cachexia often seen in end stage AIDS (Zumwalt, Schmidr, 1989; Falkanbach et al, 1989).

Inadequate diet and malabsorption have been frequently noted previously in AIDS patients (Gillin et al, 1985; Hickey, Weaves, 1988). Bacterial contamination of the small intestine is an important cause of occult malabsorption in the elderly (McEvoy et al, 1983).

Malabsorption of vitamin B\textsubscript{12} and intrinsic factor secretion during Biguamide therapy 30% had malabsorption of vitamin B\textsubscript{12} with drawal of the drug resulted in normal absorption in only half of those with malabsorption. The concept that biguamide can induce malabsorption by two different mechanism. One of these temporary and unrelated to intrinsic factor secretion and other is permanent and mediated by depression of intrinsic factor secretion (Adams et al, 1983).

Kinetic analysis of D-xylose absorption in normal subjects and in patients with chronic renal failure shows that nonrenal clearance of D-xylose is markedly reduced in chronic renal failure patients. D-xylose is less completely absorbed in patients with chronic renal failure than in normal subjects. The absorption rate of D-xylose is slower in these patients than in normal subjects. The absorption rate is positively correlated with the extent of D-xylose absorption (Robert, 1983).
A case of a syndrome of malabsorption associated with Prurigo nodularis was reported. Her malabsorption syndrome was an idiopathic sprue. Five months after treatment with gluten free diet supplement with vitamin and iron, the disappearance of the clinical and analytical alteration was compared (Suareg et al, 1984).

A study was done that is intestinal damage and malabsorption after treatment for cervical carcinoma malabsorption was found in 22% and 13% had vitamin B₁₂ deficiency. Intestinal damage in tumour free patients occurred in 3% patients (Lantz and Einhorn, 1984).

A stiffman with malabsorption study was done, in which it was stated that pancreatitis has been found in patients of scleroderma (Greef, 1979; Davidson, Epstein, 1983; Rai et al, 1986).

In a study duodenal pH in cystic fibrosis and its relation to fat absorption conclude was that a wide range of duodenal pH values found in patients with cystic fibrosis and that the efficiency with which enzyme supplements work is closely related to these pH levels (Pancreatic enzymes). Administration of misoprostal to those patients with (misoprostal, a known acid reducing agent) excessively acidic duodenal pH levels as well as residual malabsorption appears to be of benefit in improving both the excessively acidic pH levels and the fat malabsorption (Robinson et al, 1990).
Protein and fat absorption in prolong diarrhoea in infancy (Nan et al, 1982)

In a study that fat absorption in premature infants the effect of lard (it was derived from pigs fed a diet high in polyunsaturated fatty acids in order to obtain a more "human milk like" fat profile) and antibiotic. It was suggested that no support for the use of lard in adopted cow's milk infant formulas to improve fat absorption (Verkade et al, 1989). A study lymphatic role in the pathogenesis of fat malabsorption in liver cirrhosis in rats. Data suggested that lymphostasis of the intestine may play an important role in fat malabsorption in liver cirrhosis (Soichiro Minra et al, 1982).

Another study impaired absorptive capacity for carbohydrate in the aging human it was suggested that subtle carbohydrate malabsorption should be consider when evaluating weight loss in old age and in fashioning nutrition programmes for the elderly (Joshva et al, 1982).

In a study malabsorption associated with nonmalignant immunoprofliferative small intestinal diseases (IPSID) (O' Manonsos et al, 1987).

In another study malabsorption syndrome coccidiasis combine immune deficiency and fulminant lymphoproliferative disease. It was suggested a possible role of coccidial infection in malabsorption syndrome in immuno deficients patients. It also indicates the need for further study of the relationship between malignancy and metronidazole
in immunosuppressed patients (Aharon Hallak et al, 1982).

In a study, familial amyloidosis with polyneuropathy, aspect of the relationship between gastrointestinal symptoms, EMG finding, and malabsorption studied. The steatorrhoea was found in 58% and an impaired D-xylose absorption in 52%. It was suggested that the main reason for the gastrointestinal dysfunction is a disruption of the gut autonomic system rather than a barrier to the absorption of nutrients across the intestinal wall (Steen and Ek, 1984).

**CLINICAL MANIFESTATIONS**

**HISTORY**

Although many of the symptoms of malabsorption are non specific, for example, diarrhea, weight loss, and symptoms of anaemia, clinical history can provide clue to the etiology of malabsorptions in some patients. Early symptoms of intestinal or pancreatic disease include fatigue bloating, anorexia, and passage of two to three loose stool per day. An increase in bulk may be the first change noticed by the patient. However, more advanced pancreatic insufficiency may be associated with classic symptoms of fat malabsorption, which include the passage of bulky, floating, malodorous stools. Although stools were considered to float because of a high fat content, they actually float because of increased gas (Levitt et al, 1972).

Some common clinical features of malabsorption and their pathophysiology are summarized in table 3.
Both small intestinal or pancreatic disease may result in profound weight loss. Although anorexia is more characteristic of small intestinal disease or pancreatic carcinoma than chronic pancreatitis.

**TABLE 2 : Condition associated with impaired micelli formation.**

<table>
<thead>
<tr>
<th>Pathophysiology</th>
<th>Associated diseases</th>
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<tbody>
<tr>
<td>Decreased bile salt formation.</td>
<td>Severe parenchymal liver disease.</td>
</tr>
<tr>
<td>Decreased bile salt delivery to the duodenum.</td>
<td>Cholestatic liver disease (Primary biliary cirrhosis, drug induced cholestasis) bile duct obstruction (Cholangiocarcinoma, pancreatic carcinoma, gallstones, sclerosing cholangitis).</td>
</tr>
<tr>
<td>Decreased ionization of conjugated bile salts.</td>
<td>Zollinger - Ellison syndrome.</td>
</tr>
<tr>
<td>Decreased intraluminal bile salt concentration</td>
<td>Binding agents (Cholestyramine)</td>
</tr>
<tr>
<td>Bile salts deconjugation.</td>
<td>Bacterial overgrowth in jejunal diverticula, small intestinal fistula and strictures in Crohn's disease, scleroderma, intestinal pseudoobstruction, diabetes and elderly.</td>
</tr>
<tr>
<td>Increased intestinal bile salt loss.</td>
<td>Crohn's disease, small intestinal resection, cholecystocolonic fistula.</td>
</tr>
</tbody>
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Patient with chronic pancreatitis tend to have hyperphagia, which may contribute to the marked fat excretion. Anaemia (due to vitamin B12, iron, or folate malabsorption) may present with dyspnoea, dizziness, fatigue and pallor.
Diffuse abdominal pain is not usually associated with malabsorption unless extensive small intestinal disease with partial intestinal obstruction is present (as in Crohn's disease or radiation enteritis, for example). Patients with chronic intestinal ischemia classically have pain 20 to 60 minutes after meal and usually have other evidence of peripheral vascular disease. The abdominal pain of chronic pancreatitis tends to be epigastric with radiation into the back. Patient with small intestinal lymphoma frequently have severe periumbilical or generalized abdominal pain.

Recent foreign travel may be associated with parasitic diseases including giardiasis, and tropic sprue. Homosexual contact, intravenous drug abuse, or multiple blood transfusion predispose to infection with the human immunodeficiency virus (HIV). Patients with infected with this virus are prone to develop opportunistic infections caused by a variety of organisms including mycobacterium avium intracellular. Alcohol is toxic to the small intestinal mucosa affecting absorption (Green, 1983) and chronic alcoholism abuse may cause pancreatic insufficiency and fat malabsorption. In a child small stature or failure to thrive are features of celiac disease and of cystic fibrosis. Malabsorption and concomitant bronchitis or bronchiectasis also suggest cystic fibrosis.

Patient with disaccharidase deficiencies experience abdominal distension, nausea and water diarrhoea 30 to 90
<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Pathophysiology</th>
<th>Laboratory findings</th>
</tr>
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<tbody>
<tr>
<td>Diarrhoeas</td>
<td>Increased secretion and decreased absorption of water and electrolytes: unsorbed fatty acids and bile salts.</td>
<td>Increased fat excretion, decreased serum carotene, &quot;Osmotic gap&quot; in stool electrolytes</td>
</tr>
<tr>
<td>Weight loss with hyperphagia</td>
<td>Decreased absorption of fat protein and carbohydrate.</td>
<td>Increased fat excretion.</td>
</tr>
<tr>
<td>Bulky foul smelling stool</td>
<td>Decreased fat absorption</td>
<td>Increased fat excretion.</td>
</tr>
<tr>
<td>Muscle wasting oedema</td>
<td>Decreased protein absorption</td>
<td>Decreased serum albumin.</td>
</tr>
<tr>
<td>Flatulence borborygmi abdominal distension</td>
<td>Fermentation of carbohydrates by intestinal intestinal bacteria</td>
<td>Increased fat excretion.</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Small intestinal stricture, infiltration of peneosse intestinal ischaemia.</td>
<td>Decreased D-xylose absorption.</td>
</tr>
<tr>
<td>Parasthesia tetany</td>
<td>Decreased vitamin D and calcium absorption</td>
<td>Hypocalcemia, hypomagnesaemia.</td>
</tr>
<tr>
<td>Bone pain</td>
<td>Decreased calcium absorption</td>
<td>Hypocalcemia, increased alkaline phosphatase.</td>
</tr>
<tr>
<td>Muscle cramps weakness</td>
<td>Excessive potassium loss.</td>
<td>Hypokalemia, abnormal ECG.</td>
</tr>
<tr>
<td>Easy bruisability</td>
<td>Decreased vitamin K absorption</td>
<td>Increased prothrombin time, increased fat excretion.</td>
</tr>
<tr>
<td>Hyperkeratosis, night blindness</td>
<td>Decreased vitamin A absorption</td>
<td>Decreased carotene, increased fat excretion.</td>
</tr>
<tr>
<td>Pallor</td>
<td>Decreased vitamin B12, folate or iron absorption</td>
<td>Macrocytic anemia, microcytic anemia.</td>
</tr>
<tr>
<td>Glossitis, stomatitis, Cheilosis</td>
<td>Decreased vitamin B12, folate or iron absorption</td>
<td>Decreased vitamin B12, folate or iron.</td>
</tr>
<tr>
<td>Acrodermatitis</td>
<td>Zinc deficiency.</td>
<td>Decreased serum zinc.</td>
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minutes after ingesting a particular disaccharides sugar (milk sugar in lactose deficiency). Eosinophilic gastro-enteritis should be suspected in any patient with malabsorption and a history of food allergies. A history of peptic ulcer disease and diarrhoea raises the positivity of Zollinger Ellison syndrome. Abdominal surgery, particularly or Billroth II partial gastrectomy can lead to the creation of a blind loop of small intestine. It is also a cause of malabsorption, small intestinal resection may interrupt the enterohepatic circulation of bile salts with resulting fat malabsorption and if extensive may impair the absorption of other nutrients. In patients with malabsorptions, nondeforming arthritis neurologic symptoms or valvular heart disease. Whipple's disease should be considered. Scleroderma can lead to small intestinal dismotality and bacterial overgrowth. Certain small intestinal diseases have dermatologic manifestations (for example, dermatitis herpetiformis in celiac disease). Some endocrine disorders (diabetes mellitus, addition's disease, hypoparathyroidism and thyrotoxicosis) are also associated with malabsorption.

Finally a careful drug history should be taken because certain drugs (for example, colchicine, cholestyramine, neomycin and cathartics) may cause malabsorption.

**PHYSICAL EXAMINATION**

If malabsorption is not severe, the physical examination may be normal or there may be minor physical
abnormalities including smooth lateral margins of the tongue and hyperactive bowel sounds. With more severe malabsorption, patients may show evidence of malnutrition, with muscle wasting particularly in the temporal areas, pallor of mucous membranes suggests anaemia (which may result from malabsorption of iron, vitamin B_{12} or folate). Deficiencies of fat soluble vitamins can produce hyperkeratosis of the skin (Vit. A), ecchymosis and hematuria (Vit. K) and paraesthesias, tetany, positive Chvostek and Trousseau signs and bone pain with vertebral collapse (Vit D and calcium). Patients with intestinal disease may have malabsorption of & water soluble vitamins (Notably B vitamins) with resulting glossitis (riboflavin and niacin deficiency) and peripheral neuropathy (Vit B_{12} deficiency).

The prognosis of patients with malabsorption is determined by the nature of the underlying disease.

The clinical features and investigation of specific diseases will now be considered according to their pathophysiological classification.

**INTRALUMINAL STAGE - DIGESTION**

**PANCREATIC DISEASE**

Pancreatic proteases lipase and amylase are essential for normal digestion of nutrients and diseases of the pancreas typically produce significant fat malabsorption (commonly more than 25 gm of fecal fat excretion per day). Pancreatic bicarbonate secretion neutralizes gastric acid and maintains the duodenum at the alkaline pH
required for pancreatic enzyme activity. Profound destruction of the pancreas must occur before significant steatorrhoea results (Gastin et al., 1984; Dimagno, 1982).

Although chronic alcoholic pancreatitis is the commonest cause of pancreatic exocrine insufficiency, in one study 75% of patients with pancreatic carcinoma had fat malabsorption some of whom improved with exogenous pancreatic enzyme replacement (Perez, 1983). Symptoms of fat malabsorption predominate in patients with pancreatic exocrine insufficiency, but symptoms of impaired protein absorption (for example, muscle wasting and edema) also occur. Patients typically have hyperphagia and are able to maintain their weight despite significant malabsorption. Impaired vitamin $B_{12}$ absorption is common but the $B_{12}$ deficiency is rare. Symptoms result from malabsorption of the fat soluble vitamin (A, D, E and K) and from hypocalcemia caused by chelation of calcium by excess fatty acids in the institute.

Pancreatic disease should be suspected in any patients with steatorrhoea (determined by fecal fat excretion), normal small intestinal function (determined by D-xylose absorption) and without evidence of terminal ileal disease (determined by a small intestinal barium contrast radiograph). Pancreatic dysfunction may be confirmed by bentilromide test. The specific pancreatic disease (chronic pancreatitis, pancreatic resection or carcinoma) may be diagnosed by computerized tomography, endoscopic retrograde cholangio pancreatography, and if
necessary fine needle aspiration of the gland. If patients with known pancreatic disease fail to improve after pancreatic enzyme replacement, coexisting small intestinal disease should be sought (Lembe et al., 1985).

Pancreatogenous malabsorption in children is most commonly associated with cystic fibrosis. Rare syndrome as a sidroblastic anaemia (Pearson et al., 1979) or neutropenia (Schwachman syndrome (Gaskin et al., 1984) has been described.

**ZOLLINGER - ELLISON SYNDROME**

High gastric acid production stimulated by gastric secreting tumours of pancreas or duodenum results in impaired fat absorption. Excess acid in the duodenum had a dual effect on fat digestion by (a) inactivating pancreatic enzymes and (b) decreasing bile salt ionization. Acid suppression (by cemetidine or surgery) results in reversal of the malabsorption (King and Toskes, 1983; Kingham et al., 1981).

**SURGERY FOR PEPTIC ULCER DISEASE**

Malabsorption of fats and carbohydrates occurs after total or partial gastrectomy and is multifactorial in etiology. Gastric emptying rate is increased and gastric antral function is lost, resulting in inadequate grinding of food particle and inadequate mixing of nutrients with gastric secretion, as well as dilution of pancreatic enzymes.
with decreased proteolysis and lipolysis (MacGregor et al., 1977).

Because the pancreas is innervated by the vagus, absolute levels of pancreatic enzymes are reduced after vagotomy and fat malabsorption results. Rapid gastric emptying after a partial gastrectomy or vagotomy and pyroplasty causes a 10 to 50 percent reduction in glucose absorption (Radzink and Bondy, 1982). Following a Billroth II anastomosis bacterial overgrowth in the jejunal loop causes both bile salt and vitamin B₁₂ malabsorption.

**INTRALUMINAL STAGE: SOLUBILIZATION**

**DISRUPTION OF THE ENTEROHEPATIC CIRCULATION OF BILE**

Bile salts are necessary for the effective solubilization of fats in the small intestinal lumen and any disease that interrupts the normal enterohepatic circulation of bile can result in decreased micelle formation and fat malabsorption where low bile salt concentration in the duodenum are due to decreased production (severe parenchymal liver disease) decreased delivery (cholestatic liver disease, Biliary tract obstruction). Bile salt deconjugation to free bile acids (bacterial overgrowth), or increased bile salt loss (terminal ileal disease or resection). Symptoms relate to impaired absorption of fat and fat soluble vitamins. In these disorders protein and carbohydrate absorption remain normal. The absorption of vitamin B₁₂ is impaired in bacterial overgrowth, as
intestinal bacteria compete with intrinsic factor for binding to vitamin B₁₂ (Giannella et al., 1972) and intestinal ileal disease when receptors for the vitamin B₁₂ intrinsic factor complex are lost.

Regardless of the cause patients with reduced bile salt concentration have significant steatorrhoea (15 to 20 gm excreted fat per day). The specific disorder resulting in decreased bile salts may be identified by routine liver function tests, small intestinal contrast radiographs and sonograph imaging of the biliary tract and pancreas. An abnormal $^{14}$C D-xylose breath test is diagnostic of small intestinal bacterial overgrowth and an abnormal choyl $-^{14}$C glycine breath test is suggestive of terminal ileal disease or resection or bacterial overgrowth. Finally cholecystokinin pancreozymes (CCK-PZ) a gut hormone secreted by I cells in the proximal small intestinal mucosa is essential for normal gallbladder contraction. Any disease that destroys the intestinal mucosa (for example, celiac disease) may reduce CCK-PZ release, reduce gallbladder contraction, reduce bile salt and pancreatic enzymes delivery to the duodenum and hence result in impaired fat absorption.

**INTESTINAL STAGE : EPITHELIAL CELL DIGESTION**

**Disaccharide Deficiency**

Aquired lactose deficiency is the most common disorder of carbohydrate absorption in humans. Lactose in
intestinal brush border epithelial cells is important for lactose hydrolysis in neonates but level decline after weaning (Kretschmer et al, 1981), so that by adulthood most humans are lactase deficient (Nuang and Bayless, 1968). The rate of fall of lactase levels differs in different ethnic groups (Ravich and Bayless, 1983) and there is considerable variation in the prevalence of lactase deficiency among different races, occurring in more than 65% of people of Asian and African origin.

Symptoms of abdominal distension, flatulence and diarrhoea after ingestion of milk products commonly begin in adolescence. Diagnosis is best made by measurement of breath hydrogen after ingestion of lactose. Lactose levels in a small intestinal mucosal biopsy may be measured directly, although this rarely necessary clinically. (Hyams et al, 1980). As the symptoms of lactose intolerance are non specific and lactase deficiency is very prevalent diagnosis ultimately depends on the resolution of symptoms after elimination of milk from the diet. Lactose can be more readily absorbed from yogurt as intraintestinal lactase is released by bacilli in Yogurt, facilitating digestion of lactose (Kolars et al, 1984).

Lactase deficiency also results from diseases that damage the small intestinal mucosa (celiac disease, tropical sprue, radiation enteritis) (Weiss and Styker, 1982) chronic alcoholics have reduced level of intestinal lactase which improve with abstinence (Perlow et al, 1977).
Although lactose malabsorption was thought to influence the severity of symptoms in children with inflammatory bowel disease (Pena and Truclone, 1973; Sciaretta et al, 1984) a recent study of breath hydrogen elimination after lactose ingestion in 70 children with inflammatory bowel disease found to increased incidence of lactose intolerance (Kritschner et al, 1981). Milk intolerance may contribute to symptoms in patients with irritable bowel syndrome (Sciaretta et al, 1984).

Congenital lactase deficiency is a rare disorder in mucosal lactase levels are low at birth. Infants have watery diarrhoea, irritability and weight loss from the first feed of breast milk (Kritschner et al, 1981) and improve on a lactose free diet.

Other rare inherited disorders of brush border enzymes include alpha dextrinase deficiency (Gray et al, 1976) and the lactose deficiency. In all these disorders the nonabsorbed carbohydrates are fermented by colonic bacteria to produce short chain fatty acids, CO₂ and hydrogen, which result in symptoms of abdominal distension flatulence and diarrhoea after ingestion of relevant sugar.

**INTESTINAL I STAGE - EPITHELIAL TRANSPORT**

Many small intestinal diseases results in dysfunction of epithelial cells and loss of normal absorptive functions. Patients with celiac sprue (glutin sensitive
enteropathy) may have profound malnutrition secondary to mucosal distruption. Elimination of gluten from the diet usually reserves the small intestinal damage with improvement of enterocyte absorption. A variant of celiac disease has recently been described in six patients with loss of small intestinal villi, atrophy of the spleen and cavitation of mesenteric lymph nodes (Matuchansky et al., 1984). All patients had abnormal D-xylose absorption, and four had steatorrhoea.

Small intestinal involvement in sarcoidosis is rare but can cause malabsorption with increased fecal fat excretion and abnormal D-xylose absorption (Sprague et al., 1984). Small intestinal biopsy reveals villous atrophy and multinucleate giant cells in the mucosa which resolves with steroid therapy. Other disorders causing loss of intestinal surface area for absorption are summarised in table 1 (Crohn's disease, radiation enteritis, Whipple's disease, tropical sprue, eosinophilic gastroenteritis) specific defects in amino acid transport (Hartnup disease, cystinuria) and vitamin B₁₂ and folate transport already discussed.

**ALCOHOL**

Acute and chronic alcohol ingestion directly damages the small intestinal mucosa with resulting altered absorption of nutrients.
Acute alcohol administration produces haemorrhagic erosion of the intestinal villous tips in alcoholic volunteers (Gottfried et al, 1976). Chronic alcohol ingestion in alcoholics produces ultrastructures changes in the mitochondria and endoplasmic retinaculum of the crypt and villous epithelial cells but no light microscopic changes to the intestinal mucosa (Rubin et al, 1972).

Steatorrhoea in alcoholic is primarily due to pancreatic insufficiency rather than mucosal disease. Alcohol administration in healthy volunteers causes impaired absorption of methionine, thiamine and D-xylose (Green, 1983) presumably due to intestinal epithelial cell damage. Small intestinal motility is also increased (Robles et al, 1974) and may contribute to the diarrhoea in alcoholics.

**Small Intestinal Resection or Bypass**

Resection of the small intestine is most commonly performed in patients with Crohn's disease with severe mucosal damage and stricture formation. Jejunooileal bypass was frequently used for the treatment of morbid obesity before the severe metabolic consequences were appreciated (Adibi and Stanko, 1984). Surgical resection of the small intestine decreased the surface area available for absorption. The affected nutrient and degree of malabsorption depend on a number of factors:

1. The extent and site of intestine resected.
2. The absorptive function of remaining small intestine.
   and the functional integrity of the liver and pancreas.
3. Adaptive responses of the remaining intestine and
4. The presence of the ileocecal valve (Weser, 1976).

   1. Patients who have had more than 75 percent
      of their small intestine resected have severe malabsorp-
      tion with diarrhea caused by the rapid transit of nutrients
      into the colon. If the jejunum alone is resected steato-
      rrhea is typically mild (approximately 10 gm of fecal fat
      per day) and the specific functions of the terminal ileum
      (Vitamin B₁₂ and bile salt absorption) are maintained.
      However, after terminal ileal resection, the bile salt
      pool is reduced and micelle formation is inhibited,
      resulting in marked steatorrhea (20-40 gm of fat daily).
      In addition, the unabsorbed fats and bile salts which
      reach the colon inhibit colonic water and electrolyte
      absorption and may stimulate colonic electrolyte secretion
      causing watery diarrhea (Mckhian et al 1971; Ammon and
      Phillips, 1973). Bile salt induced diarrhea occurs after
      as little as 100 cm of ileum is resected but steatorrhea
      is usually mild (Hofmann and Foley, 1972).

2. Patients who have disease in the remaining
small intestine have major difficulties in absorbing
nutrients (for example, Crohn's disease). Similarly
patients with concommitant liver or pancreatic diseases
may have reduced bile salt or pancreatic enzyme secretion
with aggravation of steatorrhoea. In patients who have a total colonic as well as ilial resection, water and electrolyte absorption in the colon is lost, and fluid losses in the ileostomy may become unmanageable.

3. There is good evidence from animal studies, that after resection of the jejunum adaptive changes occur in the remaining ileum. As early as one week after the resection, transit time is decreased (Curtis et al, 1984). The height of the intestinal villi and mucosal enzymes contents increase and intestinal absorption improves (McCarthy and Kim, 1973).

4. Nutrient malabsorption and diarrhoea seen to to less in patients who do not have resection of the ileo-cecal value. Intestinal transit time is prolonged and small intestinal contamination by colonic bacteria is reduced with preservation of the ileocecal value (Weser, 1976)

Following intestinal resection or bypass patients may have impaired absorption of time elements (Calcium, magnesium, and vitamins, A, D, E and \( B_{12} \)). In normal individuals, oxalate in the diet is precipitated by calcium and little is absorbed. In patients with severe steatorrhoea, calcium binds to the excess fats and is unavailable for binding to oxalate, which remains soluble. Hence, oxalate absorption from the colon is increased, explaining the high incidence of oxalate renal stones in patients with terminal ileal disease.
For the management of patients with extensive small intestinal resection and an excellent review by Weser (1976). Although long term survival of patients with only 6-8 inches of remaining jejunum, in addition to duodenum is reported (Winawer and Zameneck, 1968). Life long intravenous hyperlimentation is usually necessary.

**ABETALIPOPROTEINEMIA**

A group of rare inherited defects in chylomicrons formation have been described. Following lipolysis fatty acids are passively transported into the enterocyte where chylomicrons are formed from phospholipids, cholesterol, triglycerides and apoproteins in the endoplasmic reticulum prior to transport to the Golgi apparatus, children with abetalipoproteinemia or with homogygous Hypobetalipoproteinemia are unable to synthesize chylomicrons (Isselbacher et al, 1974; Cottrill et al, 1974). The enterocytes become filled with fat and patients have fat malabsorption with steatorrhea. A progressive sensory neuropathy, ataxia and retinitis pigmentosa are also characteristic of these diseases. Chylomicron retention disease is a redently described varient of abetalipoproteinemia with similar features of steatorrhea and neurologic impairment (Roy et al, 1987). Both disease have an autosomal recessive made of inheritance and can be distinguished by the lipoprotein profiles in serum (Roy et al, 1987). Treatment consists of substituting medium chain triglycerides for dietary fat and supple-
menting with fat soluble vitamins, particularly vitamin E.

**ADULT FAMILIAL HYLINE MEMBRANE DISEASE**

A familial syndrome of progressive hyalinosis of capillaries, veins and arteries have recently been described (Ramband et al, 1986). Clinical manifestation include hypertension retinal ischemia and subarachnoid hemorrhage.

**ABNORMALITIES OF LYMPHATIC TRANSPORTS**

Intestinal lymphoma should be considered in any patients with profound steatorrhea and hypoalbuminemia. Lymphatic transport of chylomicrons and proteins is obstructed with consequent fat malabsorption and protein loss in to the intestine. In developed countries the disease is usually a localised ileal tumour, which may present with obstructive symptoms, where as in third world countries intestinal involvement is often diffuse and symptoms of malabsorption predominate (Mondhiry, 1986).

Other causes of obstruction of mesentric lymphatics include tuberculosis (Hanson, 1985), metastatic carcinoma, metastatic mesothelioma (Raptopoulos, 1985) and metastatic carcinoid (case records of the massachusetts general hospital, 1986, Seigel et al, 1980). Retractile mesenteritis and retroperitoneal fibrosis and disease of unknown etiology which cause lymphatic obstruction (case records of the Massachusetts General Hospital, 1984).
Lymphatic duct obstruction of any etiology is frequently associated with ascites. Primary intestinal lymphangiectasia is a genetically determined structure disorders of the lymphatics. Intestinal biopsy characteristically shows dilated lymphatics and the villi may also be distended or may appear normal.

Differentiation between these different causes of lymphatic obstruction may be difficult, lymph nodes in tuberculosis enteritis may be calcified, small intestinal biopsy may show malignant lymphocytes in primary lymphoma, and urinary 5-hydroxy indole acetic acid level are usually increased in metastatic carcinoid disease. But often definitive diagnosis is only made at laparotomy.

**DISEASES OF UNEXPLAINED MECHANISMS**

**Enteropathy of the Acquired Immune Deficiency Syndrome (AIDS)**

Diarrhoea and weight loss occur in approximately two thirds of male homosexual with the acquired immune deficiency syndrome (AIDS). Many of whom have malabsorption (Gillin et al, 1985; Koller et al, 1984). Although enteric pathogens may be present (Giardia, Cryptosporidium Isospora belli). In one recent study no identifiable pathogen could be identified by stool culture in 20/72 patients with AIDS and diarrhoea (Gillin et al, 1985). D-xylose absorption was impaired in all patients, fat malabsorption was common. Intestinal biopsy revealed mycobacterium avium intra-
cellular in 5 of the 20 patients and specific inflammation without pathogens in 13 of 20. Jejunal biopsy in some patients revealed partial villous atrophy, but the causative agent was not identified. Thus, these seems to be an enteropathy associated with AIDS which present with diarrhoea and symptoms of malabsorption but without an identifiable etiology.

Even when organisms are seen on intestinal biopsy, the pathophysiologic mechanism of the malabsorption in these patients is unexplained. Infection with cryptosporidium in immunocompetent hosts causes an acute self limited diarrhoea. However, in AIDS patients cryptosporidium produces a severe incapacitating diarrhoea with major fluid and electrolyte loss and occasionally nutrient malabsorption. (Rodgers and Kagniff, 1987). Isospora belli may be identified by acid fast stains of stool specimens or by electron microscopy of a small intestinal biopsy (Schun and Gelb, 1984). Light microscopy of the small intestine typically reveals partial villous atrophy. Microsporidia have been found in the intestinal mucosa of patients with AIDS and diarrhoea but malabsorption has not been associated with the organisms and their importance in the pathogenesis of diarrhoea is unclear (Rodgers and Kagniff, 1987).

*Myobacterium avium intracellulare* is an important pathogen in patients with AIDS and is known to produce PAS positive inclusions in intestinal macrophages, similar to
the lesions identified in whipple's disease (Strom and Gruninger, 1983). Although malabsorption is commonly associated with this pathogen the pathophysiologic mechanism is not known (Gillin et al, 1985).

Cytomyalovirus infection in AIDS patients typically cause diarrhoea and occasionally colonic perforation. Although small intestinal involvement has been described, diffuse colonic ulceration is seen more commonly (Rodgers and Kagnoff, 1987) and malabsorption has not been reported. AIDS patients with gastrointestinal kaposi sarcoma are usually asymptomatic (Friedman et al, 1985).

ENDOCRINOPATHIES

A number of endocrine disorders are associated with malabsorption. Abnormalities of gastrointestinal motility have been documented in patients with thyroid disease, and rapid intestinal transit may cause the impaired fat absorption which is frequently associated with thyrotoxicosis (Shofer et al, 1984; Thomas et al, 1973). Similarly the steatorrhoea observed in patients with addison's disease improved with steroid replacement. Mild steatorrhoea is also reported in patients with deficient parathyroid function, in whom diagnosis may be made by measuring parathormone levels. Treatment with vitamin D and calcium will improve the steatorrhoea as well as other symptoms of the disease. Patients with long standing diabetes mellitus frequently have diarrhoea and
may have mild steatorrhoea (Wruble and Kalser, 1964). Although a few patients have associated pancreatic exocrine insufficiency and some have intestinal bacterial overgrowth, in most diabetes small intestinal histologic findings and pancreatic exocrine function are normal autonomic neuropathy is common in these patients and dysmotility may predispose to bacterial overgrowth but small intestinal culture rarely reveal increased organisms and steatorrhoea rarely improves with antimicrobial therapy.

MALABSORPTION IN THE ELDERLY

Poor intake is probably the major cause of malnutrition. But in a recent study 45% of elderly patients were found to have bacterial overgrowth of the small intestine (McEvay et al, 1983). Impaired absorption of fat (Webster et al, 1977) and carbohydrate (Feibusch and Halol, 1982) has been reported in patients over 65 years of age, although mechanism is unclear. Investigations of these patients may reveal unsuspected anatomic abnormalities (for example jejunal diverticular).

OTHER DISORDERS

Both primary and secondary amyloidosis may involve the small intestine and cause malabsorption. proposed mechanism include small intestinal ischemia from amyloid infiltration of mesenteric arterioles, amyloid deposition in the lamina propria inhibiting transport of
nutrients and altered intestinal motility. Of note as only 50 percent of the patients with intestinal amyloidosis have impaired D-xylose absorption, damage to the small intestine seems to be variable (Steen and Ek, 1984). Giardiasis is known to cause steatorrhoea, but the mechanism is unclear. However, there is evidence that giardiasis lamblia trophozoits can take up bile salts and may thus reduce intraluminal bile salt concentration, leading to fat malabsorption (Farthing et al, 1985).

**DRUG INDUCED MALABSORPTION**

Colchicine, a drug commonly used in the treatment of gout, inhibiting epithelial crypts cells division (Race et al, 1970). Mild steatorrhoea and impaired D-xylose absorption may result. Neomycin produce partial villous atrophy and impaired D-xylose and fat absorption in doses as low as 4 gm per day. The pathophysiologic mechanism is unclear although lipolysis of fats is reduced and bile salts in the intestinal lumen may be precipitated by the drugs (Rodgers et al, 1966). Bacitracin polymyxin and kanamycin any cause malabsorption. Clindamycin in therapeutic doses inhibits jejunal water and electrolyte absorption, which may in the absence of pseudomembranous colitis. Contribute to diarrhoea that occur during Clindomycin therapy (Spiller et al, 1984). Methotrexate (Gwavava et al, 1981) an irritant laxatives appear to impair absorption by directly damaging small intestinal epithelial cells. Cholestyramine in the doses of 12 gms
or more per day, binds bile salts in the intestinal lumen and impaire fat absorption. The oral anticoagulant phenindione also cause steatorrhea by an unknown mechanism. Aluminium containing anacids bind dietary phosphate and can lead to hypophosphatemia hyper calciuria and nephrolithiasis.

**CLINICAL TESTS OF DIGESTION AND ABSORPTION**

Numerous tests are available for evaluating patients with symptoms of maldigestion and malabsorption. A logical approach to investigating such patients can be made if attention is given to clinical features suggestive of specific etiologies during a careful history and physical examination (for example excess alcohol intake causing shall intestinal or pancreatic disease). Routine laboratory tests may also be helpful. Thus, a macrocytic or microcytic anaemia would suggest deficiency of vitamin in $\text{B}_{12}$, folate or iron, respectively and hypoalbuminemia might indicate protein malabsorption or a protein losing enteropathy. A low serum carotene level would suggest impaired fat absorption, which would then be investigated directly by a quantitative sudan stain and then measurement of quantitative fecal fat.

In patients with chronic pancreatitis, a plain abdominal X-ray may demonstrate pancreatic calcification (this is present in 30 percent such patients) (Robet et al, 1978) whereas an abdominal CT scan may demonstrate a pancreatic mass in patients with pancreatic carcinoma.
If fat malabsorption is due to small intestinal disease, carbohydrate absorption as determined by D-xylose absorption a hydrogen broth test or a bile acid breath test is likely to be abnormal.

Small intestinal barium X-ray may show evidence of previous intestinal surgery (subtotal gastrectomy or massive small bowel resection) or may show partial intestinal obstruction in a patient with Crohn's disease or lymphoma. Distortion of the second portion of the duodenum by pancreatic carcinoma may also be seen on barium contrast radiographs. A small intestinal biopsy may provide diagnostic information in patients with specific mucosal diseases and occasionally may be used to measure disaccharidase activities in patients with suspected disaccharidase deficiencies.

A schematical approach to investigating the patient with suspected malabsorption is summarized in figure-1. The range of normal values for the different test is given in table 4. Some of the more frequently used tests will now be considered in further detail.
<table>
<thead>
<tr>
<th>Tests</th>
<th>Test reflects</th>
<th>Normal values</th>
<th>Abnormal results indicate</th>
<th>Factors affecting interpretation of the test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum carotene</td>
<td></td>
<td>70.06 mg/dl</td>
<td>Pancreatic insufficiency, small intestinal disease.</td>
<td>Inadequate dietary fat</td>
</tr>
<tr>
<td>Qualitative fecal fat</td>
<td>Fat digestion and absorption</td>
<td>a few fat globules per high power/field</td>
<td></td>
<td>Incomplete collection</td>
</tr>
<tr>
<td>Quantitative fecal fat</td>
<td></td>
<td>16 gm/day</td>
<td></td>
<td>Inadequate dietary fat.</td>
</tr>
<tr>
<td>Schilling test</td>
<td>Vitamin B₁₂ absorption</td>
<td>77%/24 hours</td>
<td>Pernicious anemia primary vitamin B₁₂ malabsorption.</td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td>X-xylose (25 gm orally)</td>
<td>Carbohydrate absorption</td>
<td>74 gm/5 hr (urine)</td>
<td>Small intestinal mucosal dysfunction bacterial overgrowth</td>
<td>Renal insufficiency, age, ascites</td>
</tr>
<tr>
<td>Lactose tolerance test</td>
<td>Lactase activity of enterocytes</td>
<td>720 mg/dl, rise in blood</td>
<td>Acquired lactase deficiency, congenital lactase deficiency, Crohn's disease, radiation enteritis, celiac sprue.</td>
<td>Renal or liver disease, diabetes</td>
</tr>
<tr>
<td>Bentimidide test (PABA).</td>
<td>Pancreatic secretion</td>
<td>75% amylase excretion/6 hrs.</td>
<td>Pancreatic insufficiency extensive small intestinal wall damage.</td>
<td>Renal or liver disease, diabetes</td>
</tr>
<tr>
<td>Breath tests</td>
<td></td>
<td></td>
<td>Bacterial overgrowth</td>
<td>Delayed gastric emptying</td>
</tr>
<tr>
<td>a. ¹⁴C-xylose</td>
<td>Carbohydrate digestion and absorption</td>
<td>0.001% of administered dose at 30 min.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Choly ¹⁴C-</td>
<td>Enterohepatic circulation of bile acids</td>
<td>3% of administered dose any time within 4 hours.</td>
<td>Bacterial overgrowth, terminal ileal disease/ resection.</td>
<td></td>
</tr>
<tr>
<td>c. Lactase H₂</td>
<td>Lactase activity of enterocytes</td>
<td>20 ppm rise in breath H₂, any time within 3 hours.</td>
<td>Lactase deficiency.</td>
<td></td>
</tr>
<tr>
<td>Small intestine culture</td>
<td>Bacteria in the small intestine</td>
<td>10⁵ organisms/ml</td>
<td>Bacterial overgrowth</td>
<td>Unrepresentative sampling of the small intestine inadequate culture techniques.</td>
</tr>
<tr>
<td>Small intestinal biopsy</td>
<td>Small intestinal morphology</td>
<td></td>
<td></td>
<td>Unrepresentative sampling of the small intestine.</td>
</tr>
</tbody>
</table>
SELECTION OF TESTS IN THE EVALUATION OF MALABSORPTION

qualitative or quantitative
fecal fat

Normal special test
- Serum folate
- Serum B₁₂ (Schilling test)
- Serum Iron
- Stool electrolytes
- Lactase breath test

Abnormal
D-xylose absorption test (Blood or urine)

Normal
- Abdominal radiograph
- Small intestinal barium X-ray
- Bantiromide test
- Abdominal CT Scan

Abnormal
$^{14}$C-D-xylose breath test

Normal
Small Intestinal biopsy

Abnormal
- Jejunal culture
- Tetracycline
- The repeat Breath test.

Figure 1.
HISTORY AND PHYSICAL EXAMINATION

(Diarrhoea, weight, Nutritional deficits)

Initial Laboratory

( | Hemoglobin, iron, calcium, albumin, cholesterol)

( | Prothrombin time, bone demineralization)

Stool volume appearance

( | Volume, bulky, watery, silver gray, foul)

    | Serum carotene

Stool fat qualitative

Quantitative fecal fat (selected patients)

Percentage of fat intake

\[
\leq 6\% = \text{normal} \quad 76\% = \text{further work up}
\]

D-xylose absorption

25 gm oral dose, 5 hr urine collection.

\[
\begin{array}{c|c}
75 \text{ gm} & \leq 5 \text{ gm} \\
\text{Pancreas ?} & \text{Jejunal biopsy} \\
\text{Bile salts ?} & \text{Small bowel X-ray} \\
\text{Lymphatics ?} & \\
\end{array}
\]

Fig. 2: Format for malabsorption work up by Roger and Gebhard (1983).
SUDAN STAIN

If abnormal    If normal but still highly suspicious    If normal
             end of work up

72 hours fecal fat test

If normal    If abnormal
             End of work up

UGI/SBFT + D-xylose test + Serum Trypsinogen RIA

If abnormal
Benbtiromide or Secretin CCK test
If abnormal
Small bowel biopsy with fluid aspirate for parasite and culture for bacterial overgrowth.

Fig. 3 : Decision tree for suspected malabsorption UGI/SBFT upper gastro intestinal series and small bowel follow through RIA - Radio-immunoassay CCK cholecystokinin (By Igram M Roberts, 1987).
TESTS OF FAT ABSORPTION

Qualitative fecal fat

This simple test is useful for screening individuals with suspected fat malabsorption and correlated well with the quantitative fecal fat (Doummey et al, 1961; Ghosh et al, 1977). The qualitative fecal fat test is most useful in patients with moderate to severe fat malabsorption (excreting more than 10 percent of a daily intake of 60 gm of fat) in whom it is positive in 94 to 100 percent of cases. In patients with mild to moderate fat malabsorption (Excreting 6 to 10 percent of dietary fat), the test is less sensitive and will be positive in only 75 percent of cases. In addition, 14 percent of fecal specimens from healthy individuals (excreting 7 percent of dietary fat) will have a slight increase in microscopic estimate of fecal fat (Drummey et al, 1961). The test is performed on a stool specimen which is placed on a glass slide and mixed with two drops of glacial acetic acid and two drops of Sudan III in 95 percent alcohol.

In moderate steatorrhoea many fat globules the size of erythrocytes are present, and in severe steatorrhoea many fat globules greater in size than erythrocytes are seen. In patients with a positive test the degree of fat malabsorption should be further evaluated with a quantitative fecal fat measurement. Patients ingesting minerals, oils may have a false positive test.
False negative qualitative fecal fat tests arise in patients with inadequate dietary fat intake or mild steatorrhoea.

**Quantitative Fecal Test**

Measurement of the amount of fat in the stool excreted in three days by a patient on a daily diet containing 80-100 gm of fat is the best method for evaluating fat malabsorption. The stool specimen is analysed by the Van de Kamer method (Van de Kamer et al 1949), which is based on extraction and titration of long chain fatty acid by NaOH. Fecal fat levels greater than 6 gm per day are abnormal and suggest unduly small intestinal, pancreatic or hepatobiliary disease. If the patient is on a 100 gm per day fat diet and a complete three day stool specimen is collected, the test provides a useful measure of the amount of fat which is not absorbed by the small intestine and it remains the "Gold standard" to which all other tests of fat absorption were compared. Small errors arise in patients taking medium chain triglycerides (Braddock et al, 1968) or mineral oils (Drammey et al, 1961) which interfere with fecal fat analysis. It must be remembered that fecal fat level may be normal in patients with advanced destruction of the pancreas since pancreatogenous steatorrhoea will not usually appear until the enzyme output of the gland has been reduced to ≤2 percent of normal values(Gaskin et al, 1983).
Recent attempts have been made to introduce less cumbersome tests of fat absorption which avoid the problem of inadequate dietary fat intake and inadequate collection of excreted fat. The most widely used of such test is the "C-triolein breath test". A new double-isotope method using radiolabelled triglycerides and free fatty acids, as well as a nonabsorbable marker to assess the adequacy of the fecal collection promises to overcome some of the deficiencies of the quantitative fecal fat test but requires further evaluation (Thorsgard Pedersen and Hølgaard, 1985).

\textbf{\(^{14}\text{C-TRIOLEIN BREATH TEST}\)}

Triolein is a triglyceride (glyceryl trioleate) that normally is hydrolyzed by pancreatic lipase in the small intestine and after absorption and further metabolism contributes to the CO\textsubscript{2} in exhaled air. Following oral administration of glycercyl tri (1-\(^{14}\text{C}\)) oleate, exhaled \(^{14}\text{CO}_{2}\) is trapped by hyamine, then quantitated by scintillation counting. In patients with impaired fat absorption the amount of \(^{14}\text{CO}_{2}\) exhaled in six hours after an oral dose of \(^{14}\text{C}-\text{labelled triolein is reduced. This test has been validated in patients with steatorrhoea (Newcomer et al, 1979; Butler et al, 1984). It is easier to perform than the 72 hours fecal fat test but as with other tests of fat absorption, provides little information about the
cause of malabsorption in any particular patient. In addition result may be misleading in patients with altered metabolism of absorbed $^{14}$C-triolein or impaired excretion of $^{14}$CO$_2$ in breath (for example in patients with diabetes, obesity, thyroid disease, pulmonary disease and liver disease, a condition which are often associated with chronic pancreatitis) it is also insensitive in detecting early pancreatic insufficiency and is a qualitative rather than a quantitative test. A variant of this test employs triolein labeled with the non-radioactive isotope $^{13}$C, which is quantitated by mass spectrometry.

In an attempt to differentiate patients with pancreatic and small intestinal disease, Goff has repeated the test after pancreatic enzyme replacement (The two stage triolein breath test) and found an increase in $^{14}$CO$_2$ excretion in patient with pancreatic insufficiency (Goff, 1982). At present the triolein breath test is available only in research laboratories.

**SPECIFIC PANCREATIC FUNCTION TEST**

Radiographic techniques (ultrasounds Computerised tomography and cholangiopancreatography) have greatly improved our ability to diagnose chronic pancreatitis, but tests of pancreatic function are helpful in establishing whether structural abnormalities of pancreas are the cause of the patients symptoms. Pancreatic function tests measure the ability of pancreatic acinar cells to
secrete enzymes and bicarbonate into the duodenum following certain stimuli. However, most of these tests are insensitive in detecting pancreatic insufficiency, as they are only abnormal when enzyme secretion is reduced to less than 10 percent of normal level (Di Mago et al., 1973).

**Bentiromide Test**

The underlying principle of this noninvasive test of pancreatic function is that an adequate duodenal concentration of chymotrypsin is necessary to cleave free para-aminobenzoic acid (PABA) from the synthetic peptide N-benzoyl-L tyrosylparaaminobenzoic acid (Bentiromide) (Toskas, 1983; Weizman et al., 1985).

After a 500 mg oral dose of bentiromide free PABA is released in the duodenum absorbed conjugated in the liver and excreted in the urine, where it is measured in 6 hour urine sample. PABA excretion is reduced in severe pancreatic insufficiency when enzyme output is less than 5 percent of normal. In addition, patients with defective intestinal absorption, renal disease, diabetes or severe liver disease may have diminished urinary PABA excretion in the absence of pancreatic insufficiency (Di Magno, 1982; Neideran and Grendell, 1985). Modification of the test involving measurement of plasma PABA levels have increased its accuracy (Weizman et al., 1985).
PANCREATIC STIMULATION TESTS

In these tests the duodenum is intubated and the duodenal contents are aspirated after a specific stimulus (Intravenous secretin or cholecystokinin or a liquid meal containing fat, protein and carbohydrate, known as the lundh meal). Duodenal fluid is analysed for pancreatic enzymes (lipase, colipase trypsin or chymotrypsin) and bicarbonate content. Although these test remain the "Gold standard" by which other pancreatic tests are measured they are cumbersome to perform and are uncomfortable for the patients and are rarely used clinically.

SCHILLING TEST

Approximately 50 percent of patients with pancreatic exocrine insufficiency have impaired absorption of vitamin $B_{12}$, as measured by the standing Schilling test (Brugge et al, 1980). The standard schilling test measures vitamin $B_{12}$ absorption and is used to detect the intrinsic factor (IF) deficiency in patients with pernicious anaemia. The test is also abnormal in patients with genetic defect in vitamin $B_{12}$ absorption, bacterial overgrowth of small intestinal extensive mucosal destruction resection or bypass of terminal ileum and pancreatic insufficiency( for which the dual label schilling test was developed).
In the standard schilling test an oral dose of vitamin $B_{12}$ (0.5 to 2.0 ug radiolabelled with either $^{57}C_{O}$ or $^{58}C_{O}$) is given with a simultaneous intramuscular injection of 1 mg of nonradioactive vitamin $B_{12}$ (which saturate hepatic binding sites for vitamin $B_{12}$ and reduces the amount of radio-active vitamin $B_{12}$ retained by the liver). The urine is collected for 24 hours following the administration of vitamin $B_{12}$ and the amount or radio-activity determined. Patients with normal absorption and normal renal function excrete more than 7 percent of the radioactive vitamin $B_{12}$ in 24 hours and those with impaired of collection. The low level of urinary radiolabelled vitamin $B_{12}$ in patients with pernicious anaemia is corrected when the test is repeated and 60 mg of intrinsic factors is given orally with the test dose of labelled vitamin $B_{12}$ (second stage schilling test). Patients with small intestinal bacterial overgrowth often show malabsorption of vitamin $B_{12}$ with the first stage schilling test because of bacterial utilization of the vitamin which however is not corrected in the second stage test by administration of intrinsic factor. In such patients the absorption of vitamin $B_{12}$ plus intrinsic factor remain low, but usually a week of antibiotic treatment for example, metronidazole, 250 mg three times/day) eliminates the intestinal bacteria and restores the vitamin $B_{12}$ absorption of the first stage test to normal.
The dual label schilling test was developed to provide information about pancreatic exocrine function because proteases are required for the release of vitamin B₁₂ from so called R-proteins of gastric juice which preferentially bind the vitamin (Allen et al, 1978). For vitamin B₁₂ to become bound to intrinsic factor the action of proteases in the duodenum is essential. The vitamin B₁₂ thus released will then be bound to intrinsic factor in the duodenum. This test compares the absorption of ⁵⁸Co labelled vitamin B₁₂ given orally bound to R-protein and ⁵⁷Co labelled vitamin B₁₂ is given orally bound to intrinsic factor. In pancreatic insufficiency, the ⁵⁸Co labelled vitamin B₁₂ is malabsorbed and the ratio of ⁵⁸Co / ⁵⁷Co in a urine specimen is lower than if pancreatic function is normal (Brugge et al, 1980). In patient with bacterial overgrowth of the small intestine or distal ileal disease both forms of vitamin B12 are malabsorbed, but the ratio of the cobalt isotops in the urine is normal. The dual label schilling test is no longer in clinical use because attempts to standarized this test by different laboratories have not been successful. Normalization of vitamin B₁₂ absorption after pancreatic enzyme replacement as measured by the standard schilling test suggests pancreatogenous malabsorption.

TESTS OF CARBOHYDRATE ABSORPTION

HYDROGEN BREATH TEST:

In normal individual, hydrogen in produced
exclusively by the bacterial metabolism of carbohydrates. This test measures the hydrogen exhaled at times intervals during the first three hours after ingestion of carbohydrate under investigation (for example, lactose, lactulose, fructose or sucrose) (Levitt, 1969; Perman et al, 1984). Patients who are unable to digest or absorb carbohydrates in the small intestine have increased delivery of carbohydrates to the colon and hence increased production of hydrogen, which is then absorbed in the colon and exhaled by lungs. Patients with small intestinal bacterial overgrowth have increased hydrogen production by the ingested bacteria. The peak excretion is early i.e. within 3 hours. Patients with small intestinal disease and carbohydrate malabsorption have a later peak of hydrogen release as do patients with disaccharidase deficiency who have ingested the appropriate disaccharide.

The hydrogen breath test is now the most commonly used test to diagnose lactose deficiency (Newcomer et al, 1975) and is more sensitive than the lactose tolerance test. After measurement of basal breath hydrogen levels. An oral dose of lactose (1 gm per kg of body weight) is given. A rise of 720 ppm in exhaled hydrogen is diagnostic of lactose malabsorption. Patients with bacterial overgrowth of small intestinal bacteria in response to ingested carbohydrate (50 or 80 gm of glucose or 10 gm of lactulose) and an early peak of hydrogen exhalation after carbohydrate ingestion. The hydrogen breath test appear to be comple-
mentary to other breath test in diagnosing small intestinal bacterial overgrowth (Metz et al., 1976). A controlled diet on the day before the test affects fasting breath hydrogen levels and may improve the accuracy of this test (Perman et al., 1984; Kerlin et al., 1984). Because it is simple to perform and does not involve radioisotopes. This test is commonly used to study carbohydrate absorption in children. Of note, patients with severe pancreatic insufficiency may have impaired carbohydrate absorption and positive hydrogen breath test (Kerlin et al., 1984).

**D-XYLOSE ABSORPTION TEST**

Xylose is a five carbon sugar that is incompletely absorbed in the small intestine by the same transport mechanism as glucose and galactose. Intestinal uptake of xylose occurs by both passive diffusion and active transport, but unlike glucose and galactose, xylose is not completely metabolised after it is absorbed but it largely excreted unchanged in the urine. The xylose absorption test has been used extensively to assess the functional integrity of the small intestinal mucosa. After an overnight fast a 25 gm (less commonly, 5 gm) dose of D-xylose a given orally and the patient is encouraged to drink fluids to maintain a good urinary output. Approximately 25 percent of the administered dose is excreted in the urine (Normal values in a five hour urinary collection after a 25 gm oral doses, 75 gm). In patients with fat malabsorp-
tion this test is useful to differentiate between small intestinal disease (in which xylose absorption is diminished and pancreatic insufficiency (in which xylose absorption is normal) however, xylose absorption may be normal in patients with only mild impairment of small intestinal mucosal function and in patients with predominantly distal small intestinal disease (Ryan and Olsen, 1983). The accuracy of the test is increased by measuring serum D-xylose levels one or two hours after the oral dose (normal levels more than 20 mg/dl two hour after a 25 gm dose or 11 to 22 mg/dl one hour after a 5 gm dose(Finley et al, 1964; Sladen and Kumar, 1973; Kaeney et al, 1978).

After an oral dose, serum D-xylose level should be normal in patients with impaired renal function (elderly individuals or patients with renal parenchymal disease in whom urinary xylose level will be diminished) and in patient with ascites (in whom xylose is retained in the ascitic fluid). Serum D-xylose levels will also be decreased in more than 85 percent of patients with bacterial over growth of the small intestine as bacterial metabolism of xylose in the intestinal lumen decreased the amount available for absorption (Haeney et al, 1978). In patients with bacterial overgrowth and small intestinal mucosal function D-xylose absorption any urinary excretion are likely to increase after oral administration of antibiotics.
In summary, the D-xylose absorption test is useful for evaluating patients with steatorrhea. If serum and urinary levels are reduced, the patient should be further investigated with a jejunal biopsy or test for bacterial overgrowth. If D-xylose absorption is normal steatorrhea is likely to be due to pancreatic insufficiency.

LACTOSE TOLERANCE TEST

This test is performed to identify patients with either a specific defect in lactose absorption (congenital or acquired lactase deficiency) or a more generalised defect in carbohydrate absorption (for example, mucosal abnormalities associated with Crohn's disease). After oral administration of 50 gm of lactose, plasma glucose is measured at one and two hour. In normal subjects, the plasma glucose rises by more than 20 mg/dl whereas little increase in plasma glucose level is seen in most patients with lactase deficiency. The lactose tolerance test may not detect certain patients with biopsy proved lactase deficiency (6 to 25 patients in one study) (New Comer et al, 1975) and has largely been replaced by the more sensitive breath hydrogen test.

ILEAL INTUBATION TESTS

Intubation tests have been recently described which directly quantify the unabsorbed carbohydrate reaching the ileocecal value (Stephen et al, 1983; Higachi et al, 1986).
These tests are easier to interpret than the D-xylose absorption or hydrogen breath tests as carbohydrate fermented by colonic bacteria is not measured by the tests. Intubation tests provides promise in the investigation of carbohydrate absorption, but further validation and comparison with the other tests are necessary.

**TESTS FOR BACTERIAL OVERGROWTH**

**QUANTITATIVE BACTERIAL CULTURE**

To quantify bacteria in the small intestine, the jejunum is intubated either with a peroral small intestinal tube passed under fluoroscopy or with a tube passed through an endoscope and the intestinal aspirate culture for both aerobic and anaerobic bacteria. In normal individuals, $\lesssim 10^3$ bacteria per milliliter (usually streptococci and staphylococci) are cultured. The presence of $7 \times 10^5$ bacteria per milliliter (commonly coliforms and anaerobes) has been used as the minimum concentration for diagnosis of small intestinal overgrowth. However, this test requires special culture techniques to detect anaerobic bacteria and is not as useful for diagnosing bacterial overgrowth as the breath tests.

**Breath Tests**

Bacteria in the small intestine metabolized only administered carbohydrate bile salts with the release of $\text{CO}_2$ in exhaled air. This is the underlying principle of
the $^{14}$C-D-xylose and chaly1$^{14}$C-glycine tests. Both these tests are in clinical use.

$^{14}$C-D-xylose Breath test

This clinical breath test measures $^{14}$CO$_2$ in exhaled air following oral administration of 1 gm of $^{14}$C labelled D-xylose. In patients with small intestinal bacterial overgrowth, gram negative aerobic bacteria metabolize $^{14}$C-D-xylose to $^{14}$CO$_2$ which following absorption is exhaled. Eighty five percent of these patients will have a diagnostic elevation of exhaled $^{14}$CO$_2$ within 60 minutes of ingesting $^{14}$C-D-xylose (King and Toskes, 1983). In patients with delayed gastric emptying and small intestinal bacterial overgrowth (for example, in scleroderma), the release of $^{14}$CO$_2$ may be delayed until three hours confirmation of bacterial overgrowth is obtained by the normalization of this test and resolution of the malabsorption after antibiotic administration. The labelled xylose breath test has been shown to be more reliable than quantitative bacterial culture for diagnosing bacterial overgrowth because multiple test of xylose absorption give reproducible results in 95 percent of patients compared to only 38 percent for bacterial culture (Tillman et al, 1981). In addition because xylose is absorbed in the proximal small intestine, little is available for metabolism by
colonic bacteria and $^{14}\text{CO}_2$ release is not increased in patients with small intestinal resection.

**CHOLYL-$^{14}$C-GLYCINE BREATH TEST**

The bile and breath test is based on the normal enterohepatic circulation of bile salts. In contrast to the normal situation following the oral administration of choly1 $^{14}$C-glycine anaerobic bacteria in the small intestine of patients with the bacterial overgrowth deconjugate the bile salt with the release of glycine. The glycine is then absorbed and after further metabolism, $^{14}$CO$_2$ is released, resulting in an early peak of radioactivity in the expired air. Unfortunately this test cannot easily differentiate between bacterial overgrowth and small intestinal disease or resection, in which unabsorbed choly1 glycine is metabolised by colonic bacteria with a delayed release of $^{14}$CO$_2$. Comparisons of the radiolabelled choly1 glycine and D-xylose breath test in the patients with culture proved bacterial overgrowth have shown that the latter test more accurately identifies patients with blind loop syndrome (King et al, 1980; Schneider et al, 1985).

**TESTS OF BILE SALT ABSORPTION**

The choly1 $^{14}$C glycine breath test may also be used to identify patients with impaired ileal absorption of bile salt (King and Toskes, 1983) although it cannot
reliably differentiate patient with bile salt deconjugation
due to small intestinal bacterial overgrowth from patients
with bile salt malabsorption secondary to small intestinal
disease or resection. The measurement of fecal $^{14}$C may
increase the accuracy of the cholygl glycine breath test,
but it also decrease the facility with which those test
is performed (Rutgeerts et al, 1979). The recently
developed $^{75}$Se MCAT test overcomes some of these
difficulties and attempts to measure the total bile salt
balance in patients.

$^{75}$Se MCAT TEST

This radioactive taurocholic acid analogue (23-
Selena-25-Homotaurocholic acid) undergoes a similar
interohepatic circulation to taurocholic acid and has
recently been used to detect patients with increased
bile acid loss. After oral administration of the compound
the patient is screened under a gamma camera on sequential
days and the amount of retained bile acid is quantitated,
patient who retain less than 34 percent of the administered
dose after three days are considered abnormal (Sciaretta
et al, 1986). This test has been used to identify patients
with bile acid malabsorption secondary to vagotomy or ileal
resection many of whom have improvement in their diarrhoea.
When treated with cholestyramine (Sciaretta et al, 1986;
Merrick et al, 1985). In these small studies 20 to 50
percent of patients with idiopathic diarrhoea had decreased
retention of 75 Se HCAT suggesting bile acid malabsorption and 75-100 percent of these patients had symptomatic improvement when taking cholestyramine. Although the 75 Se HCAT test is not in general clinical use. It is simple to perform and promise to be helpful for identifying patients who have idiopathic bile acid malabsorption (Popovic et al, 1987) who may respond to cholestyramine therapy.

RADIOGRAPH OF THE SMAL INTESTINE

The primary role of barium contrast radiograph of the small intestine is to define anatomic abnormalities which may be associated with bacterial overgrowth. A true blind loop, small intestinal stricture (as in patients with Crohn's disease or those who have undergone abdominal surgery), multiple jejunal diverticula or marked small intestinal hypomotility (as in scleroderma) all cause stasis which leads to bacterial colonization and overgrowth with serious impairment of digestion and absorption. Pancreatic carcinoma or pseudocyst in patients with chronic pancreatitis may be detected by distortion of the sweep of the descending duodenum. Radiograph are less important in the diagnosis of infiltrative diseases of the small intestine. In patients with celiac sprue barium & x-ray typically show intestinal dilatation with little mucous thickening.
<table>
<thead>
<tr>
<th>Diseases</th>
<th>Histologic features</th>
<th>Pattern of distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celiac sprue</td>
<td>Villous flattening, crypt, hyperplasia, increased lymphocytes and plasma cells in lamina propria.</td>
<td>Diffuse in proximal jejunum</td>
</tr>
<tr>
<td>Tropical sprue</td>
<td>Shortened villi, increased lymphocytes and plasma cells in lamina propria.</td>
<td>Diffuse in proximal jejunum</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>Noncaseating granuloma with or without giant cells</td>
<td>Patching lesions particularly affecting terminal ileum.</td>
</tr>
<tr>
<td>Collagenous sprue</td>
<td>Subepithelial collagen deposits</td>
<td>Diffuse</td>
</tr>
<tr>
<td>Primary lymphoma</td>
<td>Malignant lymphocytes or histiocytes in lamina propria variable villous flattening.</td>
<td>Patchy</td>
</tr>
<tr>
<td>Whipple’s disease</td>
<td>Lamina propria laden with PAS staining, foamy macrophages bacilli in macrophages.</td>
<td>Diffuse</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>Amyloid deposition in blood vessels muscles layer.</td>
<td>Diffuse in muscularis mucosa mucosal sparing.</td>
</tr>
<tr>
<td>Abetalipoproteinemia</td>
<td>Lipid laden vacuolated epithelial cells, normal villi</td>
<td>Diffuse</td>
</tr>
<tr>
<td>Radiation enteritis</td>
<td>Flattened villi mucosal inflammation fibrosis, ulceration</td>
<td>Patchy</td>
</tr>
<tr>
<td>Lymphangiodysplasia</td>
<td>Dilated lymphatic in lamina propria</td>
<td>Patchy</td>
</tr>
<tr>
<td>Eosinophilic gastroenteritis</td>
<td>Eosinophilic infiltrate in the intestinal wall</td>
<td>Patchy</td>
</tr>
<tr>
<td>Hypogammaglobulinemia</td>
<td>Villous flattening giardia trophozoites often present few plasma cells.</td>
<td>Patchy</td>
</tr>
<tr>
<td>Giardiasis</td>
<td>Trophozoites maybe present, variable villous flattening.</td>
<td>Patchy</td>
</tr>
<tr>
<td>Opportunistic infections</td>
<td>Organism maybe seen (isospora belli, crypto sporidias, microsporidias) PAS staining macrophages (Mycobacterium avium intracellular).</td>
<td>Patchy</td>
</tr>
</tbody>
</table>
MUCOSAL BIOPSY OF THE SMALL INTESTINE

Mucosal biopsy is essential for the diagnosis of many diseases of the intestinal mucosa. Characteristics histologic changes in different diseases are summarised in table 5.

Finally if a specific disaccharidase deficiency is suspected an unfixed intestinal biopsy can be analyzed for disaccharidase activity (Dahlquist, 1968) Decreased disaccharidase levels may be secondary to small intestinal disease or may represent a primary disaccharidase deficiency.
AIMS AND OBJECTIVES OF STUDY

1. To study the spectrum of malabsorptive disorders in Bundelkhand region of Central India.

2. To evaluate the role of faecal fat estimation and D-xylose absorption test in those patients suspected of having malabsorptive disorder.

3. To establish the control values of faecal fat excretion and D-xylose absorption test in normal healthy volunteers of Bundelkhand region, India.