MALABSORPTION SYNDROME IN SINGAPORE

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and

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INTRODUCTION

The malabsorption syndrome can broadly be defined as any disease associated with impairment of digestion and/or absorption of ingested foodstuffs. Steatorrhoea is the best example of this. There is no doubt however that many patients fail to digest or absorb many things other than fat. There is thus now a wide spectrum of malabsorptive states described all over the world. Vitamin B_{12} malabsorption in pernicious anaemia and lactose malabsorption in alactasia are but two examples of this wide spectrum of diseases.

In tropical countries like Singapore and other South East Asian countries, and especially in countries like India, Ceylon, Puerto Rico and Hong Kong, tropical sprue has to be considered in any case presenting as malabsorption syndrome. Tropical sprue however is not a recent disease for it has been described for over 200 years. Hillary described it in Barbados as early as 1759, and during the 19th and early 20th centuries, Dutch physicians in Indonesia, the French in Cochin-China and the English in India and Ceylon described the disease in clinical and autopsy reports (Swanson *et al*, 1965).

With the introduction of the intestinal biopsy capsule or tube (Shiner, 1956; Crosby and Kugler, 1957) the jejunal mucosa could be studied in patients with malabsorption. In Singapore, the appearances of the jejunal mucosa in European patients with acute tropical sprue were reported by England and O'Brien (1966).

This paper is the first report of a spectrum of malabsorptive states in Asian patients in Singapore. It includes 20 cases of tropical sprue, 6 cases of chronic pancreatitis with steatorrhoea and 10 cases with various malabsorptive states (Table I). This report also shows that malabsorption in Singapore is not restricted to tropical sprue since other causes do occur not uncommonly. It is the impression however that idiopathic steatorrhoea or adult coeliac disease, so commonly seen in the Western countries is very rare in Singapore as there has been, to date, no report of any case in an Asian in Singapore.

METHOD

All cases of malabsorption syndrome were studied in the Department of Clinical Medicine, during the period from June 1966 to March 1969. The following investigations were used to test various digestive or absorptive functions in the cases reported:

Haematology: Hemoglobin, total white count and peripheral blood film were done in all cases. Megaloblastic anaemia was confirmed by sternal puncture for marrow, and the FIGLU test or more recently serum folate and serum vitamin B_{12} levels were done.

Biochemistry: Stool fat excretion (1 to 3 days collection), Xylose absorption test (25 gms. dose; 5 hour urine collection), Vitamin A absorption test, glucose tolerance test, lactose tolerance test for alactasia and sometimes serum carotene.

Jejunal Biopsy: This was done in all cases except in those who refused to give consent. A Baker-Hughes multiple retrieving small intestinal biopsy tube (Baker and Hughes, 1960) was used. The position of the tube was checked by television screening. The position of the tube was studied under the dissecting microscope and by histological sections.

Gastric Biopsy and Augmented Histamine Test: Gastric biopsy was done by the Baker-Hughes tube and the gastric acid secretion by the Radiometer automatic titrator and pH meter.

Radiology: Barium small bowel study was done and for alactasia, a lactose barium study.

Urine Isoamylase: This was done in all the cases of chronic pancreatitis with steatorrhoea.

MATERIAL

The complete list of the various malabsorptive states seen in the Department of Clinical Medicine, from June 1966 to March 1969, are

TABLE I

A SPECTRUM OF MALABSORPTIVE STATES IN ASIAN PATIENTS IN SINGAPORE

Tropical Sprue	20 cases
Chronic Pancreatitis with Steatorrhoea	6 cases
Intestinal Diverticulosis with Steatorrhoea	1 case
Tuberculous Jejunitis with Malabsorption	1 case
Diabetic Steatorrhoea	1 case
Intestinal Scleroderma with Steatorrhoea	1 case
Adult Lactose Malabsorption	2 cases
Hepatocellular Carcinoma with Malabsorption	1 case
Vit. B_{12} Malabsorption Following Oesophageal-jejunal Anastomosis	1 case
Systemic Lupus Erythematosus with Steatorrhoea	1 case
Intestinal Salmonella Infection and Malabsorption	1 case
TOTAL	36 cases

TABLE II

TROPICAL SPRUE: BASIC DATA

No. of Cases		=	20
Age:	Mean	=	55.4 years
	Range	=	24 to 80 years
Sex:	Males: Females	=	15:5
Race:	Indian	=	12 cases
	Chinese	=	4 cases
	Sikh	=	2 cases
	Eurasian	=	2 cases

TABLE III

CLINICAL FEATURES OF TROPICAL SPRUE (20 CASES)

Megaloblastic Anaemia	19/20 cases (95%)
Diarrhoea/Steatorrhoea	15/20 cases (75%)
Weakness and Muscle Wasting	13/20 cases (65%)
Weight Loss	12/20 cases (60%)
Glossitis and Angular Stomatitis	12/20 cases (60%)
Peripheral Neuropathy	8/20 cases (40%)
Congestive Cardiac Failure	6/20 cases (30%)
Hyperpigmentation	6/20 cases (30%)
Fever	4/20 cases (20%)
Abdominal Pain	3/20 cases (15%)
Lymphadenopathy	2/20 cases (10%)
Ascites (Mild)	2/20 cases (10%)

TABLE IV

HAEMATOLOGICAL INVESTIGATIONS IN 20 CASES OF TROPICAL SPRUE

Megaloblastic Erythropoiesis (Marrow)	19/20 cases (95%)
Haemoglobin:	
Mean	5.4 gms. %
Range	1.9 to 11.4 gms. %
Leukopenia (<4000/cu. mm.)	13/20 cases (65%)
Low Serum Iron (<70 mcg. %)	3/18 cases (16.6%)
Folic Acid Deficiency (Figlu/S. Folate)	9/9 cases (100%)
Serum Vit. B_{12} Deficiency (<150 uug./ml.)	2/8 cases (25%)
Low Serum Calcium (<8.5 mg. %)	3/8 cases (37.5%)
Low Serum Albumin (<3.0 gm. %)	6/11 cases (54.5%)
Low Serum Sodium (<130 meq./L)	3/13 cases (23%)
Low Serum Potassium (<3.0 meq./L)	4/13 cases (30.7%)

TABLE V

INVESTIGATIONS FOR MALABSORPTION IN 20 CASES OF TROPICAL SPRUE

Low Xylose Absorption	15/15 cases (100%)
Abnormal Small Bowel Mucosa	12/12 cases (100%)
(Partial Villus Atrophy 11/12 cases)	
(Subtotal Villus Atrophy 1/12 cases)	
Flat Glucose Tolerance Curve	12/14 cases (86%)
Low Vitamin A Absorption	10/13 cases (77%)
Abnormal Stool Fat Excretion	7/15 cases (46.7%)
Abnormal Barium Study (Small Bowel)	4/10 cases (40%)
Moderate to marked Hypochlorhydria	6/11 cases (54.5%)
Histamine-Fast Achlorhydria	2/11 cases (18.2%)
Atrophic Gastritis (Gastric Biopsy)	3/3 cases

TABLE VI

RESPONSE TO TREATMENT IN TROPICAL SPRUE

Treatment	Response	No. Cases
Tetracycline Alone	Good	2
Folic Acid Only	Good	8
Tetracycline + Folic Acid	Good	2
Folic Acid + Vitamin B_{12}	Good	4
Tetracycline + Folic Acid + B_{12}	Good	2
	Fair	1
	Poor	1 (Death)
	TOTAL	20

shown in Table I. This series can be divided into two parts: Part 1—Tropical sprue and Part 2—Chronic pancreatitis and Miscellaneous.

PART 1: TROPICAL SPRUE

Twenty cases of tropical sprue were seen and studied in the Department, during this period. The basic data and clinical features are shown in Tables II and III; haematological investigations in Table IV; results of absorptive studies in Table V; response to treatment in Table VI and diagramatic representation of the clinical course of a case in Fig. 1. The appearances of the intestinal mucosa in these cases of tropical sprue are shown in Figs. 3 to 5; the changes in the gastric mucosa in Fig. 6 and the abnormalities seen in the barium small bowel study in Fig. 7.

PART 2: CHRONIC PANCREATITIS AND MISCELLANEOUS CAUSES OF MALABSORPTION

(a) **Chronic Pancreatitis with Steatorrhoea**

Altogether 7 cases of chronic pancreatitis were seen but only 6 cases had steatorrhoea. The clinical features of these 6 cases are given in Table VII. The brief case histories of 2 representative cases of chronic pancreatitis with steatorrhoea (one secondary to chronic alcoholism and the other secondary to biliary disease) are given below:

Case L. A.: This 55 year old Indian male was admitted for alcoholic intoxication. He was a chronic alcoholic for the past 20 years. His liver was enlarged to 6 cm. below the subcostal margin but the liver function tests were normal. He also had diabetes mellitus, which was controlled with tolbutamide. He was readmitted 5 times for acute alcoholic intoxication and delirium tremens. Nine years after the first admission he began to have severe epigastric pain, which radiated to the back and was not relieved by antacids. His stools also became pale, bulky, offensive and sometimes watery. He stopped drinking by joining Alcoholic Anonymous but the pain continued to recur. A plain X-ray abdomen showed extensive calcification of the whole of the pancreas (see Figs. 8 and 9) and stool fat estimation confirmed a severe steatorrhoea of 20.0 gms./day. The serum amylase and urine diastase were normal and xylose absorption test gave a normal result of 5.5 gms., confirming that the steatorrhoea was pancreatic in origin. A liver biopsy showed essentially normal liver and cholecystography showed a normal gall bladder with no stones. A jejunal biopsy was done and showed normal intestinal mucosa. Treatment included pancreatic extract for this steatorrhoea, but he continues to have recurrent abdominal pain.

TABLE VII

SOME IMPORTANT FEATURES OF 6 CASES OF CHRONIC PANCREATITIS WITH STEATORRHOEA

Feature	Incidence
No. of Cases	6
Mean Age (years)	46.6
Males:Females	6:0
Race Distribution:	
Indian	3
Chinese	2
Malay	1
Chronic Alcoholism	4/6
Biliary Disease	2/6
Recurrent Pain	3/6
Steatorrhoea	6/6
Diabetes Mellitus	4/6
Pancreatic Calcification	5/6
Impaired Pancreatic Exocrine Function (Urinary Isoamylase)	3/6
Normal Xylose Test	5/5

Case R. P.: This 38 year old Indian male was first taken ill with obstructive jaundice, for which a laparotomy was done. A cholecystectomy was done and it was also found that the pancreas had areas of calcification and was hard and fibrotic on palpation. A diagnosis of chronic calcific pancreatitis was thus made. Surgical liver

CLINICAL PRESENTATION, INVESTIGATIONS AND RESPONSE TO TREATMENT OF A CASE OF TROPICAL SPRUE

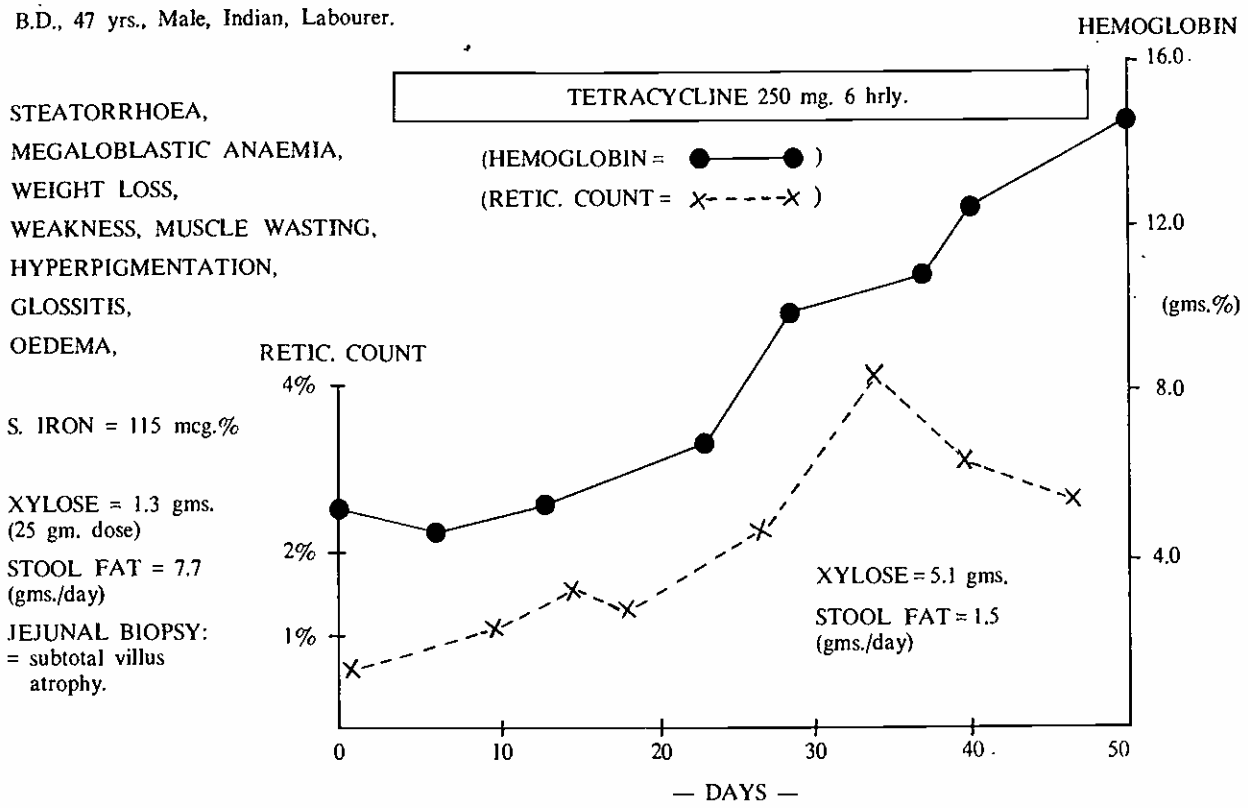

Fig. 1.

LACTOSE AND GLUCOSE TOLERANCE TESTS IN A CASE OF ADULT LACTOSE MALABSORPTION (CASE K.S.)

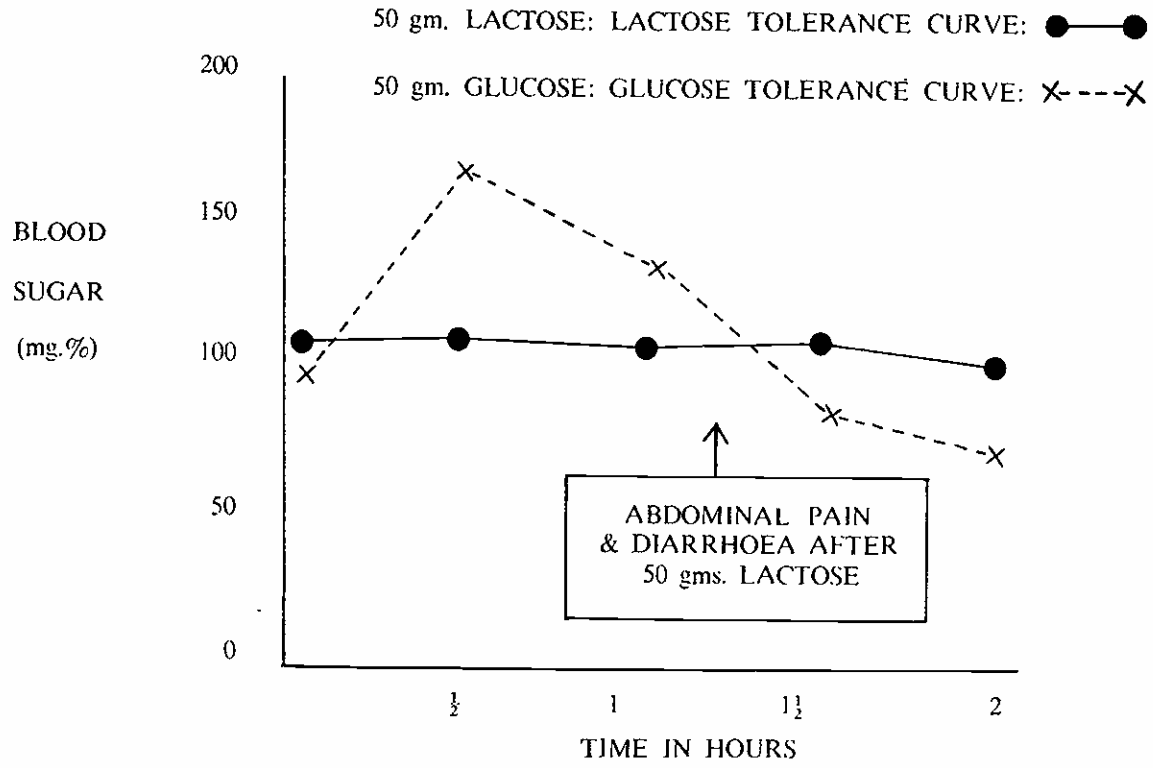

Fig. 2.

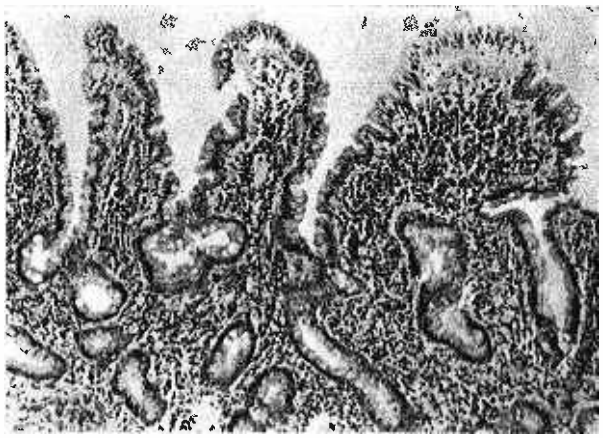

Fig. 3. Intestinal mucosa of a case of tropical sprue showing mild villus atrophy. Note the shortened and broadened villi and the marked inflammatory cell infiltration of the lamina propria. (Haematoxylin and eosin, × 100)

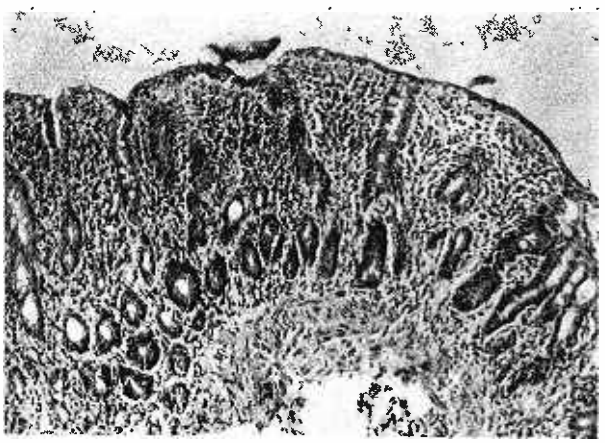

Fig. 5. Intestinal mucosa of a case of tropical sprue showing subtotal villus atrophy. Note the almost complete absence of villus structure, the marked inflammatory cell infiltration and the marked hypertrophy of the crypt zone. (Haematoxylin and eosin, × 100). Only one case had this degree of villus atrophy.

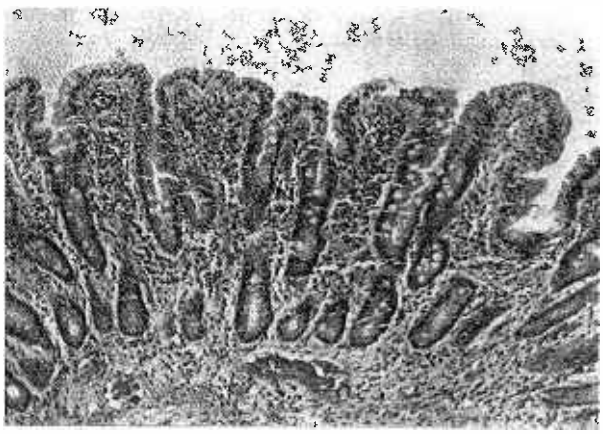

Fig. 4. Intestinal mucosa of a case of tropical sprue showing partial villus atrophy of a moderate degree. Note the stunted and broad villi, marked cellular infiltration of the lamina propria and hypertrophy of the crypt zone. (Haematoxylin and eosin, × 100)

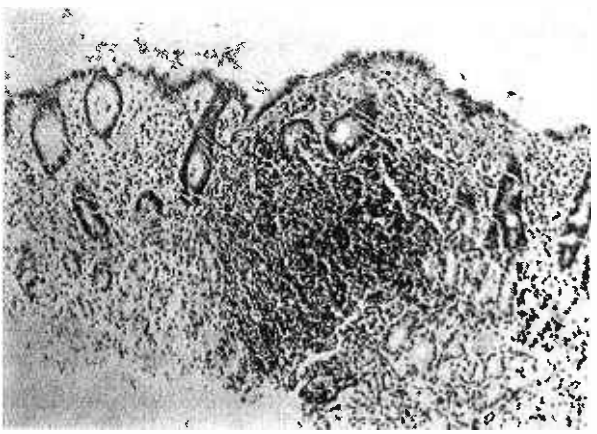

Fig. 6. Gastric biopsy of a case of tropical sprue showing atrophic gastritis. Note the scanty gastric glands and the marked infiltration with plasma cells and lymphocytes almost to the degree of follicular formation. (Haematoxylin and eosin, × 100)

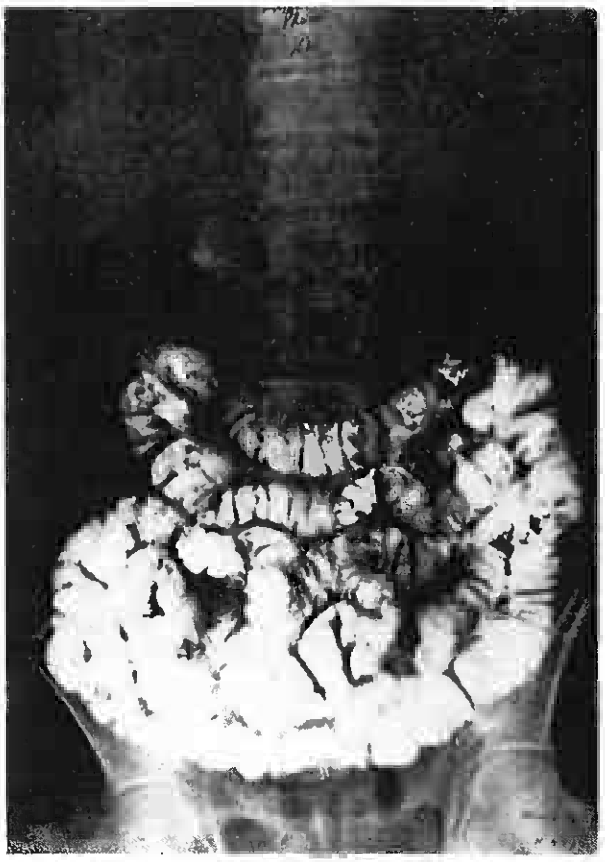

Fig. 7. Barium small bowel study of a case of tropical sprue showing dilatation of the jejunal loops and thickening of the transverse folds (valvulae conniventes).

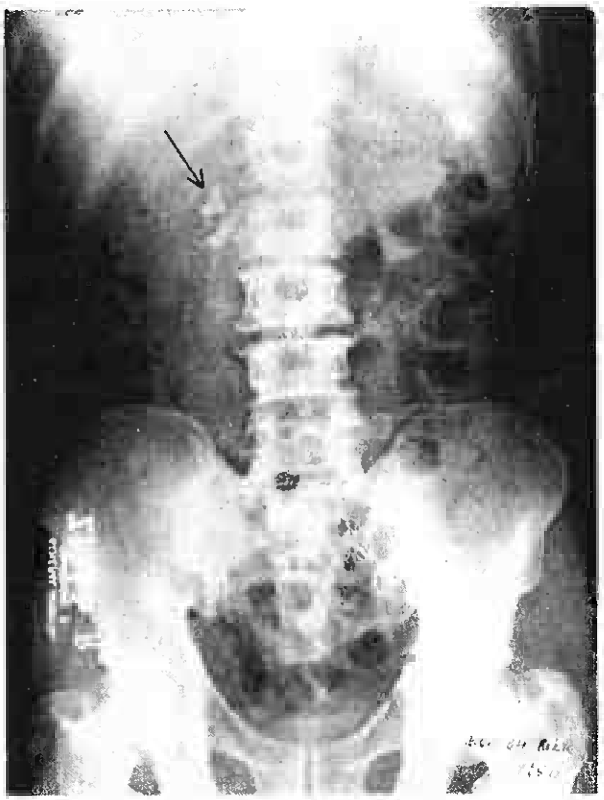

Fig. 9. Plain X-ray of another case of chronic pancreatitis showing extensive calcification of the head of the pancreas (arrow).

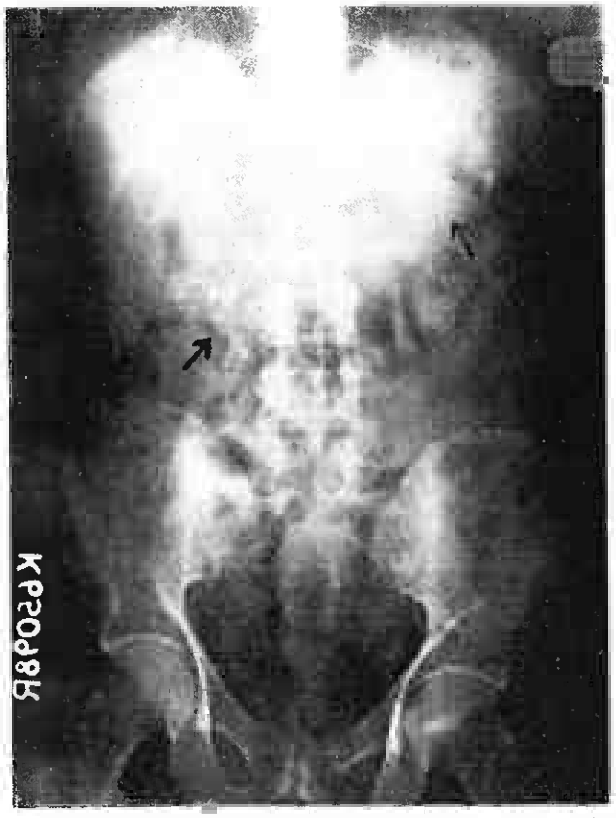

Fig. 8. Plain X-ray of the abdomen of a case of chronic pancreatitis showing extensive calcification of the pancreas (arrows).

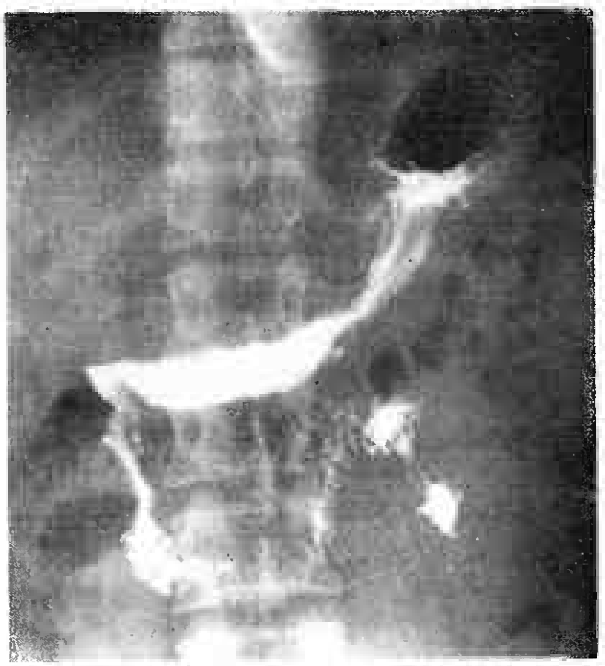

Fig. 10. Barium meal study of a case R.P. of chronic pancreatitis showing marked narrowing, rigidity and deformity of the second part of the duodenal loop, indicating an advanced degree of pancreatic pathology.

biopsy showed only bile stasis while a lymph node taken near the pancreas showed chronic inflammation. He then started to experience epigastric pain which radiated to the back. This was accompanied by anorexia, belching and bulky stools which float on water. Steatorrhoea was confirmed by a stool fat of 11.0 gms./day. This was pancreatic in origin as the xylose absorption test was normal (6.6 gms.). The serum amylase and urine diastase were normal. Although no definite calcification was seen on plain abdominal X-ray, a barium meal showed narrowing and rigidity of the second part of the duodenal loop, indicating pancreatic pathology (Fig. 10). He was treated with pancreatic extracts which cleared up the steatorrhoea but the pain continued to recur.

Urinary isoamylase was done in all these 6 cases, and showed impaired pancreatic exocrine function in 3 of the 6 cases (Table VII). These 3 cases had no abdominal pain and were therefore in remission. In the other 3 cases, who had recurrent pain, the pancreatic isoamylase was markedly higher than normal. The significance of these results is discussed in Fung and Aw, 1969.

(b) Miscellaneous Causes of Malabsorption

Intestinal diverticulosis

Case M. S.: This 60 year old Sikh male presented with marked megaloblastic anaemia, glossitis, angular stomatitis and congestive cardiac failure. Investigations showed a haemoglobin of 3.7 gm.%; total white count of 3,200/cu. mm.; reticulocyte count of 13.0% and a megaloblastic marrow. Serum iron was 141 mcg.% and serum vitamin B_{12} level was 160 uug./ml. Malabsorption was confirmed by a very low xylose test of only 0.85 gms. and he had a steatorrhoea of 19.5 gms. fat/day. Barium small bowel study showed large jejunal diverticula (Fig. 11). His steatorrhoea subsided with tetracycline and the megaloblastic anaemia improved with folic acid.

Tuberculous Jejunitis with Malabsorption and Ileal Stricture

Case W.M.C.: This 21 year old Chinese girl presented with chronic diarrhoea, abdominal pain, fever, weight loss, anaemia, ankle oedema and amenorrhoea. Her abdomen was slightly distended and had a doughy feel on palpation. She had a hemoglobin of 7.5 gm.%, reticulocyte count of 5.0% and normal serum iron. Chest X-ray revealed active pulmonary tuberculosis and laryngeal swab cultures grew mycobacterium tuberculosis. Barium enema showed stricture of the terminal ileum with hypertrophy of the ileocaecal valve (Fig. 12). Spiking was also seen in some films. Malabsorption was confirmed by a low xylose absorption of 3.5 gms., low vitamin A absorption of 95 I.U./100 ml. serum and a flat glucose tolerance curve. There was however no steatorrhoea since stool fat was only 2.1 gm./day. This was however done during the recovery phase. A jejunal biopsy, done before treatment, showed subtotal villus atrophy with marked inflammatory cell inflammation of the lamina propria (Fig. 13a). After only 4 weeks of anti-tuberculous therapy, a repeat intestinal biopsy showed a dramatic return to normal of the villus stricture (Fig. 13b) indicating the tuberculous nature of the original jejunitis. She also had atrophic gastritis on gastric biopsy, hypochlorhydria and possible protein losing enteropathy. With anti-tuberculous therapy, she made a full and rapid recovery in a matter of a few months.

Diabetic Steatorrhoea

Case S.P.: This 53 year old Indian labourer had diabetes mellitus for more than 22 years, controlled with insulin zinc suspension (lente) 40 units daily. He had peripheral neuropathy and muscle wasting. In the course of his diabetes, he developed chronic diarrhoea and steatorrhoea. There was no blood or mucus in the stools and repeated stool cultures were negative. Steatorrhoea was confirmed by a stool fat excretion of 9.3 gms./day. Malabsorption was further evidenced by a low xylose test of 3.3 gms., and a low vitamin A test of 120 I.U./100 ml. serum. A jejunal biopsy showed occasional convolutions on dissecting microscopy but sections were normal. Barium small bowel study was normal. He continues to have occasional diarrhoea and steatorrhoea in spite of adequate control of his diabetes.

Scleroderma with Steatorrhoea

Case M.A.K.: This 52 year old Chinese woman had long standing scleroderma of the skin (since 1960), confirmed by skin biopsy. She also had pericarditis and L.E. Cell test was positive once. Long term prednisolone therapy was given with little or no effect on the course of the disease. In 1968, she started to lose weight and had irregular bowel habits. Barium enema showed multiple colonic diverticula (Fig. 14) and steatorrhoea was confirmed by a stool fat excretion of 33.0 gms./day. Malabsorption was further evidenced by a low vitamin A test of 241 I.U./100 ml. serum and a flat glucose tolerance test.

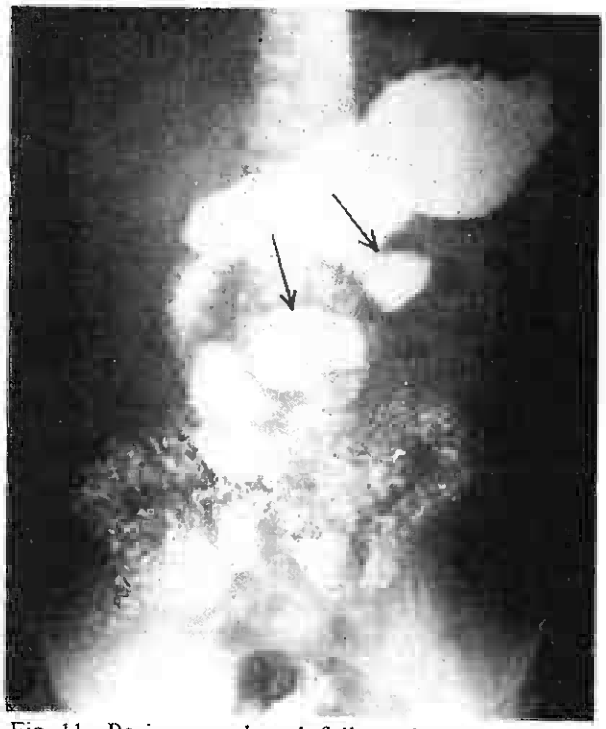

Fig. 11. Barium meal and follow through study of case M.S. showing large jejunal diverticula (arrows), one of which (upper arrow) has a fluid level.

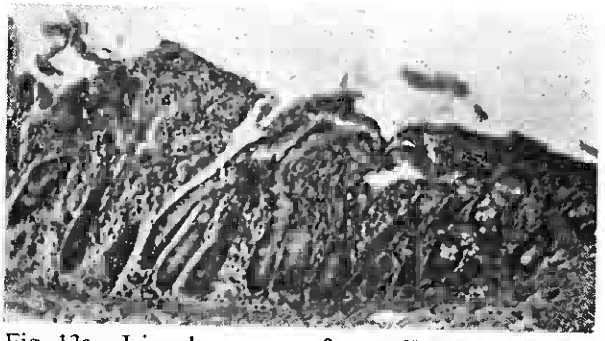

Fig. 13a. Jejunal mucosa of case W.M.C. showing subtotal villus atrophy, inflammatory cell infiltration of the lamina propria and hypertrophy of the crypt zone. (H. & E. × 100). This biopsy was seen to be flat on dissecting microscopy.

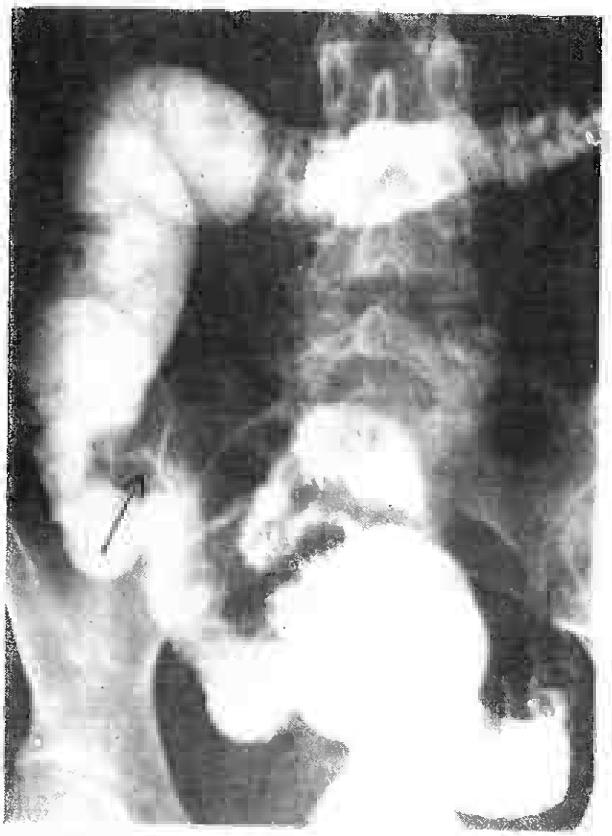

Fig. 12. Barium enema study of case W.M.C. showing stricture of the terminal ileum (arrow) and hypertrophy of the ileocaecal valve. This is most probably tuberculous in nature as this case had active pulmonary tuberculosis, chronic diarrhoea, abdominal pain and malabsorption.

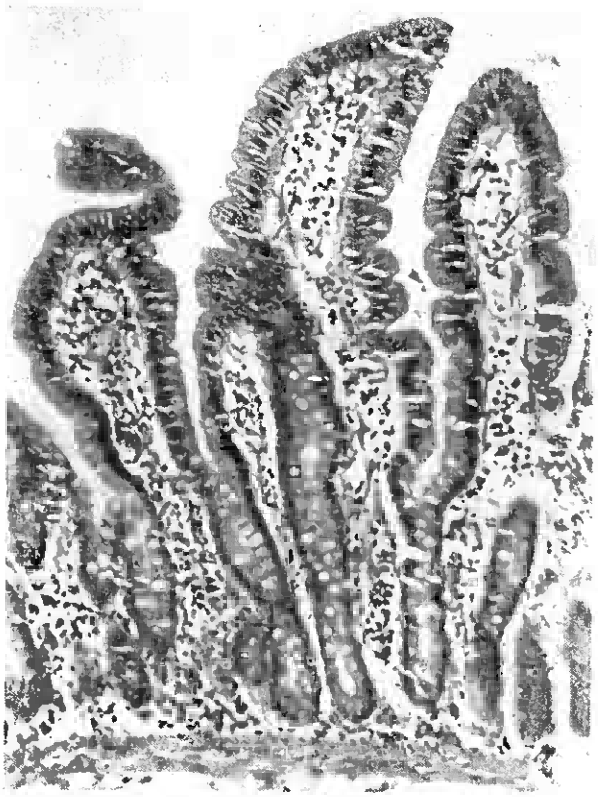

Fig. 13b. Intestinal mucosa of same case W.M.C. showing marked improvement of villus structure after only 4 weeks of anti-tuberculous therapy. (H. & E. × 100)

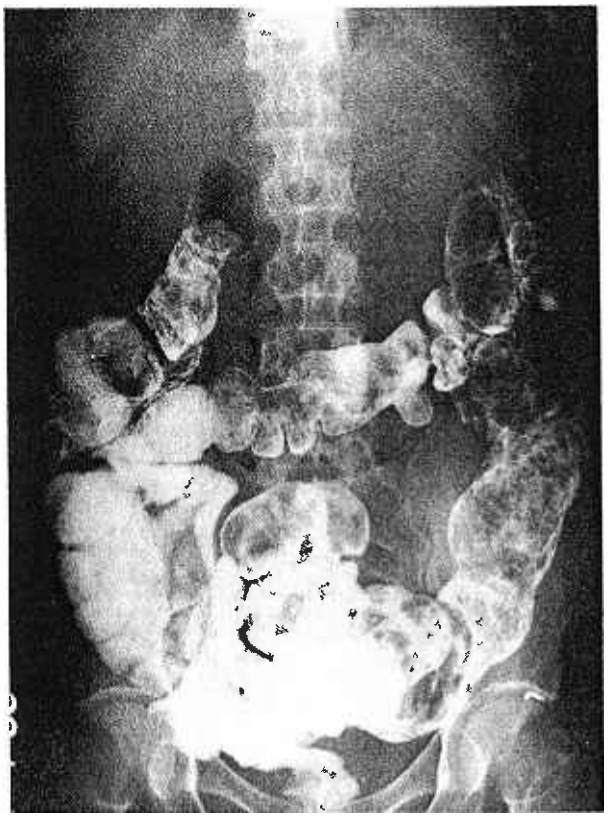

Fig. 14. Barium enema of a case of scleroderma M.A.K. showing multiple colonic diverticula characteristic of the disease.

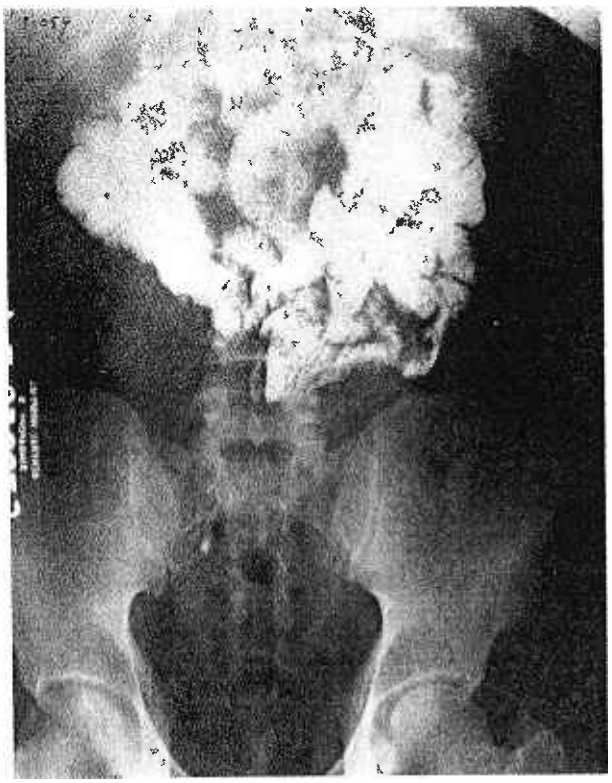

Fig. 15a. Sucrose Barium study (4 oz. micropaque and 25 gm. sucrose) of case K.S. showing normal appearance of small intestinal pattern (1 hour film).

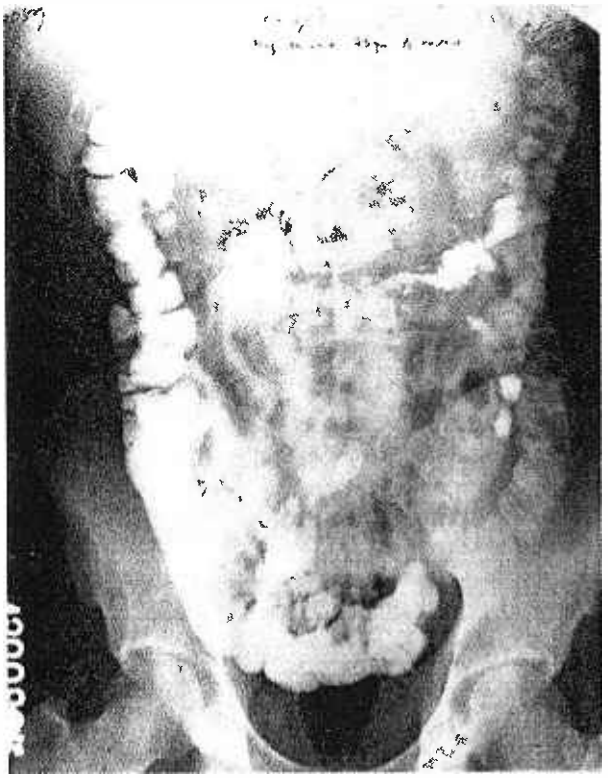

Fig. 15b. Lactose Barium study (4 oz. micropaque and 25 gm. lactose) of case K.S. showing marked dilution of the contrast and marked intestinal hurry (1 hour film), a picture typical of lactose malabsorption due to hypo or alactasia. (Courtesy of Dr. K. M. Kho)

Vitamin B_{12} Malabsorption Following Oesophageal-jejunal Anastomosis

Case P.G.S.: This 27 year old Chinese girl developed oesophageal stricture following attempted suicide with caustic soda. An oesophageal-jejunal anastomosis was done with the upper oesophageal end directly anastomosed to the proximal jejunum end to end, and the stomach (with the lower oesophageal end closed) and duodenal loop anastomosed to the lower jejunum end to side. Six years after this operation, she presented with a severe megaloblastic anaemia. The hemoglobin was 5.1 gm.%; total white count 1,400/cu. mm.; platelet count 15,000/cu. mm. and retic. count 1.0%. The serum vitamin B_{12} level was markedly decreased to 90 uug./ml., while the serum iron was 176 mcg.%. Absorptive studies showed a serum carotene of 45 mcg.% and vitamin A absorption test of 1070 I.U./100 ml. serum. Barium studies showed rapid transit of contrast but no blind loop or fistula. Oral tetracycline failed to bring improvement but parenteral vitamin B_{12} was followed by a dramatic response, with hemoglobin rising to 11.0 gm.% and retic. count to 9.0%.

Lactose Malabsorption

Two cases of adult lactose intolerance were seen. This is the typical history of one of these cases.

Case S.K.: This 29 year old Indian male had epigastric pain and vomiting in 1961, when a barium meal showed a small hiatus hernia. He was given antacids and was well until 1968, when he started to have abdominal pains and diarrhoea. The stools were soft and watery, without blood, and the diarrhoea relieved the abdominal pain. On further questioning, it was found that milk aggravated these symptoms. Stool cultures were negative. A lactose barium study showed a typical picture of alactasia (Figs. 15a and 15b), while a lactose tolerance test showed a flat curve (Fig. 2) typical of lactose malabsorption. Milk intake was stopped and the symptoms subsided completely.

Hepatocellular Carcinoma with Malabsorption

Case O.K.L.: This 53 year old Chinese male presented with chronic diarrhoea, weight loss and abdominal pain. His liver was enlarged to 5 cm. below the subcostal margin and there were spider naevi, liver palms and hyperpigmentation. Liver function tests were essentially normal and the serum albumin was 3.8 gm.%. Liver biopsy failed to confirmed cirrhosis. Malabsorption was confirmed by a low xylose absorption test of 1.5 gms. and a low vitamin A absorption test of 420 I.U./100 ml. serum. Jejunal biopsy showed partial villus atrophy, supporting the intestinal origin of the malabsorption. A laparotomy was done and the gall bladder, which had stones, was removed. A few months later, he developed ascites and chest X-ray showed cannon-ball secondaries. He died soon after and autopsy showed ruptured hepatocellular carcinoma, cirrhosis of liver and pulmonary secondaries.

Systemic Lupus Erythematosus with Steatorrhoea

Case M.K.: This 29 year old Sikh girl presented with polyarthritis and fever. S.L.E. was confirmed by a positive L.E.Cell test. A few months after onset of illness, she developed deepvein thrombosis, for which she was put on long term anticoagulant therapy (phenindione). About $2\frac{1}{2}$ years after onset of illness, she had diarrhoea and steatorrhoea. Malabsorption was confirmed by a xylose test of 2.7 gm., stool fat of 12.3 gm./day and vitamin A absorption of 240 I.U./100 ml./ serum. It is still not clear whether the malabsorption is secondary to S.L.E. or the phenindione therapy.

Intestinal Salmonellosis with Malabsorption

Case S.L.H.: A 34 year old Chinese woman presented with chronic diarrhoea, marked weight loss (80 lbs.), chronic abdominal pain and anaemia. She was also 8 months pregnant. Malabsorption was confirmed by a very low xylose absorption of 0.4 gms. (25 gm. dose). Her stool cultured salmonella bovis morbificans. After treatment with antibiotics, the diarrhoea stopped and she improved.

DISCUSSION

Of 36 cases of malabsorption syndrome (Table I) only 20 were tropical sprue. This shows that although tropical sprue is the commonest cause of malabsorption in Singapore, malabsorption secondary to other disease processes does occur. A great variety of malabsorption syndromes can thus be seen in Asian patients in Singapore.

Tropical sprue occurs predominantly in people around 55.4 years, in more males than females (3:1) and in Indians. Megaloblastic anaemia is the commonest presentation of tropical sprue, closely followed by diarrhoea or steatorrhoea. Tropical sprue should therefore be considered in every case of megaloblastic anaemia. This high incidence of megaloblastic anaemia is in sharp contrast to idiopathic steatorrhoea or

adult coeliac disease, where its occurence is considered rare. In 6 cases the anaemia was so severe that they had congestive cardiac failure. Among the tests for malabsorption, the commonest abnormalities were a low xylose absorption (100%), folic acid deficiency (100%), abnormal small bowel mucosa (100%), flat glucose tolerance test (86%) and low vitamin A absorption (77%). Stool fat was abnormally increased in only 46.7% of cases, while barium small bowel studies were abnormal in only 40% of cases. Steatorrhoea is thus not so common in tropical sprue and its absence does not exclude the diagnosis. This result agrees with that of Jeejeebhoy *et al* (1966) who also found steatorrhoea in only half their patients with tropical sprue.

The high incidence of megaloblastic anaemia can be related with the high incidence of folic acid deficiency since the serum vitamin B_{12} level was low in only 25% of cases tested. Folic acid deficiency is thus the commonest cause of megaloblastic anaemia in tropical sprue and this is in keeping with current views. In the treatment of this disease, tetracycline alone was used in some cases initially but only 2 cases responded to it (see Fig. 1). All the remaining cases required folic acid or vitamin B_{12} Eight cases responded to folic acid alone showing that folic acid is the most important form of therapy. All cases responded to treatment except an 80 year old Indian male, who died in spite of large doses of tetracycline, folic acid, parenteral vitamin B_{12} and parenteral iron. Autopsy in this case revealed only partial villus atrophy affecting the whole length of the intestine.

Intestinal biopsy was done in 12 of the 20 cases and the predominant abnormality was partial villus atrophy (Figs. 3 and 4). Subtotal villus atrophy (Fig. 5) was rare and seen in only one case. In some cases where the mucosal changes were very mild the steatorrhoea could be as high as 21.0 gm./day. On the other hand, cases without steatorrhoea may show a moderate degree of partial villus atrophy. In the only case with subtotal villus atrophy the stool fat was only 7.7 gm./day. There is thus no correlation between the degree of malabsorption, as represented by the severity of steatorrhoea, and the extent and severity of the villus atrophy. This supports the view that malabsorption in tropical sprue is independent of the mucosal lesion and is probably determined by biochemical changes in the mucosa (Jeejeebhoy *et al*, 1966).

Atrophic gastritis (Fig. 6) was found, on gastric biopsy, in 3 cases and there was also a notable incidence of achlorhydria (2 cases) and hypochlorhydria (6 cases). Gastritis seen on gastric biopsy has been reported to be present in 90% of patients with sprue. More than half of sprue cases have mild to severe atrophic gastritis and a typical sprue like vitamin B_{12} absorptive defect can progress to a pernicious anaemia like lesion (Vaish *et al*, 1965).

Radiological study of the small bowel has not been very helpful in the diagnosis of tropical sprue, in this series, since only 40% of cases studied showed abnormalities (Fig. 7). This is in contrast to Caldwell *et al*, (1965) who, in a comparison of radiology with other tests for sprue (faecal fat, xylose, vitamin A, carotene and jejunal biopsy) found radiology to be positive for sprue in 90% of cases. They concluded that radiology was a reliable and satisfactory method of diagnosing malabsorption due to intestinal mucosal lesion.

Of 36 cases of malabsorption, 6 were secondary to chronic pancreatitis, which was thus responsible for 16.6% of cases. Chronic pancreatitis is thus the second commonest cause of malabsorption in Singapore. It is interesting to note that in Uganda, East Africa, chronic pancreatitis was responsible for the majority of cases with the malabsorption syndrome (30 out of 54 cases) (Banwell *et al*, 1967). They also found that the disease occurred in young people and more closely resembled the pancreatic lithiasis in other tropical countries (Zuidema, 1959) than the chronic pancreatitis of chronic alcoholics. Tropical sprue was also found to be virtually absent in Uganda (Banwell *et al*, 1967). In this series, chronic pancreatitis was secondary to chronic alcoholism in 4 cases and to biliary disease in the remaining 2 cases. As in other reported series (Marks and Banks, 1963; Sarles *et al*, 1965) chronic alcoholism is the commonest aetiological factor in chronic pancreatitis, followed by biliary disease. There was a high incidence of steatorrhoea, diabetes mellitus and pancreatic calcification in this series. Impaired pancreatic exocrine function was detected by urinary isoamylase in 3 of the 6 cases. Urinary isoamylase was found to be a useful test for pancreatic function, provided the pancreatic disease was in remission (Fung and Aw, 1969) (Aw *et al*, 1967).

Jejunal biopsy was done in 2 of the 6 cases of chronic pancreatitis, and partial villus atrophy was found in one. This case also had alcoholic cirrhosis and it is possible that the villus atrophy maybe secondary to either the pancreatitis or the cirrhosis, although in a report of malabsorptive studies in cirrhotic patients, jejunal biopsies have been reported to be normal (Sun *et al*, 1967).

The malabsorption of case M.S., who had jejunal diverticulosis, is probably secondary to altered bacterial flora. The steatorrhoea may result from alteration of conjugated bile salts by the abnormal bacterial flora in the jejunal diverticula, with resultant reduction of micellar formation. This is supported by the fact that the steatorrhoea cleared up wtih tetracycline.

Although pulmonary tuberculosis is still a major disease in Singapore, malabsorption secondary to intestinal tuberculosis is rare. In fact this is the first case (W.M.C.) reported in Singapore of malabsorption secondary to tuberculous jejunitis. This is another instance of a flat jejunal mucosa secondary to tuberculosis. The tuberculous nature of this jejunitis is confirmed by the dramatic return to normal of the intestinal mucosa (Figs. 13a and 13b) after only 4 weeks of anti-tuberculous therapy, together with the complete subsidence of the intestinal symptoms. This supports the view that a flat intestinal mucosa is not specific to idiopathic steatorrhoea or adult coeliac disease (Hindle and Creamer, 1965). Hindle and Creamer also reported a case with flat jejunal mucosa secondary to tuberculosis.

Steatorrhoea in diabetes mellitus may be due to associated pancreatic disease, adult coeliac disease or diabetic neuropathy. In this case (S:P) of diabetic steatorrhoea, there was a severe peripheral neuropathy with muscle wasting. There was no evidence of pancreatic disease here and although he had definite intestinal malabsorption, as shown by the low xylose and vitamin A tests, the jejunal biopsy was normal. The intestinal mucosa is however usually normal in diabetic diarrhoea even in the presence of significant steatorrhoea (Wruble and Kalser, 1964). Peripheral and autonomic neuropathy and bacterial overgrowth have been suggested as possible mechanisms in the pathogenesis of diabetic diarrhoea and steatorrhoea (Katz and Spiro, 1966).

Malabsorption, including steatorrhoea, has been described in scleroderma and the role of bacterial overgrowth has been further supported (Weser *et al*, 1966). Intestinal lesions usually occur late in the disease and are invariably associated with skin lesions.

Case P.G.S. is probably the first report of vitamin B_{12} malabsorption following oesophageal-jejunal anastomosis for caustic soda stricture of the oesophagus. The mechanism in this case was most probably due to the non-mixing of the ingested foodstuffs with the intrinsic factor of the stomach, since the stomach and duodenal loop had been by-passed by this operation (Booth, 1968).

The 2 cases of adult lactose intolerance have been included in this series as they represent a malabsorption secondary to a biochemical abnormality of the enterocyte brush border. Milk intolerance has been reported to be fairly common in adults, caused by lactose malabsorption due to a selective deficiency of intestinal lactase activity (Haemmerli *et al*, 1965; Cuatrecasas *et al*, 1965; Dunphy *et al*, 1965; McMichael *et al*, 1965) and even more so in patients with irritable colon syndrome (Weser *et al*, 1965). The case history of case K.S. is typical of adult lactose malabsorption or adult alactasia. In the diagnosis of this condition, a lactose tolerance test (Fig. 2) and a lactose barium study are the two most important and practical tests. Estimation of the disaccharidase activities in jejunal mucosa, obtained by intestinal biopsy, is important for final confirmation but is not necessary for diagnosis in clinical practice.

Case O.K.L. is probably the first report, in Singapore, of malabsorption and intestinal villus atrophy in hepatocellular carcinoma, a disease so commonly seen here.

In conclusion, a wide spectrum of malabsorptive states can be seen in Singapore. Tropical sprue is the commonest and chronic pancreatitis the second commonest cause of malabsorption in the country. There is also a fairly large group of malabsorption secondary to various disease processes.

SUMMARY

Thirty six cases of malabsorption syndrome are described. There were 20 cases of tropical sprue, 6 cases of chronic pancreatitis with steatorrhoea and 10 cases of miscellaneous causes of malabsorption. The commonest presentation of tropical sprue was megaloblastic anaemia and the commonest abnormalities found were a low xylose absorption, folic acid deficiency and abnormal intestinal mucosa. Steatorrhoea was present in only half the cases and there was no correlation between the severity of malabsorption and the severity of villus atrophy. The commonest intestinal lesion was partial villus atrophy and subtotal villus atrophy was rare. Radiology was disappointing in diagnosis as only 40% of cases studied had any abnormality. There was a notable incidence of atrophic gastritis, achlorhydria and hypochlorhydria. Response to treatment with tetracycline, folic acid and vitamin B_{12} was fair to good in most cases and only one case died without responding to a combination of all 3 drugs.

Steatorrhoea due to chronic pancreatitis was seen in 6 cases. Chronic alcoholism was the commonest aetiological factor in chronic pancreatitis followed by biliary disease. There was a high incidence of diabetic mellitus and pancreatic calcification in these 6 cases. Urinary isoamylase was found to be useful in the diagnosis of impaired pancreatic exocrine function provided the patient was in remission.

Ten cases of malabsorption secondary to various disease processes are described and many interesting features are discussed.

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