MEDICAL GRAND ROUNDS

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THE DIFFERENTIAL APPROACH TO PROBLEMS OF INTESTINAL MALABSORPTION

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A. THE NORMAL MECHANISMS OF FAT ABSORPTION

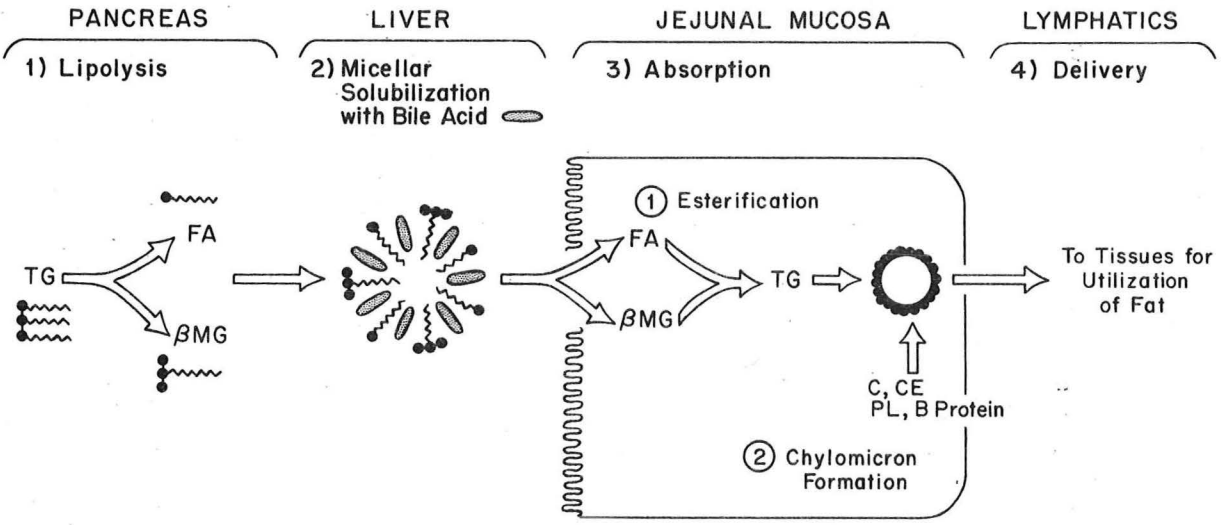

Fig. 1

As illustrated in Figure 1, the overall process of fat absorption can be divided into four distinct phases. The first two of these, i.e., lipolysis and micellar solubilization, involve the intraluminal digestion and preparation of dietary fat for absorption. The last two phases, i.e., mucosal uptake and delivery, are concerned with the actual process of absorption and transport of fat to the sites of utilization.

1. Pancreatic or Lipolytic Phase

The average American diet contains approximately 60-100 gm of fat per day--the majority of this is in the form of neutral fat or triglyceride. Triglyceride consists of the 3-carbon alcohol glycerol esterified to 3 long-chain fatty acid molecules. After ingestion, little hydrolysis occurs within the stomach (although a weak gastric lipase has been described). In the proximal small intestine, however, the triglyceride comes under hydrolytic attack by pancreatic lipase. This enzyme preferentially splits the ester bonds in the α-α' positions, although some triglyceride will be completely hydrolyzed to glycerol and fatty acids. As the result of this enzymatic attack, the two major end-products formed from triglyceride are fatty acid (FA) and β-monoglycerides (βMG).

2. Micellar Solubilization

Like the original triglyceride molecule, the end-products of fat lipolysis, fatty acid and β-monoglyceride, are essentially insoluble in water under the conditions that exist in the proximal gut lumen. Thus, lipolysis essentially does not alter solubility. Fatty acid and β-monoglyceride does, however, differ from triglyceride in one important aspect,

i.e., these two products are amphipaths, whereas triglyceride is not. Following the intake of food, gallbladder contraction occurs and bile acids, along with other biliary constituents, are secreted into the proximal small intestine. Bile acids chemically resemble detergent molecules in that a portion of the bile acid molecule is polar and water-soluble, while another portion of the molecule is non-polar and fat-soluble. Such detergent-like molecules, when present above a certain micellar concentration, cluster together in macromolecular complexes known as micelles. Like ordinary soaps, these micelles have the capacity to bring into solution other insoluble lipid materials. The amphipathic end-products of the first phase of fat absorption, i.e., fatty acids and monoglycerides, will dissolve into the micellar structure of the bile acids and so gain aqueous solubility. This process whereby the insoluble, amphipathic end-products of the hydrolysis of triglyceride are brought into aqueous solution by bile acids is known as micellar solubilization. By this mechanism, fat is brought into intimate contact with the microvillous border of the intestinal epithelium.

3. Mucosal Uptake

The fatty acid and β-monoglyceride diffuse across the cell membrane by a passive process and reach the interior of the mucosal epithelial cell. Within the cell, two very important modifications occur. First, the monoglycerides and long-chain fatty acids are re-esterified to triglyceride by one of two well-described biochemical pathways. Second, this insoluble droplet of triglyceride becomes associated with other chemical constituents including small amounts of protein, cholesterol, cholesterol ester and phospholipid, in the form of a specific class of lipoproteins, the chylomicrons. It is in this form that the triglyceride is released into the submucosal tissue of the intestinal wall and finds its way into the intestinal lymphatics.

4. Delivery Phase

The chylomicrons are released from the basal portion of the columnar epithelial cell and find their way into the central lacteal of each intestinal villus. From there, they travel in the lymph up the thoracic duct and eventually reach the general circulation. The triglyceride fat is then transported in the blood to the sites of disposal and utilization in the periphery in such tissues as the liver, muscle and fat storage sites.

B. LOCALIZATION OF SITES OF ABSORPTION ALONG THE SMALL INTESTINE

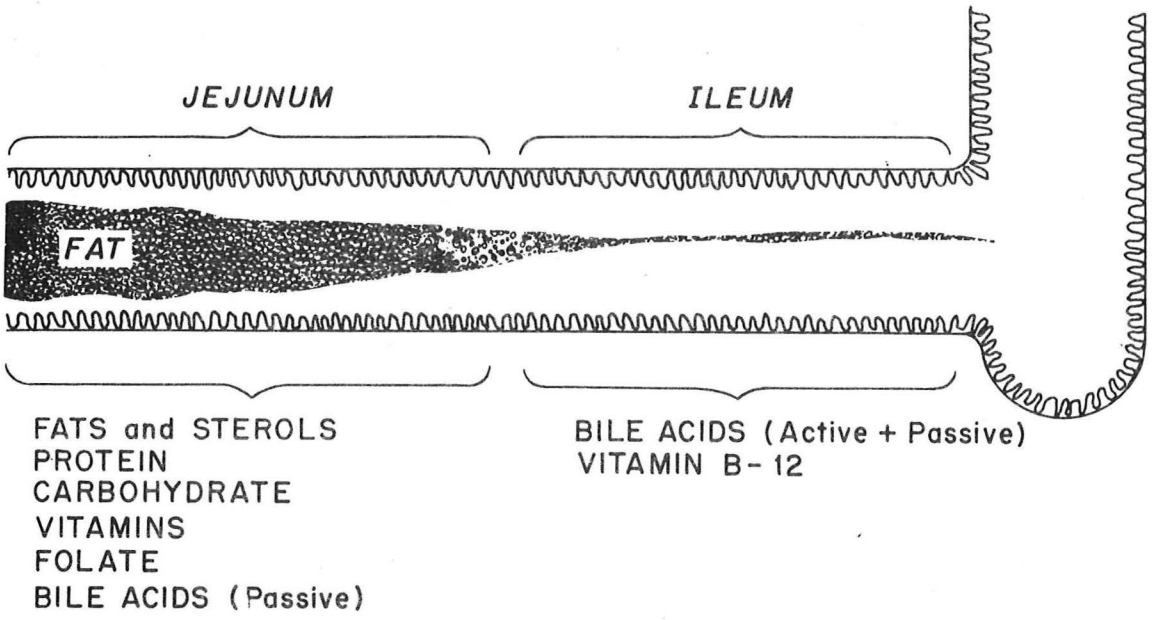

Fig. 2

As illustrated in Figure 2, the absorption of the major sources of calories, i.e., fat, protein and carbohydrate, takes place presumably in the proximal half of the small intestine. Similarly, absorption of water-soluble and fat-soluble vitamins (with the exception of vitamin B_{12}) also occurs predominantly in the jejunum. Bile acid absorption occurs by passive means across this portion of the gastrointestinal tract. The ileum also appears to be capable of absorbing fat, protein and carbohydrate, but under normal conditions absorption is complete before the distal portion of the small intestine is reached. Ileal absorption undoubtedly becomes quantitatively important, however, in disease conditions where proximal absorption is compromised. Only two transport processes appear to be specifically localized to the distal half of the small bowel; these are: 1) the active transport of bile acids, and 2) the sites for binding and the absorption of vitamin B_{12}.

C. THE ENTEROHEPATIC CIRCULATION OF BILE ACIDS

As illustrated in Figure 1, adequate concentrations of bile acid must be present within the jejunal contents if effective micellar solubilization of fatty acid and β-monoglyceride is to take place. As illustrated in Figure 3, such an effective concentration is maintained by the constant reutilization of a relatively small pool of bile acid. In response to a meal, bile acids that have been temporarily stored in the gallbladder are secreted into the proximal small bowel (approximately 3 gm in the adult human). There, bile acid participates in the micellarization phase of fat absorption. Not only are the fatty constituents of the micelle absorbed, but, in addition, the bile acid itself is absorbed. This occurs by passive mechanisms in the proximal small bowel and by

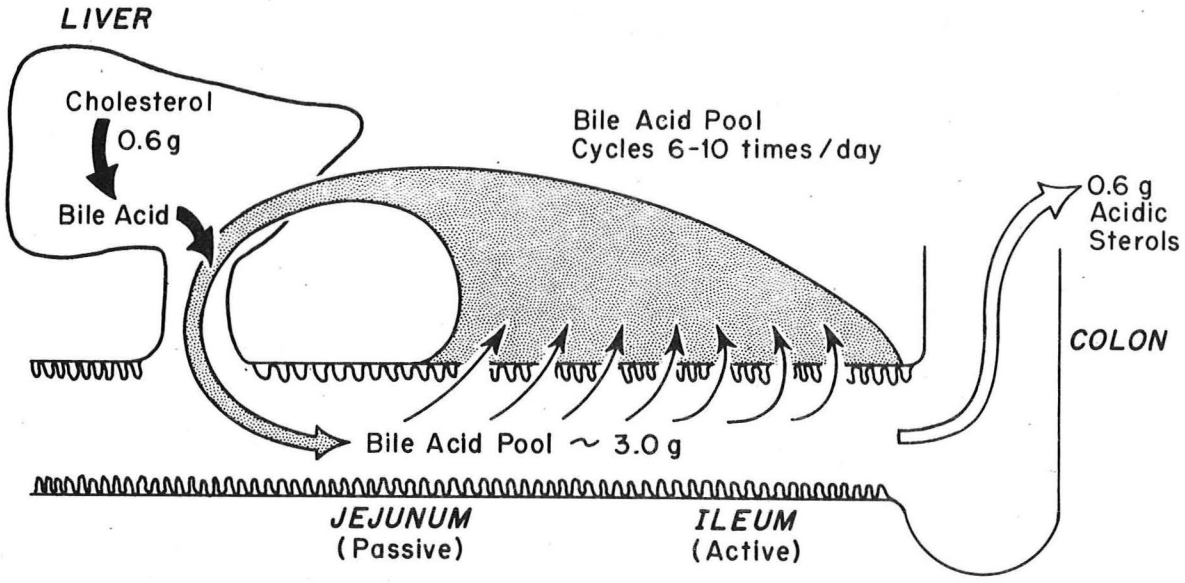

Fig. 3

a combination of passive and active mechanisms in the distal small bowel. Normally approximately 96% of the pool is reabsorbed and during each day the pool is used 6 to 10 times. Thus, each day only approximately 600 mg of the bile acid pool is lost in the feces and this is compensated for by the daily production of an equal amount of new bile acid from the metabolism of cholesterol by the liver.

It should be emphasized that the active reabsorption of bile acid by the ileum is of major importance in the maintenance of this enterohepatic circulation. Obviously, if the bile acid pool is circulating 6 to 10 times per day and if the ileal reabsorptive mechanism is impaired so that a higher per cent of the pool is lost into the feces with each cycle, then the bile acid pool might become rapidly depleted if the magnitude of the loss was greater than could be compensated for by increased bile acid synthesis by the liver.

D. COMPARISON OF THE MECHANISMS OF ABSORPTION OF PROTEIN AND CARBOHYDRATE WITH THAT FOR TRIGLYCERIDE

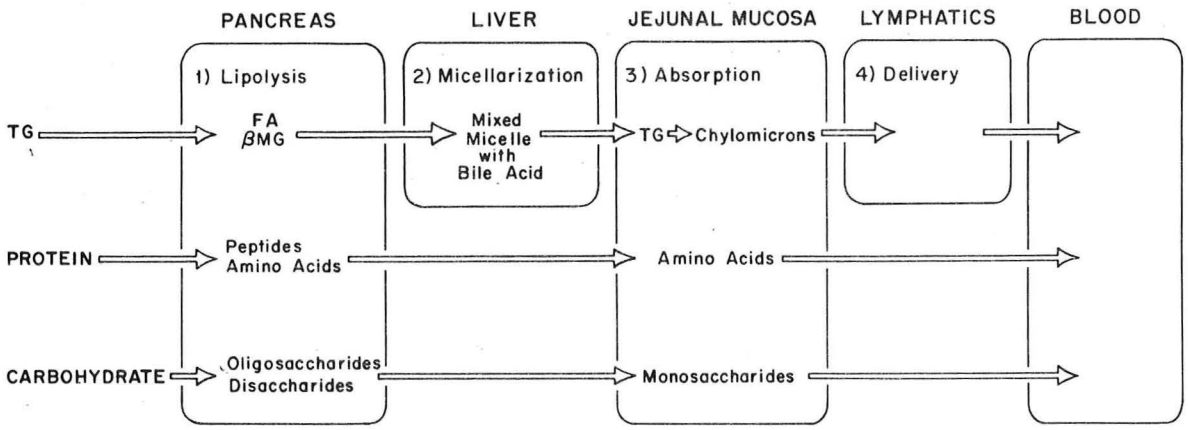

Fig. 4

As outlined above, the absorption of triglyceride can be viewed as occurring in four distinct steps: the hydrolysis of triglyceride, the formation of the mixed micelle, chylomicron formation in the mucosal cells, and delivery through the intestinal lymphatics to the circulation. In contrast to this situation, protein and carbohydrate absorption occur by mechanisms that bypass the second and fourth steps in this overall absorptive scheme. Proteins are digested by pancreatic proteinases into water-soluble oligopeptides and dipeptides. Further breakdown takes place at the mucosal membrane border and absorption of the resultant amino acids occurs predominantly by active transport. The amino acids then pass into the portal circulation and so gain access to the vascular space directly. Similarly, complex carbohydrates undergo partial digestion by pancreatic amylases to disaccharides and oligosaccharides. Further hydrolysis occurs at the brush border membrane and the resultant monosaccharides are absorbed into the cell by various active and passive mechanisms and, hence, also pass directly into the portal circulation.

As illustrated in Figure 4, the important point to emphasize is that one may have malabsorption of only fat, i.e., isolated steatorrhea, or one may have malabsorption of all three major sources of calories depending upon the site of disordered physiology. For example, destruction or loss of the pancreas will result in maldigestion and malabsorption of triglyceride, protein and carbohydrate. On the other hand, diseases that interfere with micellar solubilization (phase 2) or delivery (phase 4) cause an isolated malabsorptive defect in fat absorption while the uptake of protein and carbohydrate occurs normally.

E. TESTS TO DIFFERENTIATE TYPES OF MALABSORPTION

In this section, specific comments will be made concerning the usefulness of five commonly encountered tests of malabsorption. These include the qualitative stool fat test, quantitative stool fat, xylose absorption test, B_{12} absorption test, and small intestinal biopsy.

1. Qualitative Stool Fat

Qualitative stool fat has the advantage of simplicity, speed and low cost. A small pellet of stool is mixed with 3 to 4 drops of glacial acetic acid and 3 to 4 drops of Sudan III stain. This emulsion is covered with a coverslip and gently warmed several times. By this means all ionized long-chain fatty acids are converted to the insoluble protonated form, and the heating melts crystals of saturated long-chain fatty acids and allows coalescence to grossly visible fat droplets. These droplets will then be stained by Sudan III. The test is usually positive in cases of moderate to severe steatorrhea, but may be negative or equivocal in mild forms of steatorrhea where the quantitative stool fat is only 6-15 gm/24 hours.

2. Quantitative Stool Fat

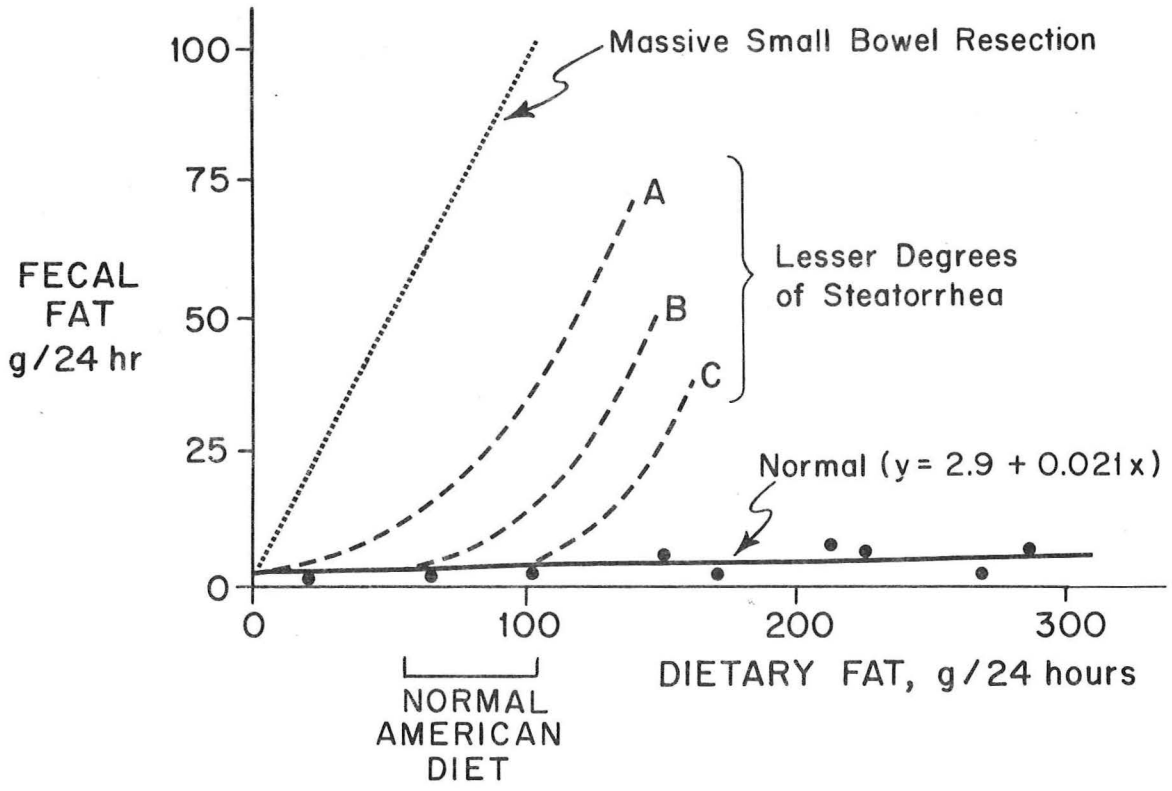

Fig. 5

The quantitative stool fat determination is the test of primary importance in defining the presence of the malabsorption of fat. As illustrated in Figure 5, in the normal individual the amount of fat appearing in the feces is relatively independent of the dietary fat intake. When the dietary fat equals zero, for example, the fecal output equals approximately 2.9 gm of fat per 24 hours. This is the amount of fat that presumably is derived from endogenous sources such as the sloughing of mucosal cells and

bacterial lipids. As the dietary intake is increased to approximately 300 gm per 24 hours, the fecal fat will increase to only approximately 9 gm per 24 hours. However, in the presence of disordered physiology at one of the four steps in the overall process of fat absorption, dramatic defects in fat absorption appear. In the presence of massive small bowel resection, there may be nearly quantitative recovery of all dietary fat in the fecal fat fractions. With less severe malabsorptive defects, one sees lesser degress of steatorrhea. The important point to emphasize, however, is that the absolute value of the quantitative fecal fat output depends upon the load of dietary fat presented to the patient. All too often this is ignored and if the patient is eating relatively little fat, one may not be able to detect a defect in fat absorption.

TABLE 1

QUANTITATIVE STOOL FAT

Measures Malabsorption of Dietary Fat	
Proper Conditions	Possible Artifacts
a) Steady state diet intake	a) Poor food intake ↓
b) Diet contains 60-100 g fat	b) Interrupted food intake ↓
c) Regular bowel movements	c) Constipation ↓
d) All stool collected for 72 hr.	d) Incomplete stool collection ↓
	e) Undigestible fats, e.g., castor oil, nut oils ↑

The data given in Table 1 outline the conditions that should be met in order to obtain a reliable quantitative fat output and also point up the possible sources of error. Briefly, the patient should be on a diet containing 60 to 100 gm of fat (standard hospital diet) for several days before beginning the stool collection and throughout the collection period. Regular daily bowel movements should be insured by the use of small amounts of laxatives if necessary. Poor food intake, interruption of food intake in order to perform some other diagnostic test, constipation, incomplete stool collection, etc., all will result in an artifactually low value for the 24-hour fecal output. An artifactually high value may be seen in the face of massive intake of undigestible fats such as castor oil or nut oils. Petroleum mineral oils will not interfere with the test.

3. Xylose Absorption Test

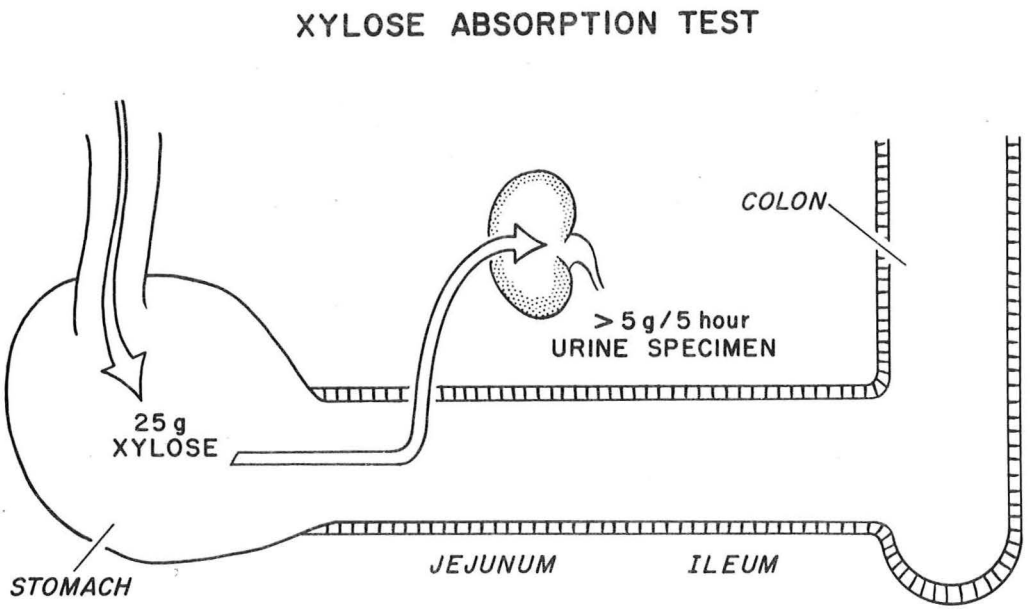

Fig. 6

As illustrated in Figure 6, xylose absorption occurs almost exclusively in the proximal small bowel and therefore it has great usefulness in measuring functional integrity of the jejunum. The test is performed by administering 25 gm of xylose to a fasting patient along with adequate fluid volume to maintain good urine flow. The patient is asked to empty his bladder at the beginning of the test and a quantitative 5-hour urine collection is then obtained. In most series, a normal value for this test is the excretion of > 5 gm of the administered dose in the first 5-hour urinary collection. As shown in Table 2, there are a number of possible artifacts in this test that must be avoided if the results are to be reliable.

TABLE 2

XYLOSE ABSORPTION TEST

Measures 1) Loss of jejunal integrity
2) Massive bacterial overgrowth in jejunum

Proper Conditions	Possible Artifacts
a) Fasting state	a) Delayed gastric emptying ↓
b) Adequate urine flow	b) Vomiting ↓
c) Complete 5-hr urine collection	c) Decreased ECV ↓
	d) Intrinsic renal disease ↓
	e) Ascitic fluid ↓
	f) Diarrheal fluid mixed with urine ↑

Delayed gastric emptying and vomiting both will lead to artifactually low urinary values. Similarly, inadequate hydration or decreased effective circulating volume and intrinsic renal disease will lead to decreased urinary clearance of xylose and, again, an artifactually low urinary excretion value. The presence of massive ascites also will lead to an erroneously low value by sequestration of xylose in the ascitic fluid. This situation is illustrated by the data in Figure 7.

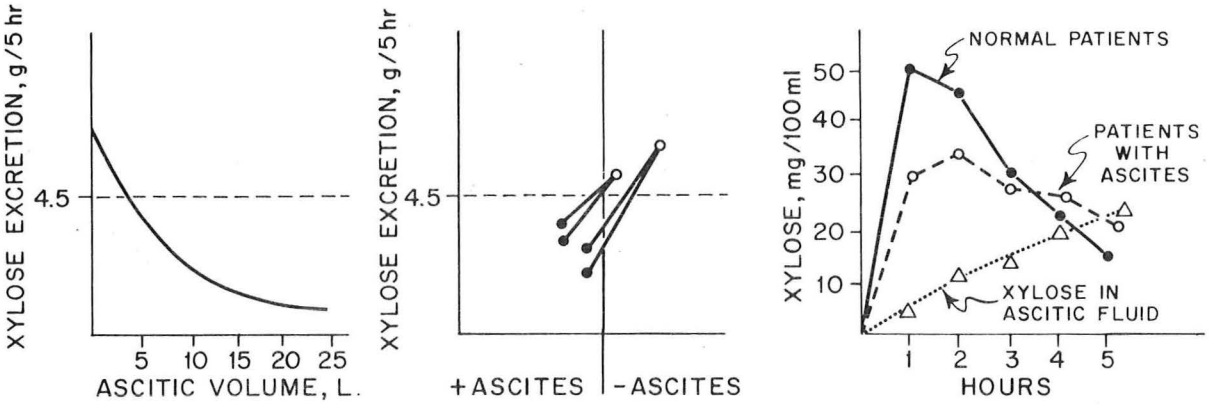

Fig. 7

In the first panel, the xylose excretion value has been plotted as a function of the estimated ascitic volume. In the second panel, the correction of a low xylose excretion is illustrated after successful therapy of the ascites. Finally, the third panel illustrates the serum levels of xylose in normal patients and in patients with ascites. In addition, the rapid entrance of xylose into the ascitic fluid also is shown by the lower dotted line. There are a number of reports in the literature that imply that malabsorption occurs in the presence of portal hypertension. One of the tests used to support this contention is the xylose absorption test. It is now apparent, however, that these represent artifactual values due to xylose sequestration within the fluid and cannot be used as evidence that there is a proximal intestinal malabsorptive defect in portal hypertension.

Another point worthy of emphasis is the value of the urinary excretion of xylose with respect to age. This is illustrated in the data shown in Figure 8. As is apparent in this diagram, the mean urinary excretion of xylose progressively falls above the age of 50. In addition, in any group of patients one may find values that are below 5 gm/5 hours (the ranges in each age group are illustrated by the thin bars). The decrease in mean excretion presumably reflects decreasing renal function with age.

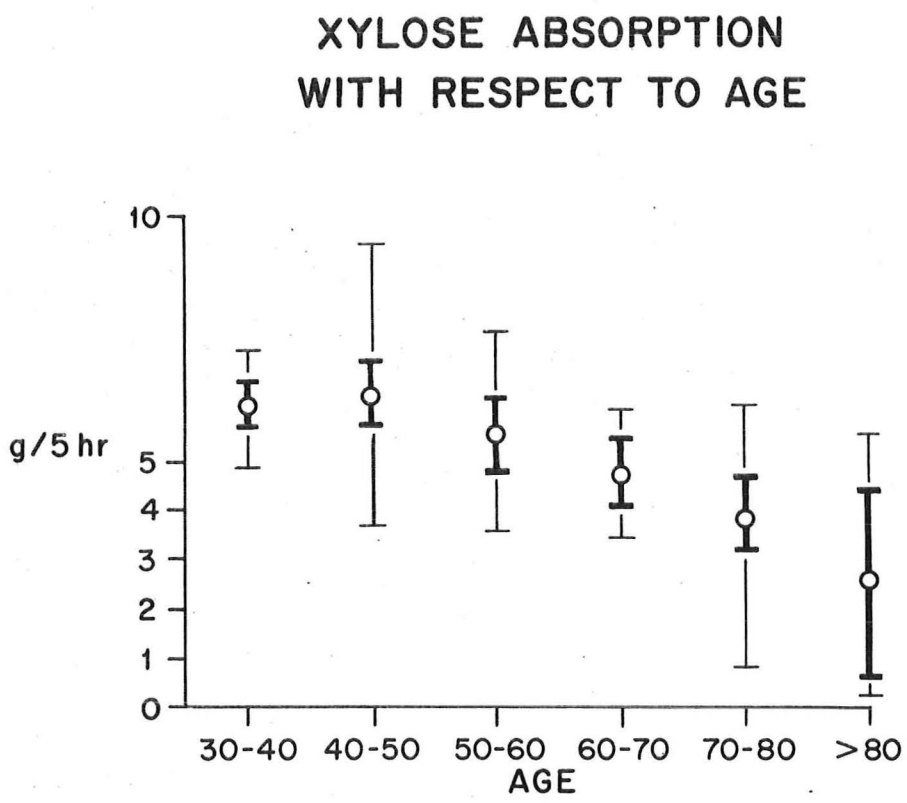

Fig. 8

In addition to measuring the functional integrity of the jejunum, the xylose absorption test may also be low in the presence of the intestinal stasis syndrome (blind loop syndrome). When there is massive bacterial overgrowth in the proximal small bowel, xylose apparently may be metabolized so that low urinary excretion values are obtained.

In summary, when properly performed and in the absence of renal disease and ascitic fluid, a very low xylose value is evidence of either 1) massive loss of jejunal function or 2) massive bacterial overgrowth in the proximal small intestine.

4. B_{12} Absorption Test

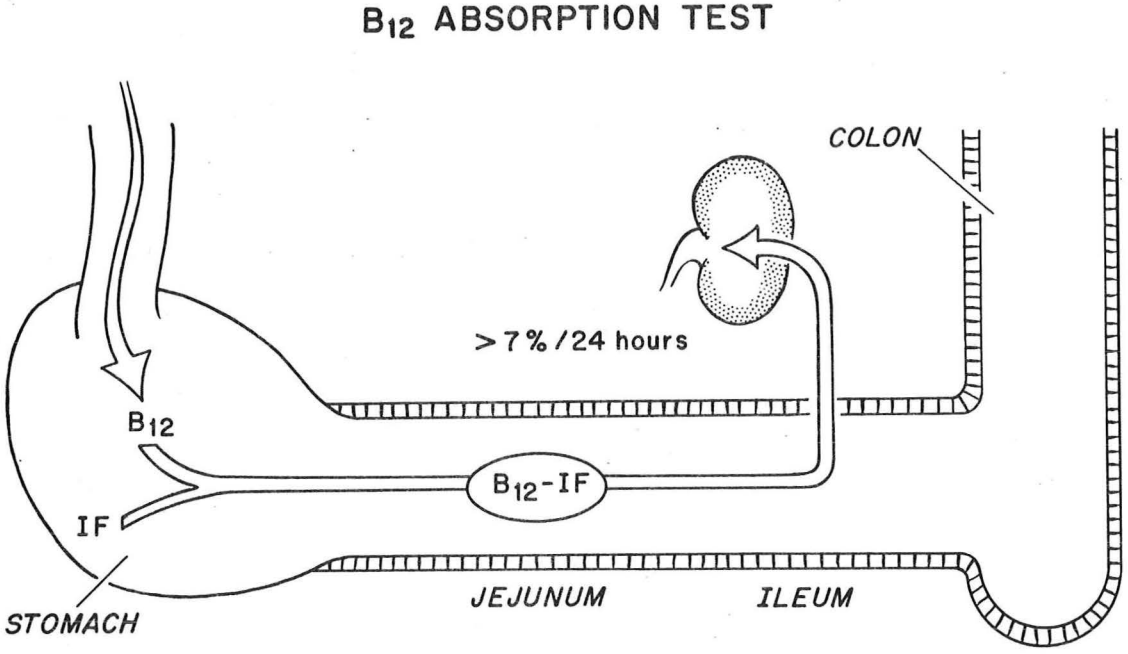

Fig. 9

As illustrated diagrammatically in Figure 9, B_{12} absorption involves the binding of vitamin B_{12} with intrinsic factor in the stomach, transport of the B_{12}-intrinsic factor complex through the proximal small intestine, binding of the complex to specific sites in the ileum, and, finally, absorption of B_{12} into the portal circulation. In the conventional Schilling test, a flushing dose of parenteral vitamin B_{12} also is administered so that a significant amount of the administered dose of radiolabeled B_{12} is excreted in the urine. Assuming that intrinsic factor is available, the Schilling test can be used to evaluate two aspects of fat absorption. First, in the presence of massive bacterial overgrowth in the jejunum, the B_{12}-intrinsic factor complex is taken up or bound to the bacterial cells causing a low urinary excretion rate. Second, in the presence of ileal dysfunction, malabsorption of B_{12} also occurs.

As outlined in Table 3, there are a number of possible sources of error in the performance of the Schilling test. Vomiting after the administration of the radiolabeled isotope or intrinsic renal disease, for example, will lead to artifactually low urinary excretory rates.

TABLE 3

B_{12} ABSORPTION TEST

Measures 1) Lack of IF
2) Massive bacterial overgrowth in jejunum
3) Loss of ileal integrity

Proper Conditions	Possible Artifacts
a) Fasting state	a) Vomiting after B_{12} ↓
b) Adequate urine flow	b) Post-gastrectomy ↓
c) Complete 24-hr urine collection	c) Decreased ECV ↓
	d) Intrinsic renal disease ↓
	e) Feces mixed with urine ↑

In summary, in the presence of adequate intrinsic factor a properly performed B_{12} absorption test will be very low in the presence of 1) massive bacterial overgrowth of the proximal small bowel and 2) loss of ileal functional integrity.

F. DIAGNOSTIC CRITERIA FOR THE INTESTINAL STASIS SYNDROME

Many anatomic and motility disorders lead to malabsorption because of bacterial overgrowth in the proximal small intestine. This is commonly referred to as the blind loop syndrome or the syndrome of intestinal stasis.

TABLE 4

DIAGNOSTIC CRITERIA FOR INTESTINAL STASIS SYNDROME

	Stool Fat	Stool N	Xylose	B_{12}
	g/24 hr	g/24 hr	g/5 hr	%/24 hr
a) Untreated	15-25	1.0-2.5	1.5-5.0	< 2
b) After tetracycline for 3 days	< 6.0	1.0-2.5	> 5.0	> 7

Diagnosis of this disorder depends not on any single test for evaluation of intestinal absorptive capacity, but rather upon a set of diagnostic tests before and after the administration of an appropriate antibiotic. This is illustrated in the data in Table 4. Typically, in the presence of intestinal stasis syndrome, there is mild steatorrhea, normal protein absorption and a very low Schilling test while the xylose absorption test may be normal or low. The critical point is that after the administration of tetracycline for 3 days, the malabsorption of fat, xylose and B_{12} will all be corrected. It is this finding, the ability to correct the malabsorption of fat, B_{12} and xylose with antibiotics, that allows one to make the diagnosis of the intestinal stasis syndrome.

G. THE VALUES OF THE VARIOUS ABSORPTIVE STUDIES IN 29 DISEASES THAT RESULT IN MALABSORPTION OF FAT

The data listed in the following charts were derived from nearly 400 case reports in the literature. Because of the limitation of space, references are given to only 122 of these at the end of the protocol. In selecting these data and preparing the charts, the following criteria were established:

1. In order to be included in this series, an acceptable evaluation of stool fat (expressed in gm/24 hours or % of intake) was required. n refers to the number of such patients in each series. It should be understood that the number of values used to calculate the other parameters of absorption were either equal to n or, in most cases, much less than n.

2. The values given represent the mean ± 1 standard error of the mean. Numbers that show no variance represent the simple mean value of 3 or less determinations.

3. Normal values for each of the major parameters of absorption in most series were as follows: Stool fat $<$ 5-6 gm/24 hours or $<$ 8% of intake. Stool nitrogen $<$ 2.5 gm/24 hours. Xylose absorption test $>$ 4-5 gm/5 hours. Schilling test $>$ 7-10%/24 hours.

DIAGNOSIS	n	TESTS THAT REFLECT ABSORPTION OF						SERUM PROTEIN and Ca^{++}		
		FAT		PROTEIN	SUGAR	VITAMINS				
		Stool Fat	Stool Fat	Stool Nitrogen	Xylose	Schilling Test	Serum Folate	Albumin	Globulin	Ca^{++}
		g/24 hr	% Intake	g/24 hr	g/5 hr	%/24 hr	mμg/ml	g/100 ml	g/100 ml	mg/100 m
I. DECREASED PANCREATIC ENZYME ACTIVITY										
1) Chronic pancreatitis	46	37 ± 4.5	34 ± 4.8	4.7 ± 0.6	6.1 ± 0.7	-	-	3.1 ± 0.6	2.1 ± 0.3	8.6
2) Pancreatic resection	37	44 ± 4.3	45 ± 4.7	7.5 ± 1.0	-	-	-	2.7	-	-
3) Cystic fibrosis	15	25 ± 4.1	30	4.2 ± 0.6	-	-	-	-	-	6.6
II. DECREASED INTRA-LUMINAL BILE ACID ACTIVITY										
1) Extrahepatic biliary obstruction	6	-	30 ± 6.0	1.2 ± 0.2	-	-	-	3.4 ± 0.4	-	8.9 ± 0.
2) Intrahepatic disease with jaundice	29	16 ± 2.0	23 ± 2.0	1.2 ± 0.1	4.3 ± 0.9	12 ± 1.0	-	3.1 ± 0.1	3.3 ± 0.2	10.2 ± 0.
3) Intrahepatic disease without jaundice	15	19 ± 3.0	19 ± 4.0	1.6 ± 0.3	5.9	-	-	2.7 ± 0.1	3.4 ± 0.4	7.4 ± 0.
4) Cholestyramine i) 12 gm/day	5	7.1 ± 1.6	-	-	-	-	-	-	-	-
ii) 24-36 gm/day	20	14.3 ± 1.6	14.3 ± 1.4	2.2 ± 0.5	-	-	-	-	-	-
5) Intestinal stasis syndrome	33	17.5 ± 1.9	20 ± 3.5	1.8 ± 0.2	3.0 ± 0.5	0.9 ± 0.3	8.9 ± 3.2	3.1 ± 0.2	2.9 ± 0.2	8.0 ± 0.

DIAGNOSIS	n	TESTS THAT REFLECT ABSORPTION OF						SERUM PROTEIN AND Ca^{++}		
		FAT		PROTEIN	SUGAR	VITAMINS				
		Stool Fat	Stool Fat	Stool Nitrogen	Xylose	Schilling Test	Serum Folate	Albumin	Globulin	Ca^{++}
		g/24 hr	% Intake	g/24 hr	g/5 hr	%/24 hr	mμg/ml	g/100 ml	g/100 ml	mg/100 ml
III. INTRAMURAL SMALL BOWEL DISEASE										
1) Idiopathic sprue	74	28 ± 1.8	32 ± 4.4	5.0 ± 1.2	2.0 ± 0.3	2.4 ± 1.0	5.7 ± 1.2	3.2 ± 0.1	2.2 ± 0.3	8.5 ± 0.1
2) Tropical sprue	305	16 ± 0.6	13 ± 0.8	-	2.2 ± 0.6	5.1 ± 1.3	3.1 ± 0.3	3.0 ± 0.4	-	7.9 ± 0.9
3) Whipple's disease	23	34 ± 4.8	50 ± 5.9	3.8 ± 0.5	3.7 ± 0.4	12.9 ± 3.7	-	2.3 ± 0.2	2.6 ± 0.1	8.5 ± 0.1
4) Amyloidosis i) Primary	7	22 ± 3.2	-	4.9 ± 0.7		6.0 ± 1.0	-	2.8 ± 0.6	3.0 ± 0.3	9.2 ± 0.1
ii) Secondary & multiple myeloma	5	15 ± 2.9	-	3.0 ± 0.1	2.1 ± 0.3	-	-	2.4 ± 0.3	2.9 ± 0.2	7.3 ± 0.8
5) A-β-lipoproteinemia	7	-	18 ± 2.4	-	6.2 ± 1.3	19 ± 2.6	-	3.8 ± 0.8	2.5 ± 0.4	9.1 ± 0.
6) Mast cell disease	3	49 ± 21	45	-	4.7 ± 0.3	6 ± 3.9	-	3.9 ± 0.1	1.7 ± 0.3	5.9 ± 0.
7) Eosinophilic gastroenteritis	4	13 ± 2.8	15 ± 4.2	-	1.5 ± 0.4	3.0	-	3.1 ± 0.4	1.8 ± 0.2	-
8) Food allergy	6	19 ± 6.1	52 ± 20	0.7	11.2	-	-	2.2 ± 0.6	1.5 ± 0.2	7.9 ± 0.
9) Nongranulomatous jejunitis	6	27 ± 5.4	-	0.6	3.4 ± 1.1	1.9	13.2 ± 5.2	2.6 ± 0.2	2.0 ± 0.3	7.4 ± 0.
10) Small bowel ischemia i) Atherosclerosis	12	15 ± 1.6	24 ± 0.2	-	2.0 ± 0.5	6.8	-	3.3 ± 0.3	3.5 ± 0.5	8.9 ± 0.
ii) Polycythemia vera	1	20	-	-	-	-	-	-	-	-
iii) Vasculitis	3	14 ± 3	-	-	-	-	-	-	-	-
iv) Kohlmeier-Degos syndrome	1	26	43	-	1.9	-	-	3.9	1.9	7.9

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		FAT		PROTEIN	SUGAR	VITAMINS				
		Stool Fat	Stool Fat	Stool Nitrogen	Xylose	Schilling Test	Serum Folate	Albumin	Globulin	Ca^{++}
		g/24 hr	% Intake	g/24 hr	g/5 hr	%/24 hr	mμg/ml	g/100 ml	g/100 ml	mg/100 ml
11) Radiation enteritis	11	32 ± 15	70	6.5 ± 2.3	3.1 ± 0.6	2.7 ± 1.5	1.2	2.7 ± 0.3	3.2 ± 0.3	8.3 ± 0.3
12) Skin disease										
i) Dermatitis herpetiform	30	9.4 ± 0.6	7.6 ± 2.1	-	3.0 ± 0.6	14.9 ± 1.3	1.8 ± 0.7	3.1	-	9.6 ± 0.3
ii) Others	28	8.4 ± 0.5	7 ± 2	-	4.0 ± 0.6	6.2	-	5.0	3.0	9.7 ± 0.3
13) Intestinal lymphangiectasia	6	23 ± 4.0	20 ± 3.0	3.2 ± 1.0	7.8 ± 0.5	-	-	1.6 ± 0.2	2.3 ± 0.2	5.7 ± 0.4
V. MALABSORPTION OF MIXED OR UNCERTAIN ETIOLOGY										
1) Zollinger-Ellison syndrome	19	24 ± 2.4	26 ± 3.6	-	3.0 ± 0.8	31	3.2	3.1 ± 0.3	2.3 ± 0.3	9.6 ± 0.3
2) Scleroderma	36	19 ± 2.0	24 ± 3.0	2.1 ± 0.2	2.6 ± 0.4	11.5 ± 2.0	-	3.4 ± 0.1	2.8 ± 0.2	8.8 ± 0.2
3) Primary acquired hypogammaglobulinemia	6	21 ± 3.0	19 ± 2.0	1.2	4.0 ± 1.4	1.9 ± 1.0	-	3.5 ± 0.2	1.6 ± 0.2	7.6 ± 0.7
4) Carcinoid syndrome	4	43 ± 20	11	-	2.4 ± 0.1	-	-	3.3 ± 0.6	2.4	7.9
5) Diabetes mellitus	26	29 ± 4.2	34 ± 5.0	5.3 ± 0.6	4.0 ± 0.7	10.8	-	3.4 ± 0.2	2.3 ± 0.2	9.3 ± 0.2
6) Endocrinopathies										
i) Hyperthyroidism	2	41 ± 6.1	-	-	5.3	-	-	3.3	3.6	-
ii) Hypoadrenalism	11	22 ± 3.4	18 ± 1.3	-	-	-	-	-	-	-

DIAGNOSIS	n	TESTS THAT REFLECT ABSORPTION OF						SERUM PROTEIN AND Ca^{++}		
		FAT		PROTEIN	SUGAR	VITAMINS				
		Stool Fat	Stool Fat	Stool Nitrogen	Xylose	Schilling Test	Serum Folate	Albumin	Globulin	Ca^{++}
		g/24 hr	% Intake	g/24 hr	g/5 hr	%/24 hr	mμg/ml	g/100 ml	g/100 ml	mg/100 ml
iii) Hypoparathyroidism	3	33 ± 20	-	2	2.5	4.5	-	3.4	2.9	4.8 ± 0.3
iv) Pseudohypoparathyroidism	3	11	35	-	-	-	-	3.9	1.8	5 ± 0.5
7) Parasitic Infestation										
i) Hookworm	19	11 ± 0.8	-	-	1.2* ± 0.1	-	-	-	-	-
ii) Strongyloidiasis	4	26 ± 5.1	-	-	-	-	-	-	-	-
iii) Coccidiosis	1	22	27.5	-	-	-	-	-	-	-
iv) Schistosomiasis	1	10	-	-	0.3*	-	-	2.8	3.0	6
v) Capillariasis	10	25 ± 6.3	-	-	2.7 ± 0.8	-	-	-	-	7.4 ± 0.3
vi) Giardiasis	17	16.6 ± 2.4	23 ± 4	2.4 ± 0.6	2.5 ± 0.3	1.7	-	2.8	2.3	7.8
8) Ileal Dysfunction										
i) Ileal resection	39	24 ± 2.8	25 ± 4.1	4 ± 0.7	4.8 ± 1.9	3.3 ± 0.4	-	3.7 ± 0.3	2.5 ± 0.1	8.9 ± 1.4
ii) Ileal Crohn's disease	9	14.5 ± 2.3	-	4 ± 1.1	5.7 ± 0.7	-	-	-	-	-

* 5 gm oral dose

Drug	n	Stool Fat		Stool Nitrogen	Xylose	Schilling Test
		g/24 hr	% Intake	g/24 hr	g/5 hr	%/24 hr
V. MISCELLANEOUS DRUGS REPORTED TO CAUSE STEATORRHEA						
1) Colchicine	6	9.6 ± 0.9	-	-	3.8 ± 0.5	8.6 ± 2.5
2) Cathartics	6	10.7 ± 2.7	22 ± 4	-	5.0 ± 0.7	-
3) Neomycin						
a) 8-12 g/day	34	19.9 ± 1.4	22.8 ± 2.3	2.87 ± 0.1	1.86 ± 0.15	-
b) 2-6 g/day	15	11.1 ± 1.5	14.9 ± 2.2	-	3.2 ± 0.4	17.1 ± 1.3
4) Triparanol	2	13.8	17.0	4.3	-	-
5) Para-amino-salicylic acid	7	11.3 ± 1.7	-	-	3.0 ± 0.9	-
6) Phenindione	1	39.5	-	-	-	-

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