CHAPTER 12 - THE DIAGNOSIS OF STEATORRHOEA/ DIARRHOEA

INTRODUCTION

We now return to physiology, and set it to work in making clinical diagnoses. This is a time to pause and introduce a few more general principles relevant to our diagnostic method.

First, we must really know what it means to put Physiology to work in making clinical diagnoses. I emphasize this because it is all too easy to do the whole exercise backwards, i.e. having recognized, derived or by some other means gleaned the diagnosis, demonstrate the most intricate details of your physiological knowledge of the subject to your colleagues, and the patient. Now, this may impress them greatly, and do wonders for your ego, but as far as actually building-up individual patient-diagnosis is concerned, it is misses the point. For example, having made a diagnosis of, say, thyrotoxicosis, it may be very impressive to demonstrate your knowledge of thyroid physiology afterwards, but that is of no relevance, because that knowledge should have been used to arrive at the diagnosis in the first place.

Second, since we are now going on to deal with the gastro-intestinal system, it is worth saying that, as with some other systems already covered, many of its aspects are relatively remote in the anatomical sense, so we become more reliant on detecting aberrations in function (Functional diagnosis) to determine the Anatomical source of the problem.

In this respect, two points are relevant. The first is that understanding and detecting malfunction of any organ or organ system requires you to have a firm grasp of that organ's function in simple terms. Only by having that basic grasp of organ function will you be able to see the wood for the trees, and hence define the essential framework of the patient's diagnosis.

The second point you will notice as we go through this chapter is that simple clinical physiology and clinical signs are not necessarily sufficient to determine aberrations of organ function. We are now beginning to embark on an area where we must add biochemical and other investigations to our repertoire, so as to be in a position to solve the problem under consideration, in this case the diagnosis of steatorrhoea.

BACKGROUND PHYSIOLOGY

The essence of gut function.

The two main tasks of the gastrointestinal system are to digest food and then absorb it. Defects can occur at either level to result, in the first case, in maldigestion from impairment of normal bile and enzyme production and, in the second, in malabsorption. The latter may be due to a disease of the
gut wall itself, but because most food-stuffs have to be digested before they can be absorbed, it can be secondary to maldigestion. In this chapter we will concentrate on hierarchically distinguishing between these two broad diagnostic subgroups of patients presenting with chronic diarrhoea. At the outset, it is important to say in this respect that the gut can only digest and absorb what is presented to it, so very poor dietary intake or starvation can produce much the same end picture as far as bodily nutrition is concerned; therefore make sure you exclude poor dietary intake before you ascribe low body levels of fat, protein, carbohydrate, minerals, vitamins etc. to either maldigestion or malabsorption.

**PHYSIOLOGY OF THE GUT RELEVANT TO DIARRHOEA DIAGNOSIS**

Broadly speaking, we can say that most of the initial coarse digestive functions of the gastrointestinal system have been taken over by organs out-pouched from it, especially the pancreas, liver and gall bladder, leaving the gut mucosa itself for the finer details of digestion (e.g. the breaking down of disaccharides to monosaccharides, and of oligopeptides to amino acids).

**Stomach**

The stomach break's down large particles of food into "chyme", mostly by churning it up in an acid medium. Protein, as well as small peptides and amino acids, liberate gastrin into the blood on contact with the antral mucosa, and this stimulates the parietal cells in the body of the stomach to secrete acid. There is also a reflex vagal phase of acid secretion, and both are important in achieving maximum gastric hydrogen ion concentration. Pepsin is also secreted by the stomach, as a pro-enzyme activated by acid.

By the time food leaves the stomach, its main components of carbohydrate, fat and protein are not much broken down to any level of molecular detail. For example, pepsin liberated from the stomach does not play a major role in breaking down protein to oligopeptides (this task belongs to the pancreas). The stomach does absorb certain simple molecules such as water, alcohol and caffeine. It also produces intrinsic factor, important in B12 absorption in the terminal ileum. The relatively gross nature of the stomach's function is reflected in the paucity of evidence for maldigestion in patients on proton pump inhibitors, which block H+ ion secretion.

**Duodenum**

When the "chyme" is passed on to the duodenum, its acid nature results in the release there of secretin, whose principal physiological action is to stimulate the pancreas to secrete water and
bicarbonate. In addition, cholecystokinin (CCK) is released in the duodenum mainly under the influence of amino-acids, peptides and long-chain fatty acids. It is actually liberated as a precursor (CCK-PZ), and its role is to induce gall bladder contraction; this releases bile into the duodenum. It also stimulates intestinal motility, inhibits gastric emptying, and most importantly, increases the secretion of pancreatic enzymes, including amylase, lipase (and co-lipase) and the protein-digesting enzymes (as pro-enzymes) trypsin, chymotrypsin (both endopeptidases) as well as carboxypeptidases (exopeptidase).

THE SITES OF DIGESTION/ABSORPTION.

1. Protein Digestion.

Virtually all ingested protein is completely broken down and absorbed as amino acids and small polypeptides. The major part of this occurs within the lumen of the duodenum and upper jejunum under the influence of the pancreatic proteases, liberated from their precursors, all of which are inactive until they reach the bowel lumen, where trypsinogen is activated to trypsin by the brush border enzyme enterokinase. Trypsin, in turn, acts autocatalytically to activate trypsinogen and other protease precursors. The endopeptidases trypsin, chymotrypsin and elastase, break down internal protein peptide bonds to produce peptides which are subsequently acted upon by the carboxypeptidases A and B to produce neutral and basic amino acids respectively, as well as small oligopeptides 2 - 4 amino acid residues long. These oligopeptides are further broken down both by enzymes released from the brush border surface of the intestinal villi and within the gut cell cytosol. Sodium dependent carriers mechanism (also used for glucose absorption) are responsible for much of the absorption of individual amino acids and glucose across the cell where they are taken up into the portal venous system.

2. Carbohydrate absorption.

Average Western diet contains 400 grams carbohydrate comprising starch, sucrose, and lactose. These are digested mostly by pancreatic amylases, but not completely, and oligosaccharides are further hydrolysed by gut brush border enzymes into their constituent hexoses and pentoses. Most sugars are absorbed by facilitated diffusion but glucose (and galactose, xylose) can also "take a ride" into the cell on the sodium cotransporter. Some monosaccharides, such as mannose and the artificial sugar lactulose, are not absorbed, and are therefore useful (osmotic) laxitives.

3. Fat Digestion and Absorption.
Dietary fat exists mainly in the form of triglycerides - long chain fatty acids linked to glycerol. Since triglycerides are not water soluble, dietary fat must first be emulsified before absorption can take place. Some emulsification occurs from the churning action of the stomach, but the major drive is from bile salts within the duodenum. Conjugated bile salts, together with lethicin and phospholipids, emulsify fat to form an emulsion particle. These are large molecular aggregates which have hydrophilic (polar) groups facing outwards and lipophilic (hydrophobic) groups facing inwards.

Co-lipase secreted by the pancreas then binds to the surface of the emulsified lipid droplet; in so doing, it intrudes between bile salt molecules and activates pancreatic lipase. This lipase, acting at the oil-water interface of the lipid droplet, hydrolyses triglyceride ester bonds to form free fatty acids and monoglycerides which are then incorporated into the bile salt micelle. When this happens, a mixed micelle results that further enhances the solution of lipids.

A key factor in increasing detergent capacity is the presence of unsaturated monoglyceride in the mixed micelles. These cause enhancement of emulsification that results in a 100-fold diminution in particle size from the initial lipid emulsion to the final mixed micelle of approx. 10 nm. This facilitates solubilization of otherwise water-insoluble compounds such as stearic acid, its monoglyceride and cholesterol to go into solution in the final tiny mixed micellar particles.

After the process of bile emulsification and lipase digestion, most ingested fat is absorbed (as fatty acids and monoglycerides) into the mucosal cell along the proximal 1 metre of the jejunum. Once inside the cell, long-chain triglycerides (16 or more carbon atoms) are re-assembled as triglycerides before being stabilised by lipoproteins and phospholipids and delivered (as chylomicrons etc.) to the lacteals, and thence to the systemic circulation via the thoracic duct. Smaller 'medium chain' triglycerides (MCT's; C6-C12 ) by contrast, are absorbed directly into the portal venous system.

Two points need emphasis. First, some fat is absorbed in the complete absence of bile - up to 50% of neutral fat, and a lesser amount of cholesterol and fat soluble vitamins.

Second, a practice point: most medium chain triglycerides (MCT's) are absorbed intact without the need for any prior fat emulsification and lipase digestion at all. These MCT's are hydrolysed within the mucosal cell by intestinal lipase, and the constituent glycerol and fatty acids so formed again pass directly to the portal blood without re-esterification. This makes MCT's useful in the therapy of two situations, firstly of maldigestion, and secondly in maintaining bodily fats in the presence of a blocked portal lymphatic lacteal/thoracic duct system.

4. Fat Soluble Vitamin and Cholesterol Absorption
The fat soluble vitamins A, D, K, and E are all solubilised in mixed micelles and are absorbed along with it in the proximal jejunum. This process depends mostly on adequate emulsification and formation of mixed micelles by bile salts and, if that is intact, to a lesser extent on pancreatic fat digestion. Hence, chronic biliary obstruction can eventually give rise to clinical vitamin D deficiency, whereas chronic maldigestion from pancreatic disease, though reducing vitamin D levels, rarely does so to a clinically important degree. The same holds true of Vitamin K and cholesterol. The intestine is normally able to convert beta-carotene into Vitamin A.

5. Bile Salt Metabolism

Important to a complete understanding of maldigestion. Conjugated bile salts are much more effective in producing fat emulsions than unconjugated bile salts. This is an important factor in situations where the small intestine is overgrown by bacteria, because these de-conjugate bile salts and so reduce fat digestion, and therefore its absorption.

A continued supply of adequate amounts of bile salts to the intestine is also dependent on bile being normally reabsorbed in the terminal ileum and recycled again as part of the so-called entero-hepatic circulation. Hence, if the terminal ileum is diseased, this process will be interrupted and hepatic secretion of bile salts will eventually become reduced, so producing a secondary fat maldigestion. The bile salt-binding agent cholestyramine, sometimes used to reduce cholesterol absorption in the gut, can have essentially the same effect.


A great deal of fluid is turned over in the intestine per day, approximately 8 litres, comprising that ingested with meals plus the secretions of the stomach, pancreas, biliary tree and the small bowel itself. All but approx. 150 mls (the 24 hour stool output) is reabsorbed. The amount of fluid present in the small intestine following a meal is mostly a function of its osmolality.

Absorption mechanisms.

Not fully understood. Water, ions and other small molecular weight water soluble substances are at least partly absorbed through the so-called "tight" junctions between cells.

Sodium is absorbed into the intestinal epithelial cell by passive diffusion in conjunction with amino acids and sugars on co-transporter proteins. But the driving force for this process is active Na+/K+ ATPase dependent Na + transport through the basal aspect of the cell into the portal capillary system.
Bicarbonate is removed both by exchange with chloride and by combination with hydrogen ions in the ileum lumen, releasing CO2.

Chloride ion is normally secreted into the lumen of the small intestine by Cl- channels that are activated by cyclic AMP. In cholera, a toxin stimulates this mechanism and results in profuse diarrhoea and (Na + )Cl - loss.

By the time the gut content reaches the lower ileum, most components other than some water and electrolytes have been absorbed. However sodium (and water) is further (actively) re-absorbed in the colon. There is normally a net colonic secretion of K+ ; in the distal colon, this occurs partly in exchange for sodium by an aldosterone effect, particularly in Na + deficiency. Diarrhoeal fluid has concentrations of sodium, chloride and potassium like that of the ileal effluent, i.e. higher in sodium and lower in potassium than the normal stool. Rapid transit is important in the appearance of high concentrations of sodium and chloride in the stool, since there is not enough time for re-absorption. However, although this also means that potassium concentration in the stool is not necessarily increased in colonic diarrhoea, the increased volume of the stool in that situation determines that total potassium loss is usually high enough for patients to become potassium-depleted. This potassium loss is compounded when concurrent sodium balance becomes negative to cause further potassium loss, in the stool as well as the urine, under the influence of aldosterone.

7. Mineral Absorption

(i) Iron: Dietary sources mostly from haemoglobins, from which iron is more readily available than from plant or inorganic iron. Low gastric pH in the stomach particularly promotes peptic digestion of haemoglobin. (Non-haem iron as poor solubility, somewhat enhanced by gastric acid and by Vitamin C.) Most released iron is absorbed in the duodenum and jejunum. Its movement into the mucosal cell is a key step in regulating absorption, and this first step is related to the incorporation into cellular ferritin, from which it is released when needed.

(ii) Calcium: Calcium is absorbed in the upper gut. The process is energy dependent, and also relies on binding proteins, the synthesis of which is controlled by 1,25-OH Vitamin D. Vitamin D is hydroxylated to 25-OHD in the liver and then converted to the active form 1,25-OHD by the kidney. Compared with vitamin D, parathyroid hormone (PTH) is of minor importance in the control of calcium absorption. But PTH does increase the conversion of 25-OHD to 1,25-OHD in the kidney, and hence has an important indirect effect. (See also Ch. 18).

(iii) Trace elements and water soluble vitamins - normally all well absorbed. Vitamin B12 absorption is particularly important to the diagnosis of maldigestion/malabsorption. Thus, its absorption depends
not only on combination with intrinsic factor in the stomach and also on the intactness of the terminal ilium, where the complex is absorbed. Moreover, the availability of any B12 for absorption can be affected by bacterial overgrowth in the small bowel. This inhibitory action occurs by direct binding of the vitamin by bacteria, particularly gram negative ones. This makes the B12 unavailable for absorption in the terminal ilium unless the organisms are killed with antibiotics (a useful diagnostic test - see below).

Bacterial overgrowth in the small intestine (as occurs in gut resection, blind loops, bowel fistulae) also results in deconjugation of bile acids, effectively blocking their all-important entero-hepatic recirculation, and so leading to secondary fat malabsorption/malabsorption. This can give rise to malabsorption of vitamin K. However vitamin K deficiency is unusual in bacterial overgrowth of the small gut (because its malabsorption in the upper gut can be offset to some degree by bacterial synthesis of vitamin K and reabsorption lower down).

8. Folic acid is absorbed maximally in the proximal intestine. Note that folates exist in food as glutamyl peptides. These polyglutamates must be converted to monoglutamates (by folate deconjugase) before absorption. Certain drugs, such as sulphasalazine, phenytoin and trimethoprim can inhibit this process, and lead to folate deficiency.

9. Other water soluble vitamins - mechanism of the absorption obscure.

SITES OF ABSORPTION OF VARIOUS MATERIALS

This is relevant to our Anatomical clinical diagnosis. To reiterate, the proximal intestine is the major site for absorption of iron, folic acid, calcium, minerals, water soluble vitamins and fat. Sugars are absorbed in the proximal and mid-intestine. While the major absorption of amino acids occurs in the jejunum, some absorption also occurs distal to this. The distal ilium is the major site for bile salts and vitamin B12 absorption. The colon is the important site for absorption of water and sodium (the latter partly in exchange for potassium). When the jejunum is diseased, the ileum provides an important 'intestinal reserve,' so that intestinal disease has to be relatively widespread before clinical manifestations occur.

FUNCTIONAL EFFECTS OF MALDIGESTION/MALABSORPTION (STEATORRHOEA)

Relevant to Functional and hence Anatomical Diagnosis
1. **General symptoms** include weight loss, (often despite reasonably maintained appetite) diarrhoea, particularly in this case steatorrhoea (greater than 18 grams fat in stool over three days on a standard 100 gram per day fat intake). Steatorrhoea gives rise to large, pale, bulky, offensive stools, difficult to flush. A stool weight of greater than 150 g per day and pale colour is a useful clue that steatorrhoea (whether due to maldigestion or malabsorption), is the basic problem, rather than some other form of diarrhoea.

2. **Vitamin Deficiency**.

(a) **Fat soluble vitamins** are especially involved.

(i) **Vitamin E** - Normal function uncertain, but plasma vitamin E is a useful determination in screening for steatorrhoea.

(ii) **Vitamin K deficiency** leads to easy bruising. It occurs in many causes of steatorrhoea, but most importantly with liver disease/biliary obstruction, and with diffuse severe small bowel disease associated with fat malabsorption. Assess by measurement of plasma prothrombin time (INR). Provided liver function is normal, a high INR indicates vitamin K deficiency due either to inadequate intake or failure of fat digestion/absorption, the latter being far more common.

**N.B.** To distinguish whether prolonged prothrombin time is due to liver/biliary dysfunction or steatorrhoea, repeat INR after 2 days of parenteral injections of vitamin K intramuscularly (not orally). In the case of malabsorption this should restore the INR to normal.

(iii) **Vitamin D** absorption is particularly affected in diffuse small bowel disease (malabsorption), and chronic biliary obstruction (fat maldigestion), such as occurs in chronic "primary biliary cirrhosis". It is not so evident in sunny countries (except in covered women) because of the alternative synthesis of vitamin D by the skin under the influence of UV light. Vitamin D deficiency interferes with calcium absorption, lowers plasma calcium (and phosphate) and so prevents proper bone mineralisation resulting in rickets in the young, and osteomalacia (bone pain and pseudofractures) in the adult. However calcium levels in these conditions vary, depending on the parathyroid gland response, which normally partially compensates to bring plasma calcium up to low-normal, even though aggravating the low serum phosphate and elevating bone alkaline phosphatase (Ch.18). However, the parathyroid gland will only compensate in this way if the level of plasma magnesium, (often reduced in steatorrhoea) is normal; as a result some patients with steatorrhoea have severe reductions of plasma calcium, even to the extent of clinical tetany. Because calcium is albumin-bound, it can only be looked at in the context of plasma albumin - the lower the albumin, the lower we expect the normal range of calcium to be in any case. Important because plasma albumin can be
reduced in malabsorption and maldigestion syndromes. Therefore better to measure calcium level adjusted for albumin level, or best early morning ionised plasma calcium.

(iv) **Vitamin A deficiency** produces skin manifestations, particularly so-called hyperkeratosis follicularis (tiny multiple areas of keratosis around hair follicles, mostly on the upper aspects of the limbs - like "permanent gooseflesh"). Confirm by low plasma Vitamin A (or serum carotene) levels.

(b) **Water Soluble Vitamin Deficiency** may also occur, particularly B12 as discussed above (with gastric disease, terminal ilial disease, and gut bacterial overgrowth), leading to macrocytic anaemia and, if severe, peripheral neuropathy &/or subacute combined degeneration of the spinal cord.

Folate deficiency may also produce macrocytic anaemia (and CNS effects), but is more common where steatorrhoea is associated with anorexia. Folic acid is largely destroyed by cooking so dietary intake (from greens) is often borderline to begin with, especially in the elderly.

Deficiencies of **Vitamin B complex** can occur in severe malabsorption. They are manifest as glossitis, stomatitis, cheilosis, neuritis, dermatitis, and muscular weakness. (Glossitis, stomatitis, and cheilosis are also seen with iron, folate, and for B12 deficiency).

**Anaemia** is common in malabsorption (e.g.coeliac disease). In some cases this is purely due to iron deficiency, mostly from poor iron absorption, in other cases from blood loss related to the pathological process. A low mean red blood corpuscular volume (MCV) is the hallmark of iron deficient anaemia. Macrocytic (high MCV) anaemia may be due to folate or B12 deficiency or both. It is not uncommon for patients with steatorrhoea to have a mixed iron/B12/folate deficiency so that mean MCV may be normal; then, the blood film RDW (red cell distribution width) index will help; also bone marrow aspiration.

Water soluble vitamin deficiency is seen more in malabsorption than maldigestion syndromes, but also vitamin B12 deficiency from bacterial overgrowth in the gut.

3. **Protein Deficiency**

This can occur in maldigestion/malabsorption syndromes solely due to poor absorption of the amino acid building blocks for albumin. But hypoalbuminaemia may also be contributed to by poor intake of protein, and by gastro-intestinal loss, particularly in patients with weeping ulcerated gut lesions, as well as in those with intestinal lymphatic obstruction. The low protein is manifest generally as wasting, particularly muscular wasting and, if severe, as low plasma albumin giving rise to oedema, even ascites.
4. Carbohydrate Malabsorption/Maldigestion

If there is solely maldigestion, orally-administered monosaccharides will be absorbed intact, and this forms the basis of a useful test for distinguishing between malabsorption and maldigestion, i.e.

**Practice point:** if monosaccharides such as xylose or mannitol are normally absorbed, then the condition is one of maldigestion rather than malabsorption.

The absorption of glucose, xylose and mannitol are usually only abnormal when there is severe and quite widespread malabsorption so that these can be relatively insensitive tests. Loss of carbohydrate per se in the stool in maldigestion is impossible to quantify because of its bacterial fermentation in the large gut.

5. Mineral Loss

Calcium deficiency (Vitamin D maldigestion/malabsorption) has been dealt with above.

Deficiencies of sodium (chloride) cause ECF volume depletion, cramps and weakness. Low potassium in chronic diarrhoea can produce proximal muscle weakness, polyuria, and abnormalities of cardiac rhythm.

Before being in a position to analyse clinical diarrhoea, we have to consider aspects other than steatorrhoea.

**WATERY DIARRHOEA**

The amount of fluid in the gut, and particularly the control of fluid and electrolyte reabsorption in the large gut has given us a background to this. Normally the stool contains less than 200 mls of water per day. In general, watery diarrhoea can come about in four ways.

1. **Osmotic diarrhoea** - an abnormal number of watery stools due to the effect action of poorly absorbed but osmotically active substances. We see this in steatorrhoea, but also in other conditions including:

   (a) **Disaccharidase deficiency** where the brush border of the gut mucosal cell fails to produce disaccharidases so that disaccharides are not split, and therefore not all absorbed. The net effect is to increase osmotically retained water to the large intestine. Along with this, there is some "solvent
drag" of sodium and therefore dehydration and ECF volume depletion. Moreover when carbohydrates reach the large gut they are broken down by bacteria and fermented, giving rise to excessive flatus, borborygmi and increased intestinal activity, sometimes producing pain. Lactose intolerance is the classic condition in this category.

(b) Osmotic laxatives will produce osmotic watery diarrhoea, particularly those compounds of low molecular weight such as magnesium sulphate.

(c) Blind loop syndrome gives rise to a mixed picture of osmotic watery diarrhoea combined with steatorrhoea. Any blind loop created from medical conditions (e.g.Crohn's), surgical fistulae or other interference with gut contiguity, leads to stasis and secondary small intestinal anaerobic bacterial overgrowth, and this causes deconjugation of conjugated bile acids with secondary malabsorption. Also, unabsorbed free fatty acids act on the colon, inhibiting absorption of water and electrolytes to produce an osmotic diarrhoea. Moreover, unabsorbed carbohydrate is metabolised by bacteria to hydroxylated fatty acids such as lactic acid and isobutyric acid, which contribute further to osmolality and aggravate osmotic diarrhoea. Finally, in this syndrome, vitamin B12 is taken up and bound by bacteria, making it unavailable for absorption in the terminal ilium.

2. Secretory Diarrhoeas

By this is meant water movements resulting from secretion of fluid, electrolytes and other substances by the gut, either because of increased hydrostatic or tissue pressure (passive secretion), exudation, or enhanced activity of the mucosal cells. Secretory diarrhoea is seen in patients with intestinal obstruction, portal venous thrombosis or thoracic duct obstruction, inflammatory/infective diseases of the bowel, mesenteric ischaemia, and antibiotic-induced (pseudomembranous) enterocolitis. Tumours may also elaborate substances which give rise to excessive secretion of hormones stimulating gut fluid secretions; these include gastrinomas, VIPomas and carcinoid tumours (all rare).

3. Defective Ion Reabsorption

Defective reabsorption of fluid normally secreted into the gut can result in diarrhoea with abnormally high losses of water and electrolytes, particularly sodium chloride. This is most commonly seen with laxatives. Important is furtive laxitive abuse causing ECF volume depletion that can be difficult to pin down.

4. Motility Disorders
These include disorders with increased motor activity of the small intestine and hence accelerated transit times of fluid through the gut. Tumours such as some of the non-beta islet cell tumours and carcinoid tumours produce diarrhoea of this type.

**PROBLEM-SOLVING COMMENT**

We are now at the stage of being able to use our physiological knowledge to approach problem-solving in a patient who presents with diarrhoea. In practice, causes and clinical presentations of diarrhoea are often complex, for example in chronic inflammatory bowel disease (particularly Crohn's disease) where the diarrhoea can be contributed to by a combination of malabsorption, exuded inflammatory fluid, increased motor activity, terminal ilial disease, and large bowel involvement. Nonetheless, if we stick to the principle of making diagnoses hierarchically in all four of our diagnostic categories, we should at least be able to solve most problems broadly at the clinical level.

**A. ANATOMICAL SITE OF THE PROBLEM**

Again broad questions first.

1. **Watery Diarrhoea or Steathorea?**

Establish that there is in fact an increased quantity of stool. Take a careful history, and examine the stool to see whether you are dealing with watery diarrhoea (increased amount of fluid), or steatorrhea with a *pale* stool of increased stool bulk and weight (greater than 150 grams per day).

2. **If Pale Bulky Stools, First Confirm Steatorrhoea.**

Thus, we must first confirm whether we are dealing with any form of steatorrhoea, whether due to malabsorption of maldigestion or both. Indirect clinical clues from functional abnormalities obtained on general physical examination include evidence of reduced fat soluble vitamin absorption - vitamin K (*easy bruising correctible with parenteral vitamin K over two days*), vitamin D deficiency (osteomalacia with bone pain) and vitamin A deficiency (follicular rash, low serum carotene). There may also be evidence of hypoproteinaemia (oedema, ascites etc.), and reduced body fat and carbohydrate and protein stores (wasting), low plasma cholesterol; also evidence of other deficiencies such as iron (anaemia), other minerals, water, and water soluble vitamins as outlined above.

In establishing that the patient does have steatorrhoea it is very important to examine the stool, macroscopically to determine its weight (normally <150 grams/day), and microscopically for fat...
globules using Sudan III stain. Quantifying the amount of fat is done biochemically using a three day stool collection with the patient on a standard 100 gram per day fat intake; greater than 6 grams per day average is diagnostic of steatorrhoea. But realistically, it is hard to persuade biochemists to enthuse over stool tests, so a more practical screening test is to measure the amount of 14CO2 exhaled in the breath after administering the oral radioactive triglyceride [14C-triolein] (normally less than 3.5% of the administered label is exhaled per hour over the next 6 hours). This test reflects fat breakdown in the large bowel by bacteria.

3. If Steatorrhoea is it due to maldigestion of malabsorption?

[Or is there generally poor gut mucosal function? Uncommon in practice]

Several points help:

(a) Microscopic examination of the stool.

(i) Unfortunately, further differentiation of malabsorption from maldigestion syndromes on the basis of fat and micelle microscopic examination of analysis in the stool is difficult. In theory, most of the unabsorbed fat should be emulsified normally into micelles in cases of pure malabsorption, whereas less than 50% of the fat will be in the mixed micellar phase in maldigestion. However, although this is true of jejunal aspirates, large bowel bacteria act on any fat micelles to make such interpretation in the faeces impossible.

(ii) Examination of the stool for undigested meat fibres can be very useful, because, if found, this strongly suggests maldigestion (from pancreatic disease).

(iii) Low faecal pancreatic elastase is indicative of pancreatic insufficiency; low faecal chymotrypsin may also help.

Accurately delineating the cause of steatorrhoea requires biochemical tests and you should know the broad principles involved in these.

(b) Biochemical differentiation of malabsorption from maldigestion

(i) With fats, one differential tests is to administer radio-labelled (14C)-triolein along with 3H-oleic acid, orally. 14C-triolein will not be absorbed in either maldigestion or malabsorption syndromes (therefore less 14*C in the breath in the form of metabolised 14*C02 over the next six hours). On the other hand, simultaneously administered 3H*-oleic acid, a fatty acid, does not need to be digested
before it is absorbed, so \(^3\text{H}^*\) (as labelled hydrogen) will only be decreased in the breath when there is intestinal wall disease causing primary gut malabsorption.

(ii) \textbf{Hypoproteinaemia} could be due to (pancreatic) maldigestion, or gastro-intestinal wall disease from either lymphatic obstruction or ulcerated weeping bowel wall lesions associated with chronic inflammatory gastro-intestinal disease. In distinguishing these, measurement of \textit{elastase in the stool} is useful, because this enzymes which survives transit through the gut into the faeces relatively unchanged.

A more specific test of pancreatic protease (chymotrypsin) function is to orally administer the amino acid tyrosine linked to para-aminobenzoic acid (PABA), and then measure the amount of PABA released in the gut (by chymotrypsin), absorbed and thus excreted in the urine over a set time. The amount will be proportional to the level of chymotrypsin in the gut. This is a simple non-invasive test of pancreatic maldigestion, but its interpretation also depends on there being a normal gut mucosa for absorption as well as a normal renal function for excretion of PABA. The "gold standard" of (pancreatic) maldigestion is the measurement of this enzyme as well as bicarbonate secretion in the duodenal aspirate (via a nasogastric tube) after maximal pancreatic stimulation with secretin and CCK intravenously.

\textbf{Protein loss in the stool}, as occurs in the so-called protein-losing enteropathies (e.g. ulcerative or weeping bowel lesions, intestinal lymphatic obstruction) can be assessed by administering I.V. radioactive chromium-labelled albumin and measuring the amount of radioactive stool chromium after a set period.

(iii) \textbf{Carbohydrate digestion/absorption} has to be exceedingly deficient before it can be detected clinically, but differential absorption of disaccharides versus monosaccharides can be very helpful in differentiating between the two. The traditional test for distinguishing malabsorption from maldigestion is the \textit{xylose absorption test}. D-\textit{xylose} is not metabolised in the gut and does not have to be digested prior to absorption (it is a monosaccharide). Xylose absorption will therefore not be affected by the maldigestion conditions of pancreatic, hepatic disease etc., but will be reduced in (fairly widespread) disease of the small bowel. However this test is relatively insensitive for malabsorption and also depends on normal excretion in the urine as the index of its absorption i.e. on normal renal function; also on accurate urine collection. D-xylose may also be broken down by bacteria in "blind-loop" syndromes.

Another test is the absorption of the monosaccharide \textit{mannitol}. In intestinal disease (particularly coeliac disease) urinary recovery of a standard oral dose of this compound is again reduced.
A low fasting plasma glucose and a "flat" glucose tolerance curve is also characteristic of malabsorption, but again, is relatively insensitive.

(iv) **Iron Absorption.**

Iron absorption is usually fairly normal in maldigestion syndromes, but reduced in malabsorption. However adequate iron absorption depends on a low gastric pH to release iron from red meats, and secondly, as with protein, iron (red cells) may be lost through weeping gut lesions. If the latter is present, radio-active chromium-labelled red blood cells injected intravenously will result in the appearance of radio-active chromium in the stool (more sensitive and specific than faecal occult blood test).

(v) **Folate deficiency** (macrocytic anaemia) and other water soluble vitamin deficiencies can also occur in malabsorption syndromes.

If there is both reduced iron and folate absorption, then you may see the blood picture of a normal mean MCV, but with an increased red cell distribution (RDW) width, i.e. a mixture of microcytes and macrocytes on the blood film - called a dimorphic picture.

4. **Localising the Site of Malabsorption.**

Having diagnosed malabsorption, our next task is to localise the anatomical site of the problem along the gastro-intestinal tract. The following can be useful in this respect

(a) If there is **iron deficiency** (microcytic anaemia) then this suggests relatively high gastro-intestinal malabsorption. Of course, if the pathological disease process involves ulceration, the iron problem may be compounded by, or due to, blood loss; any haematemesis is particularly useful in localising the problem to the upper gastro-intestinal tract (upper duodenum or above).

(b) **Macrocytic anaemia**, on the other hand, points to vitamin B12 or folate deficiency, both of which may occur in malabsorption. Low B12 is more complicated, because there are several ways in which its absorption may be disturbed.

(i) Before B12 can be absorbed, it must be complexed with intrinsic factor i.e. there must be normal gastric function. Therefore, determine whether B12 absorption can be improved by the addition of intrinsic factor.
(ii). If not, this suggests terminal ileal disease (where the B12-intrinsic factor complex is normally absorbed).

(iii). With "blind loops" in the gut (as may occur after surgical anastomoses, with fistulae between different loops of gut in Crohn's disease etc.), there may be interference with vitamin B12 absorption because of overgrowth of bacteria which then bind the B12. Fortunately, this can often be differentiated from chronic terminal ileal disease by giving a course of antibiotics, which not only eliminate bacterial overgrowth but liberate bacteria-bound B12 for absorption, with improvement of B12 levels and the anaemia. Also, lactulose is not normally metabolised or absorbed in the gut, but will be broken down by bacteria with absorption of end-products, so the finding of 14*CO2 in the breath after oral administration of 14*C-labelled lactulose helps diagnose blind loop syndromes.

(c) Monosaccharide Absorption.

Reduced glucose, D-xylose or mannitol absorption suggests (fairly widespread) disease of the small bowel causing malabsorption.

(d) Large Bowel Disease.

If severe, may lead to loss of water and sodium through intestinal hurry, and hence ECF fluid depletion. This in turn leads to aldosterone stimulation and hence to potassium loss, partly because the increased presentation of ileal fluid to the colon causes increased secretion of potassium into the stool in exchange for sodium, and partly because of the avid distal convoluted renal tubular reabsorption of sodium for potassium excretion in this situation of sodium deficiency. As a result, plasma potassium may fall substantially.

5. Localising the Defect Causing Maldigestion.

If maldigestion, our next task is to distinguish its various causes - in particular whether it is due to bile salt deficiency, pancreatic deficiency, or bacterial overgrowth in the small intestine. The following are useful pointers:

(a) Pancreatic Disease:

There may be clinical indicators of pancreatic disease, for example in chronic pancreatitis, central abdominal pain radiating through to the back, sometimes with a palpable epigastric mass (pseudo-
cyst of the pancreas), and perhaps a relevant background (aetiological) history to further point to the pancreas as the site of the problem (e.g. chronic alcoholism, familial hypertriglyceridaemia) - another example of a useful diagnostic category overlap. Other more biochemical tests of pancreatic function as outlined above.

As a practical point, vitamin D deficiency is much less common in pancreatic maldigestion than in bile salt deficiency malabsorption. Also alcoholics may have mixed liver and pancreatic disease.

(b) Bile Salt Deficiency:

This is not usually difficult to diagnose because its commonest cause is common bile duct obstruction, which is usually associated with severe jaundice and other features (Ch. 13). In the same vein, any bile salt deficiency arising from liver disease per se will usually be associated with gross liver dysfunction and the clinical manifestations thereof. But more subtle bile salt deficiency may occur in the absence of any liver disease or common bile duct obstruction at all, as for example in terminal ileal disease (reduced enterohepatic bile circulation) as well as with the administration of resins such as cholestyramine given deliberately to bind bile salts and hence reduce cholesterol absorption. The most difficult differential diagnostic problem is the delineation of terminal ileal disease from small intestinal bacterial overgrowth (see below).

(c) Bacterial Overgrowth.

"Blind Loop" Syndrome has already been mentioned in relation to the differential diagnosis of B12 malabsorption. But as we have seen, it may also cause secondary fat maldigestion by depleting the bile salt pool.

If this condition is suspected,

(i). Is there any evidence of fat maldigestion/malabsorption secondary to deconjugation of bile acids? This can be examined by the bile acid breath test, which is a simple test of either increased bile salt breakdown by bacteria or terminal ileal blockade of bile salt reabsorption. In this test, conjugated choly-14C*-glycine is ingested orally, and if this is passaged to the large gut (terminal ileal disease), or if it meets bacteria beforehand (as in "blind loop" syndrome) then bacteria will break it down to liberate cholic acid and 14C*-glycine; the latter will then be absorbed and eventually converted into 14*CO2 to be expired in the lungs. If this test is positive (increased 14*CO2 in expired air), we can then differentiate between terminal ileal disease on the one hand and small bowel bacterial overgrowth on the other by seeing whether vitamin B12 absorption (unimproved by intrinsic factor) is improved by a course of antibiotics. If so, then small bowel bacterial overgrowth is the problem.
"Blind-loop" syndromes also produce maldigestion of protein, by de-aminating gut amino acids to ammonia.

(d) Disaccharidase Maldigestion.

This results from a deficiency of the intestinal wall disaccharidases, among which lactase deficiency is most common. Unfortunately, as with protein, there is no way of quantifying carbohydrate loss in the stool, due to its bacterial fermentation in the large gut. However, this fermentation process does produce hydrogen and this forms the basis of a breath test diagnosis of this condition. Thus, the ingestion of sugars (especially lactose), in patients with carbohydrate malabsorption of this type results in the appearance of quantifiable hydrogen in the breath over subsequent hours.

The carbohydrate intolerances are mentioned last among the malabsorption/maldigestion syndromes because so far most of them have been subsumed under our hierarchic umbrella of steatorrhoea. However, disaccharidase deficiency alone does not produce maldigestion or malabsorption of either fat or protein, so what we see clinically and on examination of the stool is more akin to the watery diarrhoeas discussed below.

CLINICAL PROBLEM-SOLVING IN DIARRHOEA

In clinical practice, causes and clinical presentations of diarrhoea are often complex, for example in chronic inflammatory bowel disease (particularly Crohn's disease) where the diarrhoea can be contributed to by a combination of malabsorption, exuded inflammatory fluid, increased motor activity, terminal ilial disease, and large bowel involvement. Nonetheless, if we stick to the principle of making diagnoses hierarchically in all four of our diagnostic categories, we should at least be able to solve most problems broadly at the clinical level.

Anatomical Diagnosis

Clinical details will help diagnose the anatomical site of the problem. First, in the history, the quality, site and radiation of referred pain are useful in differentiating common bile duct obstruction from pancreatic disease causing pain. Second, the abdomen is relatively accessible to examination of its anatomy, for example an enlarged liver, distended, palpable gall bladder, pseudo-cyst of the pancreas, palpable loops of oedematous bowel in chronic inflammatory bowel disease. Rectal examination is essential because of the information it can give about steatorrhoea both macroscopically and by staining for fat globules on microscopy with Sudan III; in addition undigested meat fibres may give the clue to pancreatic maldigestion. Haematemesis indicates gastro-intestinal haemorrhage at or above the level of the proximal duodenum. True melaena, i.e. dark black liquid tar-like stools with a characteristic offensive smell, will occur with a minimum of 500 ml blood loss from the upper gastro-intestinal tract, i.e. with lesions proximal to the mid small bowel. This melena
characteristically appears within 24 hours. On rare occasions, bleeding from the distal small bowel or even proximal colon may remain in the GI tract for long enough to turn it a dark maroon colour but it will not be tarry and black. Haematemesis and melena are also relevant to our next category of Clinical Pathological diagnosis.

**Clinical Pathological Diagnosis**

This is given to us mostly by the general principles applicable to any organ system. We should first determine from the time-intensity relationships whether the condition is acute, chronic, etc. and then whether there is any evidence of inflammation (fever) or weight loss. Weight loss can be particularly helpful where there is a maintained appetite, because in that situation there are only three important conditions to consider - steatorrhoea, diabetes mellitus, and thyrotoxicosis. In relation to inflammation, in addition to fever, we also have the chance in the gut to examine for local evidence, both by palpation of the abdomen for tenderness and by rectal examination for tenderness and examination of the stool on the glove, including microscopy - especially looking for the presence of polymorphonuclear leucocytes (indicating bacterial inflammation), also for red blood blood cells (indicating an ulcerative lesion, inflammatory or otherwise, or a vascular cause).

**Functional Diagnosis**

Of importance to our anatomical diagnosis. And the functional diagnosis is important in treatment as well as diagnosis. Always include an estimate of the degree of functional disability under this category of diagnosis.

**Aetiological Diagnosis**

The background history is important here, including drug history (many drugs produce diarrhoea and some such as Neomycin do so by producing malabsorption).

Past history: Gastrectomy leads to vitamin B12 deficiency through lack of intrinsic factor, and in the elderly it may predispose to vitamin D deficiency as well, particularly in less sunny geographic areas. Also ask about any history of small bowel surgery, particularly the creation of small bowel anastomoses (blind loops and bacterial overgrowth) - can also cause B12 deficiency. A past history of alcoholism is relevant in a background to both hepatic and pancreatic disease.

Family history can help as familial hypertriglyceridaemia producing recurrent and sometimes chronic pancreatitis.
A past and family history of allergy may be important particularly in raising the possibility of food allergies. Lactase deficiency is a common cause of cow's milk intolerance (it is not due to an allergy but to an enzyme deficiency). Coeliac disease is an autoimmune allergic (malabsorption) condition, this time with the allergen being the gluten component of grain (wheat, rye and barley, but not oats). Increased levels of Anti-transglutaminase (Anti-tTG) clinches the diagnosis. Other foods may cause diarrhoea due to allergy or other intolerance, giving rise to maldigestion and malabsorption, and the only way to establish this in obscure cases is to eliminate the suspected compound from the diet and see what happens, not only during the period of withdrawal, but on re-introducing the agent into the diet.

With any obscure diarrhoea, think of factitious causes, particularly the furtive use of purgatives (urinary biochemical drug screening can be helpful).

### MCQs and PROBLEM SOLVING CASE

#### A. Mechanisms in Disease

A patient is known to have severe chronic atrophy of the gastric mucosa. Which of the following would be likely consequences:

1. A Low gastric pH.
2. Evidence of substantially reduced glucose absorption.
3. Absent gastric motility.
4. Evidence of vitamin B12 deficiency.
5. Severe protein maldigestion.
6. The presence of undigested meat fibres in the stool.
7. Detectable radio-active chromium in the stool after administration of radio-active chromium-labelled albumin intravenously.
8. Increased hydrogen in the breath after the oral administration of lactose.
B. Problem Solving

A 49 year old man (1) presents with a 10 year history (2) of upper abdominal pain of boring quality radiating through to the back (3), in the early years intermittently (4), but nagging him much more constantly over the last 12 months or so, and gradually becoming worse a (5). During the last 6 - 12 months he has noticed weight loss of approx. 10 kg, despite a relatively maintained appetite (6). Over this time he has also noticed diarrhoea in the form of passage of up to 3-4 large, bulky, pale, offensive, semi-formed bowel motions per day (7), easy bruising (8), pallor (9), weakness (10), "dermatitis" (11), and bilateral ankle swelling (12).

In the background there has been no past history of any drug ingestion (13), but he does admit to drinking up to 10 glasses of beer per day (14). There is a family history of "high blood fats" (15), and one or two others in the family have had similar clinical problems (16). No family history of ischaemic heart disease or other clinical evidence of early-onset atherosclerosis (17). Close questioning reveals that he had recurrent crops of yellow lumps over his skin as a child (18). He smokes 25 cigarettes per day and has worked for many years as a delivery man for a wine and spirits merchant (20).

On examination he looks pale (21), but palmar creases, conjunctivae and tongue appear relatively normal in colour (22). He has generalised wasting, not only of muscle bulk, but of subcutaneous fat (23). The skin shows a fine erythematous rash over upper parts of the limbs, particularly around the hair follicles, where it is associated with increased scaling somewhat like permanent gooseflesh (24). No jaundice (25). There are a number of bruises on the skin, which he says have appeared on slight trauma rather than spontaneously (26). The Hess test is negative (27), there is no sternal or other bony tenderness (28), and both Trousseau's and Chvostek's signs are negative (29).

In the cardiovascular system the pulse has a normal rate, rhythm and wave form, blood pressure 120/70 mm Hg, JVP normal, heart not enlarged; two heart sounds, no added sounds or murmurs, pulses all normal (30). Fundi show a pale yellowish appearance to both the arteries and veins, somewhat like a prominent light reflex (31). Mild bilateral pitting ankle oedema (32). Lymph node areas all clear (33). Chest NAD. Abdominal examination: upper abdominal tenderness (34) and two fingers' breadth of firm liver with 12 cm. liver span (35). Gall bladder not palpable (36). Rectal examination: no masses or tenderness, but semi-formed pale stool which shows a red staining with
Sudan III (37) but no red or white blood cells (38). There also appear to be something akin to skeletal muscle fibres in the stool on microscopy (39). On general examination there are no other relevant signs, in particular no gynaecomastia, testicular atrophy or alteration in bodily distribution or amount of hair; no spider naevi or palmar erythema (40), although both parotid glands appear slightly enlarged (41). CNS: NAD, except for some proximal myopathy; no evidence of peripheral neuropathy (42). Temperature 37 deg.C (43). Urine examination: trace glucose, otherwise NAD (44).

For this problem solving exercise, I have stopped short of giving the results of the many possible investigations because the first approach must be a clinical diagnostic one.

**Solve the problem** in the usual four-columns way: **then answer the following**.

**Which of the following statements about this patient is/are likely to be correct?**

1. The pain this patient complains of is approximately in the distribution of the first lumbar dermatome.

2. The site, radiation and character of the pain suggests involvement of a common hepatic duct.

3. The clinical evidence in this man suggests maldigestion rather than malabsorption.

4. Anatomically, the important functional abnormalities in this man are likely to have been determined by terminal ileal disease.

5. Pathologically, this is likely to be a neoplastic process.

6. Clinically, this patient has steatorrhoea.

7. He is unlikely to be anaemic on the evidence given.

8. The bruising will probably be correctible by a course of parenteral vitamin K.

9. The rash is most likely due to vitamin E deficiency.

10. The absence of bone pain, Trousseau's, and Chvostek's signs are *atypical* features in this patient's condition.

11. Serum B12 will typically be subnormal.
12. Serum iron will characteristically be within the normal range.

13. The absence of red cells in the stool is surprising.

14. There is evidence of impairment of right heart function.

15. The fibres recognisable in the stool strongly point to a protein-losing enteropathy.

16. There is good evidence of an inflammatory bacterial nature to the pathological condition.

17. Chymotrypsin and elastase-1 levels in the stool might well be increased.

18. Levels of bicarbonate and pancreatic enzymes in the duodenal aspirate following administration of secretin and cholecystokinin I.V. would characteristically be elevated.

19. Plasma alkaline phosphatase will typically be substantially raised.

20. A three day stool collection on a standard 100 gram per day fat diet will characteristically contain more than 18 grams of fat.

21. Typically, the urinary excretion of an orally administered dose of D-xylose will be reduced.

22. You would not be surprised to see a reduction in plasma carotene.

23. Excretion of hydrogen in the breath after administration of lactose is likely to be raised.

24. Excretion of radioactive CO2 in the breath after oral administration of C14-cholyglycine will characteristically be within normal limits.

25. Aetiologically, alcohol could be a contributing factor to this man's underlying problem.

26. This man's background family history suggests that he may have a familial hypercholesterolaemia.

27. The family background condition may well be relevant to his own medical problem.
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<td>? Pancreatic.</td>
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Interim conclusions - as always when time-intensity relationships change.

? Pancreas | Acute relapsing — 2° abdominal pain | ??Why

Further History.

5. 1 yr — chronic progressive.


5. Pain now more constant, nagging ← & grad. increasing.

7. Diarrhoea. — 3-4 large, bulky, pale, offensive, semi-formed stools/day = ? steatorrhoea


Why the recent progress^n ?

14. — EtOH (10 / day).
15. F.H. — ‘High blood fats’
16. Others in family have similar probs. to this pt., but,
17. No early onset athero-sclerosis = ? cholesterol not raised.
18. Recurrent crops of yellow lumps in skin as a child = ? pl. triglicerides
19. — 25 cigs/day — at occup. risk of high ETOH consumpt^n

20. —
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<td>Ch 12. (contd.)</td>
<td>Steatorrhoea Problem</td>
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### Examination Findings

21. Pale — ? anaemic,  
22. Palmar creases,  
mucous membranes normal  
   = Not clin. anaemic.  
23. Wt. loss — both of fat & muscle.  
24. Classical Vit. A defic. rash!  
   = part of a fat soluble vit. defic.  
   = 2° to steatorrhoea  
25. No jaundice =  
   no obvious liver prob. as a cause  
   for steatorrhoea.  
26. Easy bruising on slight trauma  
   rather than platelet problem.  
27. Hess test — ve + no clin.  
   platelet problem.  
28. No sternal tenderness =  
   no clin. bone marrow problem.  
29. Trousseau’s & Chvostek’s signs  
   both —ve.  
   = No clin. hyp. plasma Ca++/vit D  
   defic.  
   eg. to explain weakness.  
30. CVS. normal = no evid. of ↑ plasma  
   vol. i.e., nothing to confirm  
   ? heart failure,  
   or ? renal failure (see 12.)  
31. Strange for veins to show yellow  
   like ↑ arteriolar light reflex  
   = ↑ milky plasma  
   ↑ plasma fats (triglycerides).  
32. Mild bilat. ankle oedema  
   = prob. 2° to ↓ pl. albumin -30.  
33. Lymph nodes clear  
   = no obvious retic-endothelial  
   or immunol. prob.  
34. Abdo. — epig. tenderness  
   ? pancreatic (see above),  
   related to liver (see 35.).  
35. Liver palpable  
   = enlarged or displaced ↑ (?) COAD  
   Liver also firm (? non-tender)  
   = prob. pathological (chronic ),  
   (? 2° to ETH though no signs  
   of hepatic dysfunction clinically).  
36. Gall bladder not palpable  
   = no lower CBD. obstruction.  
37. PR. — semi-formed  
   stool stains +ve for fat  
38. Stool contains no rbc.  
   no neutrophils.  
39. ↑ undigested meat fibres in stool  
   [Confirms (pancreatic) malabsorption]  
40. Parotids enlarged  
   = ? 2° to ↑ ETH intake.  
42. No evid. of CNS. dysfunction.  
   = no serious metabolic prob.  
   (but why is he so weak?)  
44. Urine NAD.  
   = no evid of renal dysfunction,  
   no glucose, bile or urobilinogen.  

38. No evid of bowel ulceration  
   or  
   (bact.) inflammation.  

39. ↑ undigested meat fibres in stool  
   [Confirms (pancreatic) malabsorption]  

41. No evid. of hepatic dysfunction.  
40. Parotids enlarged  
   = ? 2° to ↑ ETH intake.  
42. No evid. of CNS. dysfunction.  
   = no serious metabolic prob.  
   (but why is he so weak?)  
44. Urine NAD.  
   = no evid of renal dysfunction,  
   no glucose, bile or urobilinogen.
Diagnostic Dissertation.

1. FUNCTIONAL DIAGNOSIS:
   Reduction of Pancreatic function.
   a) Steatorrhea is the main (active) problem. The clinical evidence for this is strong, but the diagnosis could readily be confirmed by a collection of stool for measurement of faecal fat. Next, in approaching the problem hierarchically, we need to be sure that this really is due to malabsorption (of whatever cause) rather than malabsorption before we further consider the detailed of the anatomical site of the lesion. In this respect, careful analysis of the stool to confirm undigested meat fibres would be critical. If present, this would not only confirm malabsorption, but at the same time further localise the anatomical site of the lesion to the pancreas which we strongly suspect on other grounds in any case (see below).
   b) Secondary effects of steatorrhea.
      i) Weakness: The cause of the weakness is unclear, and needs further investigation. First go back and re-examine limb power more carefully, paying particular attention to the proximal muscles, since they are often more involved in the sort of general metabolic condition we suspect here, viz. a metabolic myopathy or neuropathy (e.g. ? sub-clinical vit D deficiency).
      ii) Easy bruising. The precise cause of this also needs elucidating. It is very likely, in the circumstances, to be due to prothrombin deficiency, but we need to discern whether this, in turn, indeed arises from a lack of absorption of Vit. K (from malabsorption and therefore malabsorption of fat & fat-soluble vitamins) as we suspect, or from subtle liver dysfunction causing a failure of sufficient production of prothrombin. Measurement of prothrombin time before and a few days after I.V. injection of a water soluble form of vit. K would distinguish.
      iii) Vit A deficiency could be confirmed by serum carotene measurement, though the clinical evidence (classical rash) is fairly strong.
      iv) Plasma albumin measurement would be useful in determining any degree of protein malabsorption (2+ to malabsorption).

2. ANATOMICAL DIAGNOSIS.
   The anatomical site of the lesion is very likely pancreatic.
   This is because of the characteristic pain and the evidence of malabsorption (2+ to malabsorption). We would like to confirm pancreatic origin of malabsorption eg. by looking for meat fibres in the stool. Analysis of faecal elastase-1 and faecal chymotrypsin would also help.

3. PATHOLOGICAL DIAGNOSIS.
   The pathological basis for the condition.
   Probably initially recurrent inflammatory, then more chronic persistent inflammatory, this eventually giving way to atrophy.

4. AETIOLOGICAL DIAGNOSIS.
   Without further investigation it is difficult to be certain whether alcohol or hypertriglyceridaemia is the more important background factor.
   More importantly, we have not really determined why the underlying condition has become more constant and progressive in the last year. Further history would be important in this respect, e.g. does his alcohol intake been higher over this time? We may only determine that by careful discrete discussion with relatives.; if not, further examination (eg. testicular size), and investigations (eg., full blood count -? macrocytosis, ? target-shaped red cells; ? subtle liver dysfunction) may help. On the other hand, estimation of plasma triglycerides may shift the emphasis to this as the main source of the pancreatic problem.

RELATIVELY INACTIVE PROBLEMS.

B. Liver
   The liver is firm & enlarged, and therefore probably the site of some chronic (? fibrotic?? infiltrative process), but clinically appears to be fairly well compensated in terms of hepatic function. However, there may be some subtle abnormality (e.g., see above in relation to vit K), so liver function tests would be of value. Most likely aetiol. is EIOH.
C. Parotids.
   Enlarged — by fibrosis. ? Any tenderness/pain/dry mouth to suggest dysfunction?
   Pathol. — most likely a low grade inflammatory process.
   Aetiol. — chronic EIOH consumption, most likely.
MCQ ANSWERS

1. Mechanisms in Disease.
   4. Correct. All others false
   Re 1: Gastric pH would be expected to rise. It is the H+ ion that we would be expect to fall.

2. Problem Solving Case MCQs
   6, 8, 17, 19, 20, 22, 25, 26, 27 correct.
   All others false.