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DISORDERS OF THE ALIMENTARY TRACT AND THEIR NUTRITIONAL EFFECTS

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Disorders of Fat Absorption

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I have often been asked how I can keep to so narrow a field as steatorrhoea over a period of years, and my answer has always been that there are so many inviting problems in this field; my main difficulty is really one of confining my energies to a few of them. For instance, there is a wide variety of clinical conditions in which steatorrhoea is seen, often present only as part of a syndrome of generalized malabsorption, avitaminosis and malnutrition, in which many metabolic processes in the body may be upset. In Table 1 are listed several of these conditions, but this list is by no means all-inclusive as there are many other illnesses, such as Crohn's disease or Whipple's disease in which steatorrhoea is often also present.

Table 1. *Some clinical conditions in which steatorrhoea is seen*

Defective digestion and emulsification	Defective mixing and intestinal hurry	Defective absorption	'Lymphatic obstruction' ?
	Gastro-enterostomy	Coeliac disease	Mesenteric tuberculosis
Pancreatic disease			
	Gastrectomy	Non-tropical sprue	
			Malignant disease
Biliary obstruction		Tropical sprue	
			Hodgkin's disease
		Gastro-jejunocolic fistula	
	Massive intestinal resection		
		Loop syndromes	

The understanding of many of these conditions is far from complete, and treatment therefore often unsatisfactory. Pancreatic insufficiency, for example, although well understood, does not yield properly to replacement therapy, and there are many unsolved problems in connexion with post-gastrectomy steatorrhoea and the sprue syndrome, both in aetiology and treatment. In spite of a flood of studies—particularly recently—knowledge of these conditions progresses relatively slowly. There are various reasons for it, but the one with which I am particularly concerned here is the use of estimations of faecal fat as criteria of diagnosis and the control of treatment.

Assessment of defective fat absorption

It is extremely easy to measure fat in the faeces, but the only way of determining whether an abnormal amount is being excreted is by some form of balance. Unfortunately, for many years past, much good observational work has been largely wasted by use of the microscopical appearance or estimation of percentage fat in the stool as a means of detecting defective fat absorption. Both these methods may be grossly misleading and neither of them is of any value as a quantitative index of the defect (Cooke, Elkes, Frazer, Parkes, Peeney, Sammons & Thomas, 1946; Weijers & van de Kamer, 1953); although these examinations have their uses, they should be abandoned as evidence of steatorrhoea both in diagnosis and as indices of progress or recovery.

The fat balance

From an examination of the literature, and from our own experience, we know that normal people excrete faecal fat, derived from various sources, at the rate of 1–7 g/day, provided they are on a normal diet containing from 50 to 150 g fat/day (Annegers, Boutwell & Ivy, 1948). In order to make an assessment of a patient's progress, it is almost essential to have him on a known fat intake: our system is to employ a diet containing 50 or 70 g fat/day and estimate the faecal fat as fatty acid by a modification of the rapid method of van de Kamer, Huinink & Weyers (1949). On this basis, it is possible to calculate the apparent fat absorption, arbitrarily regarding the faecal fat as dietary in origin, and the mean molecular weight for faecal fatty acids as 284 (Goiffon, 1949). In a normal person, fat absorption may be regarded as 90% or over.

For diagnosis, we usually employ a 3-day balance, though a longer period of observation may be necessary in border-line cases, or when the bowels are constipated. For control or investigation of the effects of treatment, we use a continuous fat balance, the results being expressed as 3-day sliding means to even out fluctuations from irregularity of collection or evacuation.

There are three important advantages of the continuous type of fat balance in abnormal subjects:

(1) A striking irregularity of the 3-day mean absorption (or excretion) is usually seen, which cannot be accounted for simply by irregularities of collection. As

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these may occur in all types of steatorrhoea (see Fig. 1), the continuous balance must be prolonged until one is reasonably sure that the results adequately represent the absorptive defect.

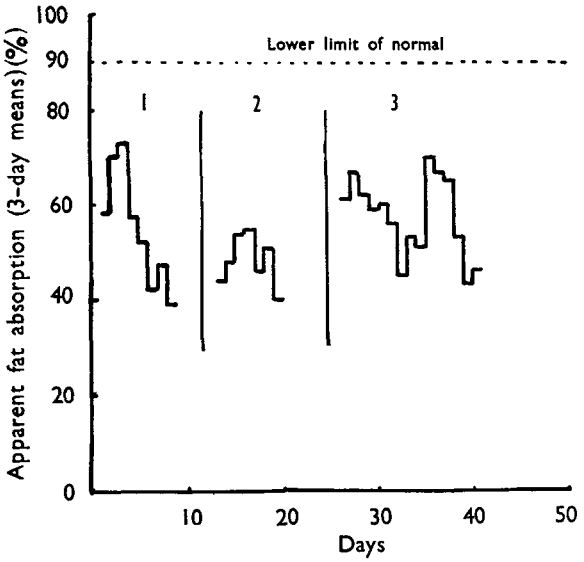

Fig. 1. Continuous fat balance used to assess the effect of treatments in a case of pancreatic insufficiency (pancreatic lithiasis). Note the wide fluctuations of the 3-day balance in the period without treatment (1), and also in the periods with treatment (2, with emulsifier, and 3 with pancreatic extract). A single 3-day balance in any of these periods would give no clear indication of the degree of absorptive defect. The patient was on a diet containing 50 g fat daily. The chart indicates no significant improvement in periods 2 or 3.

(2) Rapid alterations in the absorptive defects, which may follow procedures or treatments and be maintained, yield significant information in only a few cases. In fact important evidence may sometimes be obtained by following a single case over a prolonged period of time. Where balances at intervals of many days are employed, a much larger series of cases has to be observed in order to obtain the same information, owing to the irregularity noted above.

(3) The impact of other events, regarded perhaps as trivial at the time, may subsequently be noted to have had an effect upon absorption. For instance, it has been observed that upper respiratory infections in coeliac children depress fat absorption for several days.

The application of the continuous balance technique to specific problems

Pancreatic insufficiency. In these cases the defect of fat absorption may be attributed to a deficiency of lipase. Inadequate hydrolysis of the triglyceride fat results in faulty emulsification (Frazer & Sammons, 1945; Thompson, 1948). It might be thought that this defect could be remedied simply by the supply of pancreatic extract by mouth. However, results with active preparations of dried pancreas are disappointing, and surprisingly large doses have been recommended (up to 20 g/meal); even these have been found not to make fat absorption normal.

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There are several possible reasons for this finding: lipase is irreversibly destroyed within a few seconds in the presence of free hydrochloric acid. The pancreatic extract may not mix well with the food, particularly if supplied in tablet form. Protection of the extract with 'enteric' coatings, impervious to hydrochloric acid, necessitate the use of tablets or granules; such coatings may require for their solution the action of sodium bicarbonate (e.g. for salol coatings) or trypsin (for hardened gelatin), both of which are deficient in the patient with pancreatic insufficiency. Thus the site in the intestine at which the pancreatic extract eventually becomes freed may well be unfavourable for its action.

Coeliac disease and adult idiopathic steatorrhoea. Theories of fat and carbohydrate intolerance as a cause of coeliac disease have had to be abandoned in the face of the striking results obtained by Dicke (1950) and Weijers & van de Kamer (1950) with wheat- and rye-free diets. Their most recent publications show that administration of whole wheat protein, gluten or the gliadin fraction to coeliac children who have recovered on a wheat-free diet causes a deterioration of the clinical state into a condition indistinguishable from the original illness (Dicke, Weijers & van de Kamer, 1953): their results have been fully confirmed in this country (Anderson, Frazer, French, Gerrard, Sammons & Smellie, 1952; Sheldon & Lawson, 1952), but I have not yet seen similar reports from America.

Many cases of adult idiopathic steatorrhoea have a history—diagnosed or presumptive—of coeliac disease in childhood (43% according to Cooke, Peeney & Hawkins, 1953) and it may reasonably be supposed that the adult case would respond to a gluten-free diet in a manner similar to that of the child. The number of recorded recoveries is, however, disappointingly small: McIver (1952) reported great improvement in one case, after failure of therapy with ACTH and cortisone and Ruffin, Carter, Johnston & Baylin (1954) noted improvement in three cases; in a preliminary report (Anderson, Frazer, French, Hawkins, Ross & Sammons, 1954) we have recorded the complete recovery of five cases. The blood picture in these five cases became normal without specific haematinic therapy. A feature of the adult recovery is its slowness. We have studied a greater number of cases in whom shorter trials have been carried out (1 or 2 months) and in them no appreciable response was observed.

There are several possible reasons for the failures in the adult cases:

(1) The response is obviously so much slower than in the child that we may not have continued treatment long enough.

(2) The basic condition may have been so overlaid with vitamin or other deficiencies that reversal was not possible simply by removal of the initiating factor.

(3) If the aetiology is one of a protein sensitivity on an allergic basis, the adults may be sensitive to a variety of agents, as yet undiscovered.

(4) A vicious circle of malabsorption—increased bacterial growth in the small intestine—irritation of the small intestine—further malabsorption may be present; this may need interruption with appropriate chemotherapy, as seems possible in tropical sprue (see Fig. 4).

Tropical sprue. The great step in thought that has occurred with the discovery

of the role of gluten in initiating relàpses in coeliac disease is that we are now dealing with a positive causal factor in a condition previously thought to be some kind of deficiency disease; the same line of reasoning has been applied to the study of the aetiology of tropical sprue.

Since sprue, as I shall call it, was first described as a disease *sui generis* by Manson, (1880), when it was differentiated from dysentery, many theories have been put forward as to its causation. The most important of these are:

(1) Specific infection. There is no really acceptable evidence for it, as the disease has never been transmitted to man or animals experimentally.

(2) Dietary deficiency. For this there is plenty of evidence clinically in the fully developed case. However, all observers who have worked in areas where sprue occurs agree that they see many cases in people whose diet has been excellent; yet it is seen rarely in Africa where deficiency diseases are rife. Further, it was not seen in Japanese P.o.W. camps under conditions of extreme privation.

(3) Tropical climatic conditions. There is no adequate basis on which to explain the absence of sprue in tropical Africa.

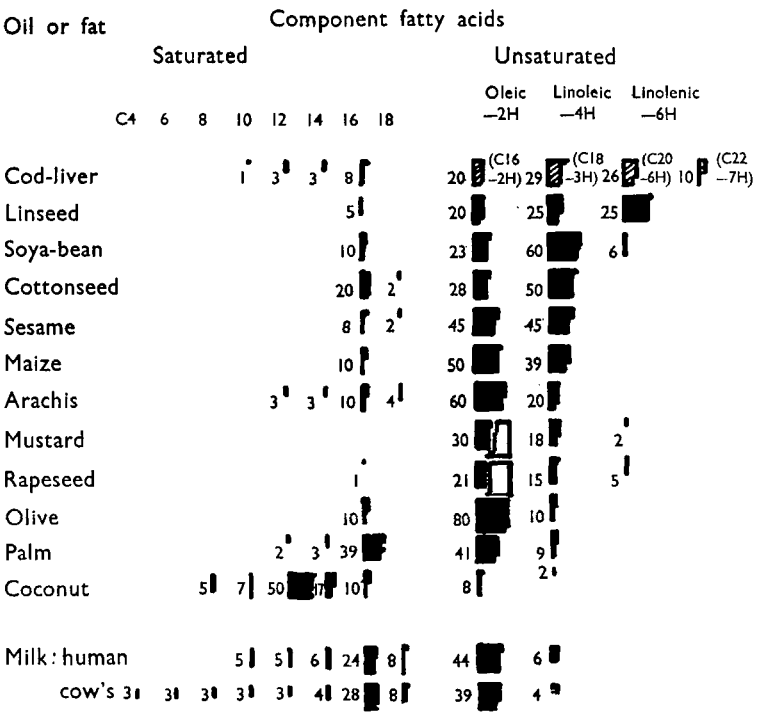

Fig. 2. Component saturated and unsaturated fatty acids of some edible fats and oils (from French, 1949). The unsaturated fatty acids are arranged to show the proportion of mono-, di- and tri-ethenoid C 18 components, with the exception of cod-liver oil (shaded blocks), which has a considerable amount of acids of greater chain length; mustard and rapeseed have a high content of erucic acid (C 22, outlined blocks).

The size of a block indicates the percentage of the total contributed by the particular fatty acid. The figure by the side of each block shows the exact value.

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(4) Rancid fat. During the war years 1940–6 I saw many hundreds of cases of sprue in both British and Indian troops and became interested in their fat intake for the following reasons. About 1942, ghee (butterfat), which was the standard source of the Indian fat ration, became almost unobtainable and many vegetable oils and fats were used as substitutes. At about the same time the fat ration of Indian troops was raised by stages to equal that of the European. Coinciding with these changes of fat intake the incidence of sprue in British and Indian troops rose to an unprecedented level and was seen in epidemic outbreaks. It was not seen in African troops, 200,000 of whom were stationed in India during this period. It is noteworthy that all their fat was sent to them from Africa (Findlay, 1949).

A study of the constitution of fats (Fig. 2) used for cooking in various parts of the world shows that the incidence of sprue roughly coincides with extensive use of certain unsaturated fats, e.g. rapeseed, sesame and mustard oil. Africans use mainly more saturated fats, such as coconut oil, palm oil and animal fats, and the virtual absence of sprue in Africans both at home and when stationed in India may be thus explained. The special feature of unsaturated fats is their liability to undergo oxidative rancidity. It was noted many years ago by Hawes (1952) that sprue almost disappeared from the Singapore area with the introduction of refrigeration; he taught that rancidity of edible oils was the most probable cause, though the idea does not appear to have been further pursued by him.

It has been known for some years that fat made rancid by oxidation will cause diarrhoea, emaciation, anaemia and death in rats (Burr & Barnes, 1943); this effect

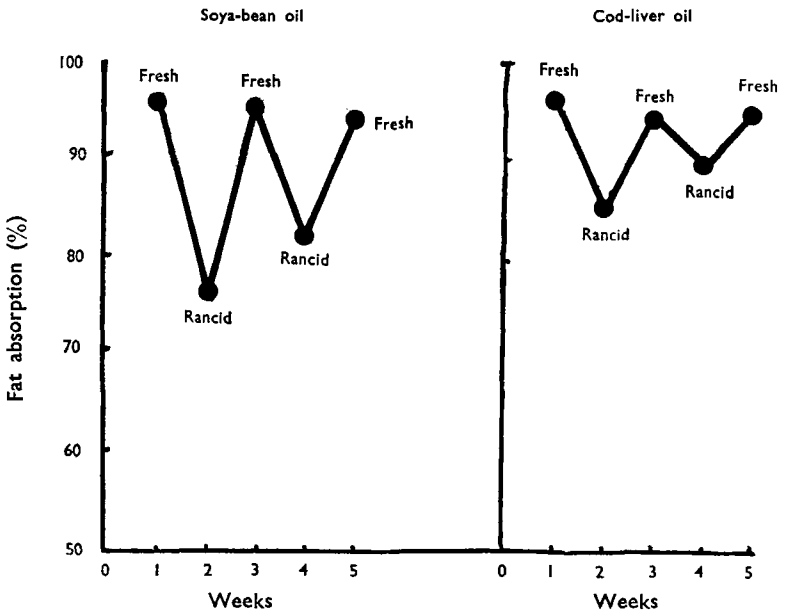

Fig. 3. Effect of rancidity of the oil on fat absorption in a group of five rats. The rats were fed on a diet containing 25% by weight of oil, fresh and rancid oil being given for alternate weeks. The fat absorption was depressed with the rancid oil, and diarrhoea and steatorrhoea began within 24–48 h, before vitamin deficiency could possibly have developed.

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has been variously attributed to the destruction of either essential fatty acids or vitamins; but it has been shown that the diarrhoea is associated with steatorrhoea (French, 1949) and that both occur within a day or so of feeding rancid fat, before vitamin deficiencies could possibly develop (Fig. 3). Rancid cod-liver oil has been reported to have caused an outbreak of gastro-intestinal disorders in a children's hospital (Whipple, 1936). It has been suggested that some factor in the rancid fat causes an excess of mucus secretion by an irritant action (French, 1949) leading to a delay in absorption as seen in coeliac disease and idiopathic steatorrhoea.

The role of bacteria in tropical sprue. The essential functional disturbance in the sprue syndrome appears to be a generalized delay in absorption from the small intestine due to an increase in secretion of mucus and loss of motility. The nocturnal diuresis, which is a feature of the condition, seems to be clearly associated with a delay in the absorption of the products of digestion (Wollaeger & Scribner, 1951; Taylor, 1954). Such a delay must lead to the presence of a rich pabulum favourable for an extravagant growth of intestinal bacteria, especially in cases with achlorhydria. Although direct evidence of such a growth within the small intestine has not

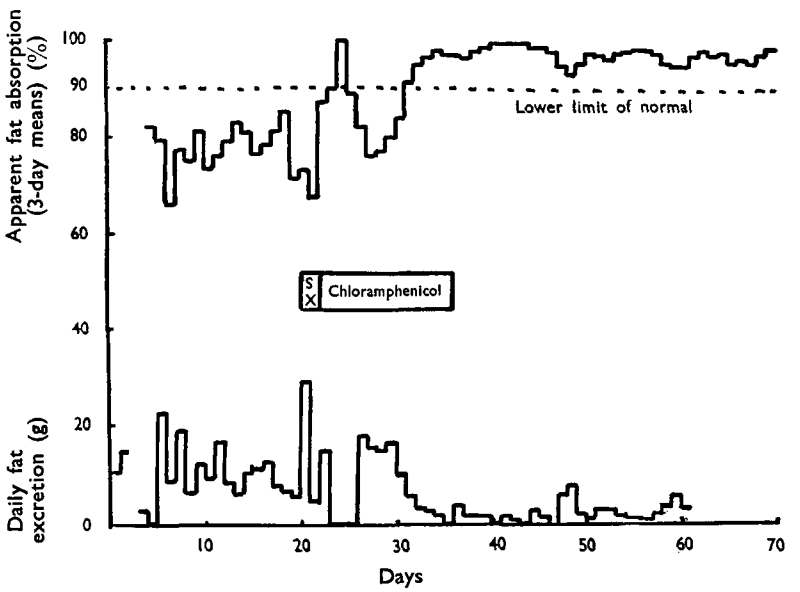

Fig. 4. Continuous fat balance in a case of tropical sprue, showing apparent recovery to normal after a course of succinylsulphathiazole (sx) and chloramphenicol.

yet been obtained, there is considerable evidence that the faecal flora is disturbed and that increased putrefaction occurs. The problem as to how high in the intestine such changes occur, and whether they affect secretion of mucus and motility seems a difficult one to assess on a quantitative basis, since gastro-intestinal motility renders the intra-luminar situation an ever-changing one. We have made an indirect attack on this problem by the employment of intestinal chemotherapy in seven cases of tropical sprue, using a continuous fat balance as an index of changes in the general absorptive situation (Anderson *et al.* 1954). It was found that if several

chemotherapeutic drugs were used *seriatim* over a total period of 10–14 days, there was an abrupt rise in the fat absorption to normal levels which subsequently remained normal; the condition appeared to be cured (Fig. 4). These patients developed sprue in the tropics, but were treated in this country after a control observational period. As most cases of tropical sprue eventually remit on return to temperate climates whatever the treatment, a natural remission cannot be entirely excluded; but the abrupt nature of the change coincident with chemotherapy suggests that a cycle of bacterial infestation of the gastro-intestinal tract had been terminated. If these results are repeatable on a wider scale, it seems that the mechanism of the

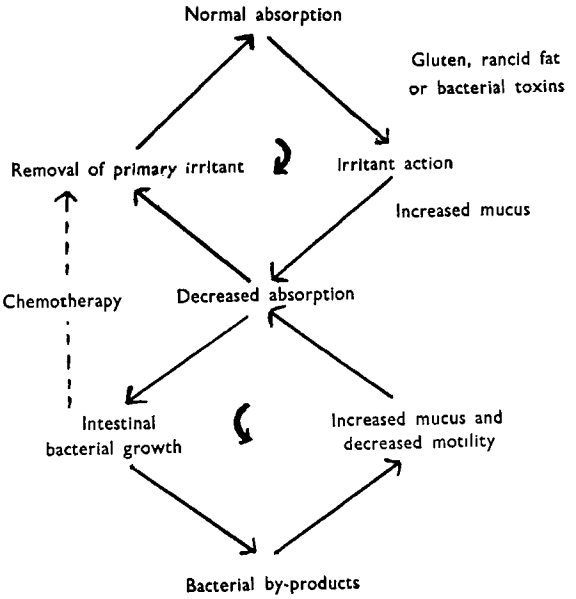

Fig. 5. Suggested scheme to show main factors causing malabsorption from the intestine in the sprue syndrome.

defect in absorption in the sprue syndrome can be described in relatively simple terms (Fig. 5). A factor in the diet, either wheat gluten, rancid fat, or possibly even bacterial toxins from an acute intestinal infection cause an irritation of the small intestine. Functional changes in the small intestine result in the development of a bacterial cycle which may prolong the condition indefinitely even when the initial irritating factor has been withdrawn. Appropriate chemotherapy looks like being a useful tool in solving some of the problems connected with these conditions.

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The Absorption of Vitamins in Disorders of the Alimentary Tract

By R. H. GIRDWOOD, *Department of Medicine, University of Edinburgh*

Space does not permit me to deal with the physiology of absorption of vitamins, but I feel that I should make some reference to the action of intestinal bacteria.

The action of intestinal bacteria

It has been shown that bacteria similar to those present in the alimentary tract, when grown under suitable conditions, can synthesize thiamine, riboflavin, nicotinic acid, pantothenic acid, biotin, *p*-aminobenzoic acid, vitamin B_{12} and vitamin K. By means of depleting organisms such as *Staphylococcus aureus* and *Bacterium coli* of folic acid and growing them under very strict cultural conditions, Lascelles & Woods (1952) have induced them to synthesize folic acid. However, other organisms in culture can destroy or absorb vitamins. Table 1 summarizes an experiment in which the mixed flora from human gastric contents was incubated for 48 h in two media with added cyanocobalamin*. Thereafter the amount of vitamin B_{12}* present was measured microbiologically with *Lactobacillus leichmannii* as the test organism. The two media used were nutrient broth and the medium of Burkholder (1952) which contains only dextrose and asparagine together with salts of potassium, sodium, magnesium and ammonia.

* Throughout this paper the terms cyanocobalamin and pteroylglutamic acid are used to denote the pure chemical substances as employed in therapy. The terms vitamin B_{12} and folic acid refer to the substances present in natural materials; they are not necessarily precisely the same chemical substances.