THE TREATMENT OF STEATORRHOEA

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Defective function of an essential organ such as the small intestine has widespread effects throughout the body. It is therefore not surprising that the treatment of the steatorrhoea syndrome offers a varied and interesting scope to the physician. Complex problems of nutrition are involved; different types of anaemia have to be corrected; and changes in the body fluids and electrolytes frequently occur. Recent knowledge is beginning to make it possible to consider treatment from a more rational viewpoint than the empiricism of the past; and new methods of fat analysis of the stools, together with radiological and other studies (reviewed by French, 1955) have enabled the effect of various therapeutic measures to be assessed more accurately.

Diet

Samuel Gee, whose original description of coeliac disease remains a classic, stated that 'if the patient can be cured at all, it must be by means of diet' (1888). Hitherto the term 'cure' has not been applicable to adult steatorrhoea, for although alleviation of the disease has resulted from the use of various empirical diets—particularly a high protein low fat one—the fat absorption has not returned to normal nor have relapses been prevented. It is only recently, when the gluten of wheat or rye has been excluded from the diet, as in coeliac disease, that apparent cure has occurred in idiopathic steatorrhoea (McIver, 1952; Anderson, Frazer, French, Hawkins, Ross and Sammons, 1954; Ruffin, Carter, Johnston and Baylin, 1954; Haax and Lips, 1955). This, unfortunately, occurs only in certain cases and there is no means of foretelling which ones will respond. It may be only those whose disease originated in childhood but a history of this is not always obtained and age does not disqualify for one of our patients showed an excellent response at 55 years. It would seem rational, therefore, to submit every patient with adult steatorrhoea of unknown (idiopathic) origin where structural changes such as pancreatitis, jejuno-ileitis, fistulae or other abnormalities of the gastro-intestinal tract have been excluded, to a

trial of the gluten-free diet. This should continue for three months or longer as the response may not be immediate. There is no doubt about the successful case. The patient notices a sense of well-being with increased energy and the attacks of soreness of the tongue disappear. The bowels become normal and the weight increases. Objective confirmation is obtained by the normal fat absorption, by the absence of flocculation pattern when the small intestine is X-rayed with routine barium sulphate and the disappearance of any macrocytic anaemia without haematinics. It appears that the exclusion of wheat gluten has to be permanent, for relapse occurs whenever it is reintroduced into the diet; all other foods, including fats, can be taken without trouble. Gluten therefore is a specific aetiological factor in certain cases of idiopathic steatorrhoea, and when a case responds no further therapy appears to be necessary.

The exclusion of wheat and rye flour eliminates bread, cake, pastry, gravy and soups that are thickened with flour, together with buns, biscuits and so on. These patients only react to the protein in wheat (gluten) and can take wheat starch without harm. Gluten is now separated from the wheat on a commercial basis and the product—pure wheat starch—can readily be obtained.* It costs about the same as ordinary flour and the patients use this substitute. The bread, though quite palatable, is less easy to make than ordinary bread; it is more crumbly and heavier because of the lack of the dough-making property of gluten. Instructions concerning foods to be eaten or avoided and recipes for making bread, biscuits and cakes are issued to these patients and do not differ greatly from the conventional ones (see Addendum).

Those that fail to respond to the gluten-free diet are best treated by a diet high in protein, usually 100 to 120 g., and low in fat, 50 g. or less.

*It is marketed as 'Special Wheat Starch' and may be obtained from Energen Ltd., Bridge Road, London, N.W.10, or Wimbush Ltd., Birmingham 9.

The quantity of protein is increased by extra meat and dried skim milk products. This should be strictly adhered to for a period of three to six months; then, if the patient's condition is satisfactory, it is reasonable to allow certain foods to be tried singly by the patient and any ill-effect recorded. Cooke (1952) emphasizes that tolerance varies to different kinds of fat; those derived from milk are often taken without trouble so that butter and cheese can be enjoyed. But serious disturbance of the steatorrhoea may result from fried foods or meat fats—particularly those subjected to repeated heating as in stews or the deep frying pan. Similarly cooking fats appear to vary in their digestibility in these patients and any may be used in making pastry and fancy cakes. It is interesting that sometimes patients are quite unable to tolerate such pastry, whereas home-made varieties are taken without trouble. The fat absorption defect is, to some extent, qualitative; for example, a patient may not only be able to eat butter but may also absorb it satisfactorily judging by faecal studies (Bassett, Keutmann, Van Zile Hyde and Van Alstine, 1939). The high protein low fat regime is an empirical one and additions are therefore made by trial and error. The responsibility of depriving a fellow-being of any of the pleasures of the table should not be lightly undertaken and certainly not continued without definite evidence—when it can be obtained—that the benefit outweighs the hardship.

The Value of Bed Rest

The success of bed rest is often striking. It is a frequent observation that actual constipation occurs in those admitted to hospital for routine investigations; a delight to the patient but a nuisance to the staff responsible for stool collection and often necessitating the use of water enemas. Rest, either complete or partial, is therefore indicated whenever the episodes of more severe diarrhoea are uncontrolled by other means. Bed rest alone may not only diminish the frequency of bowel action but may cause an improvement in fat absorption—a factor that must be taken into account in any therapeutic trial.

However, 'putting the patient to bed' is probably one of the most abused forms of therapy in medicine and must be used with discretion. It is not without its dangers such as pulmonary embolism and also may have adverse metabolic effects by creating negative balances of nitrogen, calcium, phosphorus and sodium (Cuthbertson, 1929; Deitrick, Whedon and Shorr, 1948).

Therapy for the Anaemias

Anaemia is a frequent feature of the steatorrhoea syndrome (Bennett, Hunter and Vaughan, 1932;

Cooke, Frazer, Peeney, Sammons and Thompson, 1948). It responds to treatment and is a unnecessary disability. The usual types of anaemia that occur are determined by deficiencies of either folic acid, B₁₂ or iron—or by combined deficiencies of these. Absolute values of the red blood cells are essential for accurate diagnosis of the anaemia. For the 'dimorphic' blood picture, where macrocytosis exists simultaneously with the signs of iron deficiency, may be concealed by a normal colour index.

The presence of macrocytosis indicating a deficiency of either folic acid or B₁₂ is accepted when the mean cell volume is greater than 94 cu, by the appearance of macrocytes in the blood films and a colour index greater than one. In an analysis of 100 patients with idiopathic steatorrhoea (Cooke, Peeney and Hawkins, 1953) it was found that two-thirds were macrocytic. Severe anaemia was not common, the red cell count usually being 3 and 3.5 millions per c.mm. and the haemoglobin levels between 11.4 and 13.1 g. Severe degrees of macrocytic anaemia do, however, occur and may give a peripheral blood picture identical to pernicious anaemia with a megaloblastic bone marrow. This type is sometimes refractory to B₁₂ but always seems to respond initially to folic acid. Assessment of whether B₁₂ or folic acid deficiency is present is best made by the serum level of B₁₂ (Mollin and Ross, 1953) or folic acid excretion tests (Girdwood, 1953). These are not always available for clinical work and reliance has to be placed upon the result of therapy. This may be quite difficult to estimate as the fluctuations of the red blood cells can be as much as one million in a month without treatment and the reticulocyte response may be indecisive when the red cells are fairly high. The fall in the serum iron 48 hours after a haematinic has been injected is a more precise index of effective therapy (Hawkins, 1955) and saves unnecessary visits for out-patients. The initial dose of B₁₂ is 100 µg. by injection and if there is a positive response to this the same can be given at one or two weekly intervals for about three months or longer if necessary. Similarly with folic acid. The dose of this is about 20 mg. daily but sometimes it appears that larger quantities than the conventional doses are needed. To be quite certain of the action of any therapeutic substance in the steatorrhoea syndrome it should be injected; this eliminates the unreliability of intestinal absorption. In some patients a slight macrocytic anaemia remains in spite of treatment by either or both folic acid and B₁₂; no further response is expected from refined or crude liver extracts but these can be tried. The explanation of this persistent macrocytosis is unknown.

The mean cell haemoglobin concentration is the

true indicator of the presence or absence of iron deficiency and iron therapy is indicated when this is below 32 per cent. The colour index may be low but typical microcytosis of the red cells is unusual. They are hypochromic but the size is normal—an occurrence that may be due to a latent macrocytosis which may become apparent following treatment by iron. Most patients take oral iron such as ferrous sulphate or gluconate, 5 to 10 gr., t.d.s., without aggravation of their intestinal symptoms, and may show a normal rate of rise in the haemoglobin such as 0.2 g. daily. Others give a slow response and a small group fail completely to respond to oral iron in spite of their obvious deficiency of this. Steatorrhoea is, indeed, the commonest cause of refractory hypochromic anaemia (Hawkins, Peeney and Cooke, 1950), a diagnosis that should not be made until it is certain that an effective preparation has been used for many proprietary tablets contain too little iron; there must also be indisputable evidence that the patient has taken it over a period of time—an enquiry about the colour of the stools which should be black is helpful here, and the presence of blood loss, infection, renal disease or hypoplasia of the bone marrow must be excluded. These cases respond very satisfactorily to parenteral iron and an intramuscular preparation such as the dextran-iron complex, 'Imferon,' can be used. It is obviously important to be certain that the diagnosis of iron deficiency is correct and to calculate the required amount accurately, for excess iron in the body can be dangerous and could result in an acquired haemochromatosis.

It is impossible to make any rule about maintenance treatment after any anaemia has been corrected, for each case has to be considered individually. Usually 'shot gun' therapy—to which there is no end—is avoided and, instead, these patients are kept under regular observation with blood counts at three or six monthly intervals. Any anaemia is treated at the earliest sign of its appearance. Many cases will maintain practically normal counts for months or years without any treatment, others will need repeated or continuous haematinics if their blood is to be kept satisfactory.

Relief of Diarrhoea and Other Symptoms

The mechanism of the diarrhoea in steatorrhoea is unknown. It does not seem to originate in the small intestine as the passage of barium and barium food mixtures may be slow in such cases and the coils of gut are dilated with some degree of ileus. Increased colonic movements are probably the cause for the frequency of bowel action. The stimulus for this may be the increased filling of the colon due to unabsorbed food products acting by osmosis, rather like magnesium sulphate, or from

the irritation of free fatty acids. Calcium salts have been used for many years in sprue for controlling the diarrhoea. A constipating effect may be obtained by the use of the following mixture of calcium salts which by their varying solubility may react with these fatty acids at different levels of the alimentary tract and form non-irritating calcium soaps: Calcium phosphate, 30 gr.; calcium lactate, 30 gr.; calcium carbonate, 30 gr. This is prescribed as a powder and 90 gr. or more is taken three times daily or as often as necessary. Some patients like to keep this powder available and take it whenever the frequency of bowel action becomes more troublesome than usual. Many other remedies have been advised but we have found no significant effect from such substances as folic acid, liver, detergents or antibiotics on the diarrhoea, nor have they influenced the fat absorption. Too much work or emotional disturbance will aggravate the bowel disturbance as in any patient with diarrhoea and adjustments of either of these will bring relief.

A troublesome symptom of vitamin deficiency is the glossitis; this may occasionally extend back into the pharynx and cause serious difficulty in feeding. The sore tongue usually responds quickly to riboflavin, 5 to 10 mg., or nicotinic acid, 300 mg. daily; sometimes other vitamins of the B group, such as pyridoxine or pantothenic acid, have to be tried and occasionally a crude liver extract by injection will be effective where these have failed.

Osteomalacia and Tetany

Steatorrhoea is the most frequent cause of osteomalacia in this country and the deficiency of calcium is the result of a failure to absorb it. The bones are decalcified and spontaneous fractures may occur. Chemical analysis of the serum shows a normal or low level of calcium, often a low phosphate level if the blood is taken from a fasting patient, and the phosphatase is increased. Badenoch and Fourman (1954) have demonstrated that in this type of osteomalacia there is also a failure to absorb vitamin D due to steatorrhoea. The deficiency of calcium is partly due to lack of vitamin D, partly to the calcium joining with the fatty acids to form insoluble calcium soaps and also to defective absorption of calcium itself. The implication of this is that any osteomalacia may be unaffected and even progress if the conventional doses of vitamin D and calcium are used. Large amounts of calcium have to be given orally, such as 15 to 30 g. of calcium lactate daily. The vitamin D can be given parenterally, the equivalent of 10,000 units daily are required, and an appropriate dose can be given at weekly or monthly intervals to avoid the discomfort of injection.

tions, or large doses such as 50,000 units daily can be prescribed orally. There is no risk of overdosage as long as the urinary output of calcium continues to be low and a rough estimate of the urinary calcium is easily obtained by the Sulko-witch test.

Tetany may sometimes be a presenting symptom of idiopathic steatorrhoea and requires urgent treatment. Relief is usually obtained by the slow intravenous injection of one of the organic calcium salts such as calcium gluconate, 10 cc. of a 20 per cent. solution. Otherwise treatment is directed to improve the absorption of calcium as in osteomalacia.

Dehydration and Electrolytic Disturbances

Dehydration is not usually a problem in the ambulant case but it causes much concern in the severely ill patient. For in the acute relapse the volume of a single stool may be 3 l. or more; measurement of fluid loss from the stools must be accurate for the assessment of the fluid balance. Parenteral fluids will often be necessary either subcutaneously with hyalase or intravenously.

Constant vigilance is needed to anticipate the electrolytic upsets that may result from the loss of sodium, potassium and chloride in the stools. The low serum sodium and hypotension of some of these patients may simulate Addison's disease and the salt (sodium) depletion syndrome, described by Marriot (1950), may be the cause of peripheral circulatory failure in the acute phase. This is lethal unless treated by appropriate amounts of saline.

Deficiency of potassium may arise in the ambulant patient and must be remembered as one treatable cause of the lassitude and weakness that inflicts these subjects. But it is during the episodes of more severe diarrhoea that the low potassium syndrome is serious and sometimes fatal. Clinical diagnosis is difficult because the symptoms and signs are not specific; these are listlessness, mental apathy and anorexia, skeletal muscular weakness with loss of reflexes that may cause respiratory failure (Holler, 1946), and chronic ileus. Diagnosis is difficult also because potassium deficits are frequently associated with and masked by deficits of water and other salts. Serial measurements of the serum potassium are essential in the management of such a case; the serum potassium may, however, be normal before any dehydration has been corrected and also in the presence of a cellular deficit which can only be revealed by a balance study. Electrocardiographic changes—a diminished voltage, flattening and eventual inversion of the T wave and prolongation of the Q-T interval—are not specific but give rapid presumptive evidence of potassium de-

ficiency and may be useful in assessing the effect of treatment. Potassium therapy may be life saving but can be hazardous, for excess of potassium in the serum may cause cardiac arrest, an event that has followed a too rapid intravenous infusion (Finch and Marchland, 1943). Potassium should be given orally whenever possible and a minimum dose is 6 g. of the chloride or citrate daily. Otherwise the subcutaneous route with hyalase is satisfactory; it is probably safer than the intravenous method and eliminates the danger from a faulty adjustment clip that might deliver the fluid too quickly and allow a fatal concentration of potassium to reach the heart. The safety of intravenous therapy depends upon the rate of administration and an adequate renal function. Various solutions of potassium chloride can be used such as a 0.2 to 0.4 per cent. dilution (2 to 4 g. KCl. per litre), in 5 per cent. glucose or water; these can be given at the usual rates of 1 l. in six or eight hours. The total amount of potassium needed to replace the deficit may be 20 to 50 g. or more. Hartmann's or Ringer's solutions contain too little potassium to be of any value for this purpose. Darrow's solution (2.7 g. KCl. per litre) is satisfactory but contains sodium as well and excess sodium may cause a potassium diuresis (Gamble, 1942) and have other adverse effects upon the potassium balance (Stewart and Rourke, 1942; Mudge and Vislocky, 1949). Severe deficits can be replenished by using isotonic solutions (1.1 per cent. or 11 g. KCl. per litre of water) subcutaneously with hyalase at the rate of 1 l. in six or eight hours. The effect of potassium therapy is measured by the clinical response which may be dramatic (Hawkins, Hardy and Sampson, 1951) and by the serum levels and electrocardiogram.

Adrenal Cortical Therapy

There have been several studies on the value of cortisone and ACTH in idiopathic steatorrhoea (Almy, 1951; Badenoch, 1952; Taylor, Wollaeger, Comfort and Power, 1952; Cooke, 1953; Colcher, Drachman and Adlersberg, 1953) and there is general agreement about the results. Clinical improvement takes place within a few days; there is a sense of well-being, increased activity and alertness. Appetite returns and there is a gain in weight; the diarrhoea diminishes. There may be an improvement in the fat absorption, sometimes almost to normal levels (Taylor *et al.*, 1952; Cooke, 1953), but this is not maintained when the treatment is discontinued. A daily dose of 100 mg. of either ACTH or cortisone is given by mouth or parenterally and this carries the usual disadvantages of such therapy. The possibility of it accentuating any existing potassium deficiency is avoided by giving additional potassium, such as

potassium citrate 4 to 6 g. daily by mouth, and similarly a large intake of nitrogen will prevent a serious negative nitrogen balance developing (Whitney and Bennett, 1950; Cooke, 1953). Gross disturbance in calcium and phosphorus metabolism is unlikely (Comfort, Wollaeger and Taylor, 1953).

The acute relapse of steatorrhoea carries a definite mortality rate and adrenal cortical therapy is a useful addition to the therapy for treating the condition and in some cases may be life saving.

Some workers (Colcher *et al.*, 1953; Adlersberg, Colcher and Wang, 1953) have also used corticoids for maintenance therapy in steatorrhoea. Adlersberg *et al.* (1953) made some useful observations in comparing the advantages of cortisone, hydrocortisone acetate and hydrocortisone free alcohol. They concluded that hydrocortisone free alcohol represented a valuable therapeutic agent in intractable steatorrhoea because of the need of only small maintenance doses such as 20 mg. daily by mouth and the apparent absence of adverse effects.

The Aim of Treatment

The aim of treatment is to maintain the optimum state of health for each individual patient. This is no longer a problem with the gluten sensitive case for it appears that normal health is established as long as the gluten free diet is adhered to. Many, however, will not respond to this and will require constant medical care to keep them in their best state of health. This will be assessed by their symptoms, the avoidance of the easy fatigue that is so common, the prevention of the recurrent soreness of the tongue and the minimum disturbance of bowel action and also by their appearance, weight and blood count. About 70 per cent. will be able to carry out their ordinary daily work satisfactorily (Cooke, 1952). The others will remain in only a moderate state of health with much lassitude and frequent periods of more marked incapacity when admission to hospital will be necessary. It is probable that the best results in the treatment of idiopathic steatorrhoea are obtained by a regular and adequate medical supervision.

ADDENDUM

Instructions to Patients on a Gluten-free Diet

You may eat a normal diet with the exception of any food made with wheat or rye flour. These flours contain a substance which is harmful to you. When wheat flour is specially treated to remove the harmful substance the starch portion is left behind and can be used in cooking. This 'wheat starch' can be obtained from the hospital dispensary and recipes are provided using this to make biscuits, loaves and puddings. In addition Brown and Polson's or Symmington's corn flour may be used

to make puddings, custards and sauces and cakes or biscuits if necessary. Soya flour may be used for making biscuits if you find these palatable.

You must not have the following: Bread, biscuits, pastry, cakes, shredded wheat, wheat flakes, grape nuts, semolina, vermicelli, macaroni, 'Ryvita' rye-bread, puddings containing flour or bread, custard powder, soup, gravies or sauces mixed with flour.

The following foods may be eaten: All meat, cheese, eggs, milk, vegetables, potatoes, rice, jam, honey, jellies.

For cereals: Kellogg's Cornflakes or Rice Krispies, or Quick Quaker Oats used for porridge making.

You may have any beverages including tea, coffee, Cadbury's cocoa or drinking chocolate.

Ice cream should be made at home as some commercial brands do contain flour.

The following is an example of a wheat flour free diet:

Breakfast: Kellogg's Cornflakes, Rice Krispies porridge
Sugar
Cows' milk
Boiled or poached egg, bacon and tomato
Wheat starch biscuits, or soya biscuits
cornflour biscuits or wheat starch loaf

Lunch: Average portion of meat, chicken, fish
Spinach, cauliflower, cabbage or carrots
Potatoes, boiled, baked or fried
Rice pudding, cornflour blancmange, junket jelly. Stewed fruit

Tea: Milk or weak tea to drink
Jelly, fruit, tomato, honey, jam, syrup
Wheat starch biscuits, cornflour biscuits
wheat starch loaf or cakes (from given recipes)

Supper: Milk
Egg custard, fruit purée or grated cheese and salad
Wheat starch, cornflour or soya biscuits

Gluten-Free Yeast Loaf

- 12 oz. wheat starch
- 12 oz. lukewarm water and milk mixed
- 1 oz. yeast started with one teaspoonful sugar
- $\frac{1}{2}$ oz. cooking fat
- 1 teaspoonful salt

Method:

1. Add the salt to the wheat starch and rub in the fat.
2. Mix the creamed yeast and sugar with the milk and water and stir into the starch thoroughly, seeing that no lumps are left.
3. Allow the mixture to stand in a warm place for 20 minutes exactly.
4. Pour the batter into 2-lb. bread tins previously warmed and greased.
5. Bake at regulo 5 for 15 minutes, then turn up the gas to regulo 7 (400° F.). Leave for five minutes.
6. Take the loaves out of the tins, turn upside down in the oven shelf and continue cooking for 15 more minutes.

Keeping time: About two days in an air-tight tin.

OTHER WHEAT STARCH RECIPES

Wheat Starch Cake

- ½ lb. wheat starch
- 4 oz. sugar
- 4 oz. margarine
- 1 teaspoonful salt
- 3 teaspoonsful baking powder
- 4 oz. milk
- 1 egg (optional)

Flavour with coconut, dates or chocolate

Method: Sieve the dry ingredients into a basin, run in the margarine, then make a well in the centre and mix enough to make a soft dough. Mix quickly and lightly and turn the dough into a well-greased shallow tin. Bake about 30 minutes in a hot oven (400° F.) or regulo 7.

Biscuits

- 8 oz. wheat starch
- 4 oz. margarine
- 4 oz. castor sugar
- 1 egg (small)

Grated orange rind or vanilla

Method: Cream margarine and sugar, add the egg and then the flour. Knead lightly to a small ball. Roll out thinly, prick all over and cut into shapes. Place on a greased tin. Bake in a moderate oven for 15 minutes. Regulo 4 or 250° F.

This mixture will make 1 lb. biscuits.

These biscuits can be made without sugar and may be used with butter or jam, etc.

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