COELIAC DISEASE*

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1. What is coeliac disease? It is a chronic nutritional disorder of childhood characterised by loss of appetite, loss of weight, abdominal distension, diarrhoea, and the passage of large, pale, unformed, highly offensive motions. Unless appropriately treated a fatal outcome may occur; in others the disease lingers for several years, and leads to so much interference with growth, that when eventually the child recovers, permanent stunting of growth may be the legacy. The stools in an untreated case contain a considerable excess of fat, while the gaseous distension of the abdomen and the diarrhoea are due to excessive fermentation of carbohydrate, and it is clear that the ultimate difficulty these children experience is the power to absorb from the intestine the products of digestion. This has led in past years to treatment by a diet in which fat has been almost entirely withheld, carbohydrate given very sparingly, and at any rate in the early stages of treatment protein foods have been the mainstay of the diet. I shall show later that the modern dietetic management of the disease has been considerably altered from the above. It is important to realise that the diagnosis of coeliac disease is based entirely on a clinical assessment. Although laboratory tests can be employed in order to exclude other diseases from the differential diagnosis, there is no laboratory test on which the diagnosis of coeliac disease can surely be based.

Symptoms. The onset is a gradual one, the majority of cases beginning between about nine months and two years of age, at a time when children are being weaned from a milk diet on to a variety of foods, and therefore at a time when mild digestive upsets are common. Because of this, coeliac disease is at its onset likely to be mistaken for some simple digestive disturbance, and it is only when the usual remedies fail and the child slowly drifts towards emaciation that the real nature of the condition comes to be realised. In the early stages loss of appetite is prominent, only a few ounces of food being taken at meals and that very unwillingly, the motions become lose, attacks

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of vomiting occur, and the child becomes moody and irritable, continually grizzling and resenting examination, although no actual pain or tenderness can be discovered. The temperature may be subnormal, but is as often raised a degree or two for months at a time, and at intervals may rise three of four degrees.

When the disease is fully developed the most noticeable feature is the profound emaciation. This is so extreme that the child has the appearance of being merely skin and bone, and compared with the pinched face, thin chest, and stick-like limbs the distended and tympanitic abdomen affords a striking contrast. The abdominal wall is, however, as devoid of fat as other parts, and is so tightly stretched over the distended intestines that peristaltic movements can often be seen through it. The loss of fat is also very obvious in the buttocks, where the skin hangs in loose folds. The complexion becomes sallow, the forehead appears wrinkled, and the hair becomes thinned and dry and loses its lustre. Curiously enough, the tongue is not as a rule furred—in contrast to chronic intestinal indigestion—but the breath may be sour. The abdomen is soft and can be easily palpated, which helps to distinguish it from the doughy abdomen of tuberculous peritonitis, but otherwise the only unusual feature is the smallness of the liver, which may be completely hidden behind the ribs. This has a clinical bearing, for it offers one point in differentiating coeliac disease from chronic indigestion, and from other causes of steatorrhoea, in all of which the liver can generally be felt with ease. The distension of the abdomen is accounted for in part by the excessive fermentation going on in the intestine and in part by the tonelessness of the muscles of the abdominal wall. The loss of tone also affects the muscles of the trunk and limbs to such an extent that the child is often unable to sit up or support himself, and the ligaments become so lax that the joints can be moved beyond their normal range.

Anaemia is present in practically all cases, and may reach a severe degree. As a rule it is hypochromic in type with a low colour index, due to iron deficiency, but in about 10 per cent a megalocytic hyperchromic type of anaemia develops in the peripheral blood, or can be found on examination of the bone marrow.

The stools of an untreated case are characteristic. They are large, unformed, of a porridgy consistence and colour, and are extremely offensive. They vary in number, seldom exceeding five or six a day, although sharp burst of diarrhoea may occur when their number rises, and the child's weight drops steeply. Relapses of this sort may be very dangerous, and are so often caused by incidental infections,

such as sore throats, otitis media, pyelitis, that these must be carefully searched for and be promptly dealt with.

The X-ray picture after a barium meal often shows the normal feathery pattern of the small bowel replaced by clumping of the barium into pellets, and this has been thought to interfere with the proper absorption of the products of digestion by preventing their close contact with the intestinal mucosa. Clumping, however, is not always present, and in any case is not peculiar to coeliac disease, as it may be met with in other forms of steatorrhoea.

Coeliac disease varies in its severity, and not all cases reach the degree described above. In the milder cases the stools may at times be formed, but even so are bulky and pale. Perhaps because the mild cases are more apt to be overlooked, or escape the close supervision given to the more severe, they to run just as long a course.

Complications. Oedema is a not infrequent complication, and generally appears on the top of the feet or on the back of the hands. Occasionally it is more widespread, free fluid may collect in the peritoneal cavity. The oedema develops quickly, and after lasting a variable time may suddenly disappear, but beyond emphasising the severity of the condition it makes little difference to the prognosis. It is due to a reduced level of the blood proteins. Purpura is less common than oedema, but is of more serious omen. The purpuric spots generally appear at first over the lower abdomen, in the groins, round the base of the neck, and at the edge of the axillae, places where the skin is thrown into folds, and bruising may also develop over pressure points, and may then lead to bed sores. Scurvy used to be a not infrequent complication at a time when vitamin C could only be given in the form of fresh fruit juices, which were often badly tolerated, but with the advent of the vitamin in its pure form as tablets of ascorbic acid this complication has disappered. Tetany is another complication and is due to the low level of the blood calcium. It only appears in the severe forms of the disease, and it calls for urgent treatment; this consists of intramuscular injections of 10 ml. of a 10 per cent solution of calcium gluconate, repeated daily until the blood calcium level has been restored to normal.

Rickets is a late complication of coeliac disease. This has its explanation in the fact that growth must be taking place for rickets to occur, and during the long-drawn-out active period of coeliac disease growth ceases. It is not until recovery begins to take place and the child begins to grow that rickets is likely to appear. The development

of rickets is due to the absence from the diet of vitamin D, and, except for its later age incidence, is strictly comparable to infantile rickets - and is as easily prevented by giving a concentrated form of vitamin D such as ten drops of halibut liver oil daily. Of the rachitic manifestations genu valgum is usual, and there is likely to be enlargement of the epiphyses and beading of the ribs, and fractures and bending of the long bones. The X-ray appearance shows a characteristic broadening and scooping out of the bone ends, with an irregular fluffy epiphyseal line, and the shafts of the bones are considerably rarified.

Differential diagnosis. There is a tendency at the present time to lump together all children who show wasting, abdominal distension and the passage of pale offensive motions, as instances of "the coeliac syndrome." Personally I think this is a drawback, for where these symptoms accompany such diseases as fibrocystic disease of the pancreas, tuberculosis of the mesenteric glands, or infection by *Giardia intestinalis*, a careful clinical history and examination together with the appropriate laboratory investigations, will establish the presence of these ailments, and the condition of such children bear no relation to coeliac disease.

Although fibrocystic disease of the pancreas has only been widely recognised since Andersen's description of it in 1938, it is a more common condition than coeliac disease. Unlike coeliac disease it may affect several children in a family, and another distinguishing feature is that it dates from birth. Abdominal distension, failure to thrive, and the passage of large offensive motions are all present, but, unlike coeliac disease, the appetite is voracious, yet food seems to do these children but little good. The diagnosis is made by demonstrating a lack of pancreatic enzymes, especially trypsin, either in the stool or more accurately by withdrawing a sample of the duodenal contents and failing to find trypsin in the sample. Sooner or later staphylococcal infection arises in the lungs, and may either prove quickly fatal by causing a staphylococcal pneumonia or may lead to several years of ill health with all the symptoms and signs of bronchiectasis, with death eventually coming about from heart failure. Just occasionally the disease may manifest itself in the newborn infant by intestinal obstruction, caused by a solid block of meconium- so called meconium ileus- which should have been liquified by trypsin toward the end of foetal life. A knowledge of both fibrocystic disease of the pancreas and coeliac disease enables them as a rule to be easily distinguished if a careful history is taken, the physical examination is thorough, and the absence of trypsin in the former condition can be demonstrated.

Widespread tuberculous disease of the mesenteric glands may so interfere with the absorption of fat as to lead to a clinical picture resembling coeliac disease, but the employment of tuberculin skin tests, the evidence of calcification in the mesenteric glands on X-ray examination and perhaps the recovery of tubercle bacilli from the stools will prevent error. Infection of the intestine by the protozoan *Giardia intestinalis* is usually accompanied by steatorrhoea, but the children are not so ill or so wasted as is the coeliac child, and it is not as a rule difficult to demonstrate either the protozoan or its cysts in the stools.

Pathology. For many years, coeliac disease has been thought to arise from a selective breakdown in the capacity to absorb from the bowel the products of food digestion. Failure to absorb digested fat has been given primary importance, and this has been based on analyses of the dried stools, of which in an untreated case as much as two-thirds may consist of fat (normally in a young child not more than one-third is fat) although the proportion of split to unsplit fat is unaffected. Interference with absorption of glucose has also been held to occur because the blood sugar curve after giving glucose by mouth is remarkably flat, although if glucose is given intravenously it is metabolised at a normal rate. Post-mortem investigations have been of little help as the appearances are only those consistent with profound wasting. Various theories have been put forward from time to time to account for the defect of absorption such as obstruction of the lacteals, and insufficient secretion of bile, intestinal infection, and more recently a deficiency of the vitamin B complex, but none has proved entirely satisfactory.

There are alternative explanations for the biochemical findings that have just been outlined. The flat sugar curve after giving glucose by mouth has been thought by some to be due to a slow rate of emptying of the stomach, but a relatively flat curve is obtained even if glucose is given directly into the duodenum. Emery has suggested that the flat glucose curve is attributable to the avidity of the liver for glucose owing to its deficient store of glycogen, and in this connection the constant clinical finding of a small liver, often too small to palpate, may have significance. As the disease improves, not only do the blood sugar curves become more normal, whether glucose be given orally or directly into the duodenum, but the liver returns to a normal size.

Fat Balances and the Significance of Gluten. The employment of fat-balance investigations has thrown a good deal of light on many of the basic problems of coeliac disease. In the first place, the investigations have revealed that, while normal children absorb from 90 to 95 per

cent of their dietery fat, if coeliac children are fed a normal diet, their fat absorption falls to a figure varying from 59 to 85 per cent, according to the severity of their illness. Although such a deficiency leads to the passage of unpleasant stools, from the nutritional standpoint, the amount of dietary fat absorbed is much more significant than that which is voided. If a child can absorb from half to three-quarters of the dietary fat, the fact that more than the usual proportion is voided is not a sound reason for making the diet so free of fat that the child has no opportunity of absorbing any fat at all. Indeed, if one were prepared to overlook the unpleasantness of the stool, there might be a case for feeding a high fat intake, in order that the total amount of fat absorbed daily might approximate the normal.

Fat balances have also been used to find out whether the mishandling of starchy foods by coeliac children might be the primary difficulty, the failure to absorb fat being in some way dependent on the failure to deal with starches. By feeding these children a norma amount of fat over periods when starchy foods were given, or were being withheld, it was shown that the withholding of starches led to a rise in fat absorption averaging 15 per cent. This was sufficient in some of the children to restore the fat absorption to a normal level. Altnough it was not the purpose of this investigation, it was quickly realized that a diet devoid of all starchy food, but with a normal fat allowance, led to a dramatic improvement in the state of the children viewed from all clinical angles. In consequence, the previous policy in England of feeding a very low fat intake was changed to one of simply withdrawing from the diet all starchy food.

Meanwhile, investigations in Holland were carrying our knowledge an important stage further. Dicke and Weijers and van de Kamer, using fat absorption tests as the basis of their work, showed that the harmful effect of starchy foods lay in the protein component (gluten) of wheat flour and rye flour. If this protein was removed, the remainder of these flours, consisting of pure starch, was tolerated perfectly well by coeliac children. Other starch food, such as maize, potato and rice, in which the protein was of a different nature, consisting of albumins and globulins, were without injurious effect. The adverse influence of gluten has been confirmed in Birmingham (England) by Anderson et al. and in London by Sheldon and Lawson. Thus, the problem of the dietary management of coeliac children has narrowed down to giving a diet which avoids gluten. With our knowledge at this stage, it is of interest to note that other successful diets in coeliac disease have incidentally been free of gluten, although the benefit may have been ascribed to other characteristics.

The manner in which gluten operates harmfully is not yet understood. Allergy to gluten does not seem to offer an explanation. At any rate, skin tests by scratch and intradermal application have been, in our hands, uniformly negative.

Treatment. The dietetic objective is to establish a coeliac child on a gluten-free diet. In a mild or early case, this may be a simple matter, since it merely entails the avoidance of wheat or rye protein. In England, the Energen Foods Company, Ltd., separates wheat flour into its protein and starch components in the course of preparing their particular food commodities. They are able to make available for coeliac children the wheat starch which, by means of special recipes; can be made into bread, biscuits and cakes, thus taking the place of whole wheat flour. Such recipes are necessary because in the absence of gluten, a wheat starch loaf would crumble to pieces unless some substitute for the binding properties of gluten were used. Its place is taken by fat (margarine) and milk. One may pernaps look forward to the day when coeliac disease ceases to be a hospital problem. If the early symptoms are recognized and a strictly gluten-free diet is instituted at that stage, with the child still in his own home, rapid improvement should follow, and the downward trend until admission to hospital becomes essential should be prevented.

When coeliac disease has already reached a severe degree, the problem is more complex. A gluten-free diet remains the objective, but a month or more of skillful nursing and feeding may be required before this stage can be reached. To begin with, the diet may have to consist of such simple foods as skimmed protein milk, glucose, and banana puree. If the stools are frequent and watery, the addition of a pectin preparation such as Arobon may be advantageous. In the most severe cases, it may even be necessary to spend the first day or two in overcoming dehydration and a lowered plasma protein level by intravenous fluid therapy.

As the child improves, such foods as chicken, egg custard and biscuits made from soya flour are gradually added to the simple diet outlined. The skimming of the milk is meanwhile progressively diminished. The addition of fruit and foods made with wheat starch comes next, and finally flours that do not contain gluten, such as rice, potato and maize flours are added. Care must be exercised in this last stage, for if given too soon these flours may give rise to abdominal discomfort, in which case their employment should be deferred for a fortnight or so. As soon as the child has been restored to a full diet devoid only of gluten, he is ready to return home from the hospital. It remains to

add that, of course, the diet must be supplemented with adequate vitamins.

Two other points ought to be mentioned. First, coeliac children tend to react violently to acute infections; these must be promptly recognized and treated, while the presence of foci of chronic infection, which also hinder improvement, must be sought for and eradicated. Secondly, anemia will also hold up progress. If the degree of anaemia is such that the haemoglobin is down to about 65 per cent, it is better to correct this speedily by transfusion of blood, reserving therapy with iron salts for anaemia of less degree. Should the anemia be of the relatively uncommon megalocytic type, a rapid response with Folic acid (15 mgm. daily for a week or so) can be obtained.

When a gluten-free diet is to be used in the child's home, the underlying principles are explained to the mother, and she is given a list of the foods that contain gluten which she must avoid when preparing the menu. Arrangements are also made in England for the mother to obtain regular supplies of wheat starch from the Energen Foods Company, Ltd., and she is given recipes for baking bread, cakes and biscuits with this starch. When the children are of school age and if they have their mid-day meal at school, the position is explained to the school authorities, and the child takes to school his own supplies of bread, biscuits and cakes, and does not receive any of the school food that contains wheat flour.

In our experience, the cooperation of the mothers in carrying out these directions has been all that could be wished, as has the attitude of the school authorities. The need for the strict avoidance of gluten is essential; if as little as one or two slices of ordinary bread leak into the child's diet, a deterioration of appetite and an increase in the bulk and number of stools are soon manifest. On the other hand, the disadvantage of allowing some gluten-containing foods to older children with coeliac disease, especially if treatment has been in progress for a year or more, may be difficult to realize. In them, a cheerful disposition and a fair appetite may continue, and but little alteration in the stools may be detected. The main disadvantage may be simply a slackening off in the rate of growth in both height and weight, and, unless these are being carefully and regularly recorded, several months may elapse before the deterioration is recognized.

An obvious question to ask is how long a gluten-free diet should continue, but since the diet has only been employed in this country some three years the answer cannot yet be supplied. The reply will depend to some extent on what one is trying to achieve. Already the mortality from coeliac disease has been reduced to the vanishing point.

But if these children are to survive, we surely cannot rest content if, in later life, they are to be prone to diarrheal episodes, or if their natural growth pattern, particularly as regards height, is to be at all curtailed. All one can say is that a gluten-free diet must be maintained for a minimum of two years, and that when a normal diet is restored, regular measurements of height as well as weight should be made at least every three months, and unless growth continues to be satisfactory, a return to a gluten-free diet is necessary.

The fact remains that for coeliac children in England, the use of a gluten-free diet has entirely altered the outlook. It is no longer a killing complaint; the period of stay in the hospital has been greatly reduced; the change from a wasting and miserable child to one growing and happy takes place in a few weeks; and the dietetic requirements to bring about these results are both simple and cheap and can be carried out without difficulty in the child's home.