

# Childhood Malabsorptive Disorders of Increasing Importance in Adult Life

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Diseases causing malabsorption are encountered commonly in childhood and until recent years these patients were collectively referred to by loose descriptive labels such as 'Malabsorption Syndrome' or 'Coeliac Syndrome'. However, with the recent advances in our knowledge of these disorders it has become clear that such terms are inadequate, since a multitude of distinct disease entities may cause the same clinical pattern of the child with failure to thrive, abdominal distension and recurrent or chronic diarrhoea. Among the most commonly encountered of these diseases are cystic fibrosis, coeliac disease and sugar intolerance (Anderson, 1966).

Increased knowledge of these entities has enabled more appropriate and effective therapy to be given so that some of these patients are now surviving beyond childhood and passing from the care of paediatricians to that of general physicians, who should become more aware of these conditions.

## CYSTIC FIBROSIS (CF)

This recessively inherited disorder occurs once in every 2,500 live births in communities of predominantly British stock (Danks *et al.*, 1965; Hall and Simpkins, 1968). The heterozygote frequency is thus one in twenty-five, making it the commonest lethal gene in our community.

The clinical features are very diverse (Table 1) and are related to the presence of abnormally thick mucous secretions throughout the body and abnormal sweat electrolyte concentration. In its fully manifest form these features include chronic pulmonary disease, exocrine pancreatic insufficiency, and elevated sweat electrolyte levels. The basic defect underlying these widespread features is unknown. Current research into this perplexing problem is aimed at studying: (1) the significance of a substance recently isolated from CF sera and known to disturb ciliary motility in animals (Spock *et al.*, 1967),

TABLE 1. Clinical Features of Cystic Fibrosis

Affected Area	Clinical Findings	Pathogenesis
Lungs	Chronic cough and sputum Chronic pulmonary insufficiency Cor pulmonale	Bronchial obstruction and infection
Pancreas	Malabsorption  Diabetes	Exocrine pancreatic insufficiency Endocrine insufficiency
Liver	Biliary cirrhosis	Biliary ductule obstruction
Intestine	Neonatal small bowel obstruction (Meconium Ileus) Meconium Ileus Equivalent in later life	Thick tenacious meconium  Inspissated mucofaeculent masses
Reproductive	Reduced fertility in males and females	Structural anomalies of the vas deferens ?? other factors
Sweat Glands	Heat prostration	High Sweat Na <sup>+</sup> and Cl <sup>-</sup> secretion

(2) the possibility that a generalised disturbance of water and electrolyte transport across tissue membranes is important (Johansen *et al.*, 1968), and (3) the possible role of dysfunction of the autonomic nervous system in the pathogenesis of the disease (Schwarz *et al.*, 1969). The pathogenesis and pathophysiology have recently been reviewed in detail (di Sant'Agnes and Talamo, 1967).

More patients with CF are living beyond childhood, up to 50 per cent past twenty years in reported series (Warwick and Pogue, 1969). This is due to increased knowledge of the disease, earlier and more accurate diagnosis, and more effective treatment. Furthermore, patients with milder manifestations, sometimes without malabsorption, may escape detection until adolescence or adulthood, when the diagnosis is more difficult, particularly as the sweat test is less reliable in this age group.

### *Pulmonary Disease*

This is the most important single clinical aspect of CF. Most patients are recognised because of recurrent or persistent pulmonary infection, usually associated with poor growth, in infancy or childhood. After childhood there is great variation in the extent and severity of pulmonary involvement (Gracey and Anderson, 1969). The least severely affected may be thought to have no



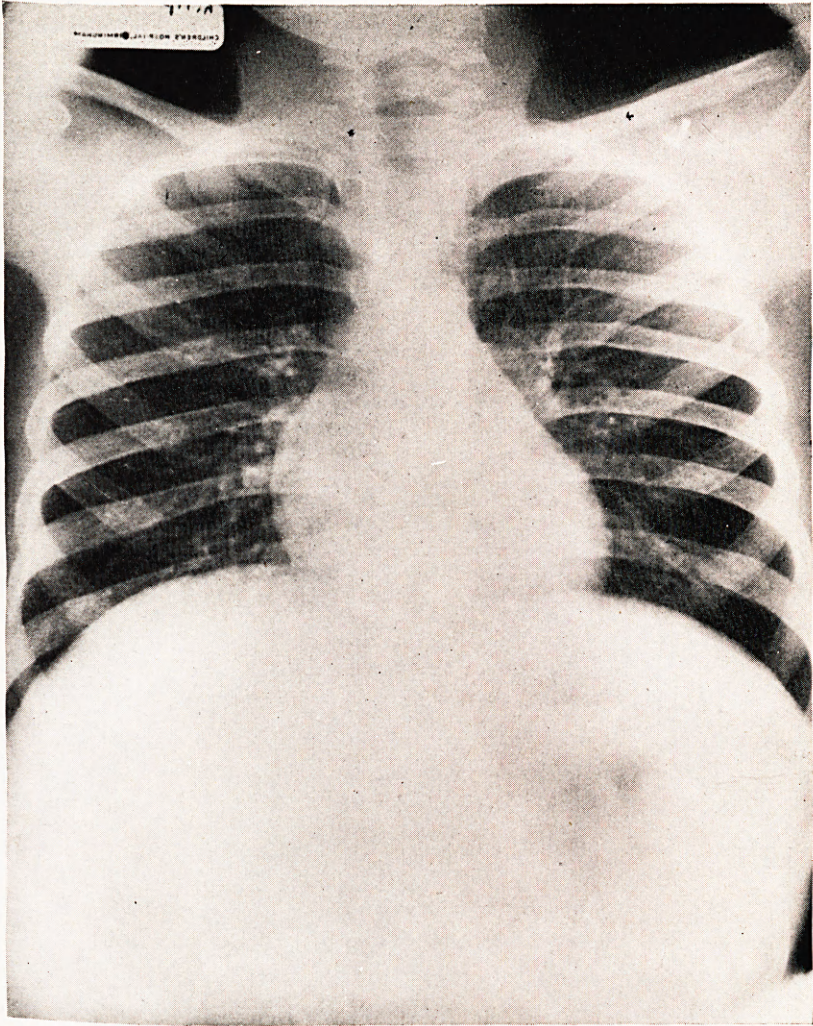


Fig. 1. Chest radiograph of an adolescent male with cystic fibrosis showing minor overflation and some increased lung markings.

abnormalities on clinical or even radiographic examination (Fig. 1) and these individuals may be apparently healthy and able to cope with full-time occupations. The other end of the scale contains the unfortunate few with severe incapacitating chronic pulmonary infection and insufficiency (Fig. 2), occasionally with cor pulmonale. Between these extremes are the majority of patients with intermediate degrees of pulmonary disease who require careful treatment to remain well.



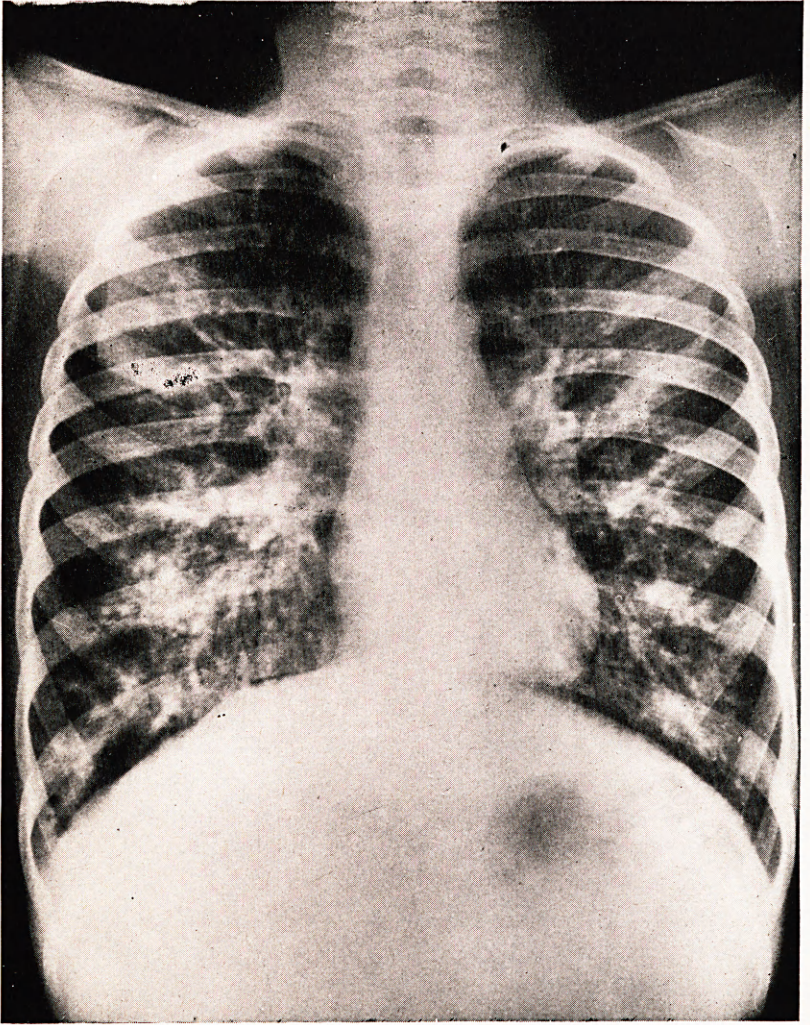


Fig. 2. Chest radiograph of 20-year-old man with cystic fibrosis showing moderately severe changes, with extensive airways obstruction and increased lung markings.

The important principles in the management of the pulmonary aspects of cystic fibrosis are—

1. Regular and carefully administered physiotherapy and postural drainage. Patients can be taught to continue this at home.
2. Intermittent inhalation aerosol therapy used with physiotherapy. The



aerosol is based on a diluent of 10 per cent propylene glycol to which antibiotics, mucolytic agents, and bronchodilators can be added when indicated.

3. The judicious use of systemic antibiotics. Our practice is to use these frequently, and sometimes continuously, in most patients, depending on the severity of the disease; the antibiotic given is altered according to the clinical course and results of bacteriological investigations. This is not prophylactic therapy, as these patients have persistent pulmonary infection which necessitates this form of treatment.

Application of these principles can lessen the incapacity resulting from chronic pulmonary insufficiency.

The place of mist tent therapy is still not established (Fifth International Cystic Fibrosis Conference, 1969; Parks, 1970).

*Cor pulmonale.* In some patients, chest infection and respiratory insufficiency lead insidiously to right-heart failure. The cardiac signs are frequently masked by the extensive pulmonary signs, and the usual diagnostic aids, including chest X-ray and electrocardiogram, are often unhelpful (Liebman *et al.*, 1967). For these reasons prophylactic digitalisation of all patients with severe disease has been recommended (Moss, 1967). We have not followed this practice but have occasionally used digitalis, without electrocardiographic evidence of cardiac failure. Caution must be taken in the use of diuretics, as excessive loss of electrolytes in the sweat of these patients may cause hyponatraemia.

#### *Exocrine Pancreatic Insufficiency*

Approximately 85 per cent of patients have gross steatorrhoea due to deficiency of exocrine secretions of the pancreas. The use of orally administered pancreatic extracts may help to reduce this abnormality but steatorrhoea is rarely eliminated. Excessively bulky, frequent and offensive stools and the passage of large amounts of flatus may sometimes be uncomfortable or embarrassing. The avoidance of particularly fatty foods or the substitution of long-chain fats by medium-chain triglycerides may be helpful.

#### *Liver Disease*

Biliary cirrhosis occasionally appears in adolescence and may progress rapidly, leading to portal hypertension and gastro-intestinal haemorrhage. Abdominal discomfort and anorexia may be overriding clinical problems in those with cirrhosis. In this situation medium-chain triglycerides may provide a readily absorbed source of calories and thus help maintain nutrition (Gracey

*et al.*, 1970). By the time liver disease becomes an overt clinical problem the presence of extensive pulmonary disease will usually preclude surgical treatment for portal hypertension, and in the few patients where surgery may be considered, the high risk of postoperative deterioration in pulmonary disease is a deterrent.

#### *Meconium Ileus Equivalent*

Recurrent abdominal pain is not uncommon in older patients with CF. This is thought to be due to inspissated, thick mucofaeculent material within the caecum or small intestine. Sometimes an abdominal mass, usually in the right iliac fossa, can be palpated. This syndrome may simulate surgical emergencies like appendicitis or intestinal obstruction, and untimely operation may produce disastrous results such as galloping chest disease and chronic intestinal fistulae. The oral administration of a mucolytic agent, n-acetyl cysteine, has recently produced encouraging results in several of these patients (Gracey *et al.*, 1969).

#### *Diabetes Mellitus*

This is a well recognised associated feature of CF (Rosan *et al.*, 1962) and usually responds well to therapy; diabetic ketosis is uncommon.

#### *Reduced Fertility*

Several females with CF have had babies, although their overall fertility is reduced (Grand *et al.*, 1966).

Among the survivors beyond childhood there are inexplicably twice as many males as females (Shwachman *et al.*, 1965; Gracey and Anderson, 1969). The males are almost invariably sterile due to the presence of anatomical abnormalities of the vas deferens (Kaplan *et al.*, 1968), and only one satisfactorily documented case of paternity is on record (Feigelson *et al.*, 1969).

#### PANCREATIC INSUFFICIENCY AND NEUTROPENIA

Physicians caring for adults should also be aware of pancreatic insufficiency and neutropenia (Burke *et al.*, 1967), the only other significant cause of pancreatic disease in childhood. This may be the explanation for abnormal pancreatic function or neutropenia in some adults and should be suspected particularly in patients with short stature, since metaphyseal dysostosis is a common associated feature. In this disorder, steatorrhoea is usually maximal in early childhood, decreasing in older children in spite of persisting abnormalities of pancreatic function. Insufficient adult patients have been reported to allow assessment of its clinical course in later life although attention has



recently been directed to the disorder in the adult literature (Hudson and Aldor, 1970). It seems reasonable to investigate pancreatic function in adults with unexplained neutropenia, and in those with abnormal pancreatic function frequent leucocyte counts should be done during a three-week period to exclude neutropenia, which may be cyclical. Steatorrhoea is controlled with pancreatic supplements but neutropenia is unaffected. However, infections seem less severe and frequent in this disorder than in other types of chronic neutropenia.

#### COELIAC DISEASE

By using the following criteria:

- (a) intestinal malabsorption,
  - (b) abnormal jejunal mucosal histology,
  - (c) clinical and mucosal response to gluten-free diet, and
  - (d) clinical and mucosal relapse following re-introduction of dietary gluten;
- the term 'coeliac disease' will include 'adult coeliac disease' (Cooke, 1958), 'gluten induced enteropathy' (Frazer *et al.*, 1959) and 'coeliac sprue' (Rubin, 1961). The earlier arbitrary separation of childhood and adult coeliac disease is no longer tenable (Hanes and McBryde, 1936).

The inability of patients with coeliac disease to tolerate gluten is lifelong (Gerrard *et al.*, 1955). However, after some years of gluten restriction many patients have been able to resume ingestion of dietary gluten without obvious subjective deterioration (Sheldon, 1959). Recent evidence has shown the long-term effects of such relaxation of gluten restriction to be deleterious (Sheldon, 1969), and experimental studies (Rubin *et al.*, 1962) confirm that re-introduction of gluten during remission will rapidly produce mucosal damage. These findings, together with the possibility that the susceptibility of adults with coeliac disease to develop malignancy (Harris *et al.*, 1967) is increased by non-adherence to gluten restriction (Jeffries *et al.*, 1964), indicate life-long abstinence from gluten.

The establishment of gluten-free diets in infancy and childhood is usually not unduly difficult for parents and patients. However, during adolescence many patients 'experiment' with their diets and may become lax in their adherence to gluten restriction. It is at this difficult stage that many patients are passing from the care of their paediatricians to general physicians. It is important that the patients are aware of the principles of gluten restriction and of at least some of the dangers of deviation from this regime.

#### SUGAR INTOLERANCE

In 1921, Howland prophetically suggested that an enzyme defect was

responsible for diarrhoea caused by dietary sugars, and that 'when new methods are devised that make possible an attack upon the problem from this quarter, information of the most fundamental nature may be derived'. However, it was not until 1963, after the introduction of the peroral intestinal biopsy capsule, that intestinal disaccharidase deficiency was demonstrated in patients whose symptoms were related to ingestion of sugar (Anderson *et al.*, 1963).

The intestinal disaccharidases are found in the brush border of the mucosal cells of the small intestine (Miller and Crane, 1961) and disaccharide hydrolysis normally occurs at this site prior to absorption of the component monosaccharides by the cell.

Disaccharidase deficiencies are recognised by paediatricians as a common and important cause of diarrhoea during infancy and childhood. The commonest form is secondary lactase deficiency, which may be secondary to several conditions such as gastroenteritis (Table 2); prematurity and malnutrition are important predisposing factors.

TABLE 2. Types of Sugar Intolerance

	Disaccharidase Deficiency	Monosaccharide Malabsorption
Primary	Sucrase/isomaltase deficiency Adult lactase deficiency	Glucose-galactose malabsorption
Secondary	Lactase and/or sucrase deficiency. May be associated with coeliac disease, regional enteritis, ulcerative colitis, Kwashiorkor, post-operative, gastroenteritis and others.	In infants following neonatal intestinal surgery or gastroenteritis.

The typical clinical picture is of a child, often under the age of two years, and often with a preceding illness resembling gastroenteritis, developing profuse, watery diarrhoea following ingestion of the offending sugar. If appropriate treatment is not given, diarrhoea continues, the patients become dehydrated and wasted 'to skeletons' (Howland, 1921), and the buttocks excoriated. The stools are characteristically acidic, fluid and frothy and contain abnormal amounts of sugar. Lactose-free feeding will be followed by a rapid improvement in the nature of the stools. Usually this disturbance subsides spontaneously within several weeks if the correct feeding is given, when the normal dietary sugars can be re-introduced (Burke and Anderson, 1965).



Other forms of sugar intolerance (Table 2) are less common in childhood but present a similar clinical pattern precipitated in each case by ingestion of the affected sugar.

Sugar intolerance appears to be much less common in adults, and the symptoms are milder, colicky abdominal pain and vomiting being more usual. However, numerous reports indicate that impaired sugar digestion and absorption, associated with various disorders such as coeliac disease, ulcerative colitis, and regional enteritis (Littman and Hammond, 1965) may occur in adults, and recent reports indicate that the entity of lactase deficiency in adults, which is distinctly different from the childhood disorder mentioned above, is more common in certain racial groups (Chung and McGill, 1968). Apart from these, the congenital disorders of sugar absorption, such as sucrose-isomaltase deficiency and, very rarely, glucose-galactose malabsorption, may occur. Mortality in childhood from such disorders was high until recent years, but with appropriate dietary sugar restriction we can anticipate that these patients will soon be transferred to general physicians.

In sucrose-isomaltase deficiency the severity of symptoms depends on the patient's age, the amount of sucrose ingested, and whether the patient is homozygous or heterozygous. Diarrhoea is most dramatic in infant homozygotes following weaning and the introduction of sucrose-sweetened feedings. In older patients bloating and abdominal cramps following the ingestion of sucrose are usual (Burke, 1970).

In glucose-galactose malabsorption, diarrhoea begins in the neonatal period following the first sugar-containing feed. The mortality is high if the condition is not recognised and appropriately managed in early life. However, very infrequent reports indicate (Neale *et al.*, 1965) that presentation of this disorder may be delayed until adult life.

*This article is based on a paper read by Dr Anderson at the Paediatric Conference held at the Royal College of Physicians in October 1969.*

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### The Physician

'His practice is some business at bed-sides, and his speculation an urinal. He is distinguished from an Empericke by a round velvet cap and doctor's gown, yet no man takes degrees more superfluously, for he is a doctor howsoever. He is sworn to Galen and Hippocrates, as University men to their statutes, though they never saw them, and his discourse is all aphorisms, though his reading be only Alexis of Piedmont, or the Regimen of Health. The best cure he has done is upon his own purse, which from a lean sickness he hath made lusty and in flesh. His learning consists much in reckoning up the hard names of diseases, and the superscriptions of gallypots in his apothecaries shop, which are ranked in his shelves and the doctor's memory. He is indeed only languaged in diseases, and speaks Greek many times when he knows not.'

(A view of the profession by John Earle, Bishop of Salisbury 1663-5, chaplain and clerk of the closet to Charles II of France, who died of the plague at Oxford in 1665.)