The child with cystic fibrosis who fails to gain weight

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INTRODUCTION

Since the 1970s we have recognized that a high-fat high-calorie diet promotes a normal growth pattern and leads to improved survival in children with cystic fibrosis (CF)[1]. This approach to nutrition has been endorsed by most major centres and has resulted in an overall improvement in respiratory prognosis. Good nutritional status can be achieved in the majority of CF patients by combining a high-calorie diet with adequate pancreatin supplements. However, for some, nutrition remains a problem. Poor nutrition in CF results from factors that are often interlinked:

- Anorexia and poor dietary intake
- Increased stool energy losses
- Increased energy demands of the disease
- Other factors.

Although dietary advice on increasing energy intakes has become an important part of CF management, deficient calorie intake remains the chief reason for growth failure in CF children. This is a particular problem during pulmonary exacerbations, where energy requirements increase to meet the immune response to infection yet the appetite usually diminishes. Subsequent dietary intake is often inadequate. Thus in children catch-up may be incomplete, leading to a pattern of slow weight loss punctuated by acute step-like episodes of weight loss associated with further chest infections. This may lead to a reduction in respiratory muscle strength and, subsequently, impaired lung function[2].

Despite more effective pancreatin replacement therapy, increased energy losses in the stools may still contribute towards an energy deficit sufficient to limit growth[3].

The energy needs of CF patients are 25–80% higher than in healthy individuals of the same age, sex and size[4]. This reflects an increase in the basal metabolic rate (BMR), which in sedentary adults accounts for three-quarters of daily energy expenditure. In the CF lung, a combination of obstructive and restrictive changes increases the work of breathing and hence the BMR by 30%[5]. This figure approximates with more extensive studies in adults with chronic bronchitis and emphysema, where the resting energy expenditure is increased to 140% of that predicted. An increased energy requirement at the cellular level has also been proposed[6], although recent data collected from babies with cystic fibrosis strongly suggest that this is not the case, and previous data were confounded by subclinical lung disease.

Treatment may also be a factor in increasing energy demands by as much as 10%, as Vaisman *et al.* demonstrated by studying the effects of salbutamol, a β-agonist, on heart rate and resting energy expenditure[7].

GROWTH FAILURE IN CYSTIC FIBROSIS

Newborns with CF are small at birth (standard deviation (SD) scores: length −1.24, weight −0.72)[8] but experience a period of catch-up growth to fall within −0.5 SD of the population mean by 2 years[8,9]. Recent data from the UK Cystic Fibrosis Survey confirms these earlier reports and shows that height and weight gain remain within this range throughout the first decade of life[10]. Thereafter, growth slows in both sexes, with weight more affected than height and males more affected than females[10,11]. This partly reflects pubertal delay, which is common in CF, and a reduced peak height velocity[12]. However, the final height for most CF patients may not differ significantly from that of the normal population[12] (Table 1).

Table 1 **Peak height velocity (PHV) and final height males and females with cystic fibrosis**

	Mean Z score	
	Males	***Females***
PHV (cm/year)	7.7 −6.5	6.4 −8.4
Age at PHV (years)	14.6 3.0	12.6 2.9
Final height (cm)	174.3 −1.2	163.5 −0.1

MONITORING OF GROWTH

In order to detect growth failure it is necessary to monitor height and weight gain. Thus, all children with CF should have their weight and height recorded every 3 months. Head circumference should also be measured for children under 5 years of age. Methods used for assessment must be

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consistent and performed by experienced staff. These measurements should be plotted on the 1990 Nine Centile United Kingdom Charts[13]. The age-related definition of nutritional/growth failure is given in Box 1. Percentage weight for height and percentage weight and height for age are perhaps the best measures for growth assessment in children. The body mass index (BMI, wt/ht^2) is also widely used to assess nutritional status, particularly in adults. Recently it has been validated for children[14], and BMI values for CF children in the UK have been reported[15]. Although BMI percentile charts are now available[16] care must be taken in their interpretation, as inaccurate assessment can follow in children with short stature and/or delayed puberty.

GROWTH FAILURE IN INFANCY

Neonatal screening (immunoreactive trypsin ± mutation testing) has enabled the early diagnosis of CF and the opportunity to prevent nutritional problems in infancy[17]. Case-controlled studies suggest that appropriate growth rates can be achieved in infants with CF, whether receiving hydrolysed formulae, standard formulae or breast milk[18]. However, as dietary fat provides approximately 50% of the energy intake of young infants, adequate control of fat absorption is important. Approximately 92% of CF patients have pancreatic insufficiency by 1 year of age[19]. Steatorrhoea can be confirmed by direct microscopy for fat globules or measurement of faecal elastase1. This latter test appears simple and reliable, with concentrations $< 100\,\mu g/g$ indicative of severe pancreatic insufficiency[20]. Pancreatin therapy should be introduced once there is evidence of steatorrhoea. Enteric-coated enzyme microspheres are well tolerated by neonates and appear more effective at controlling symptoms of malabsorption than older preparations[21]. They can be administered by teaspoon at intervals throughout the feed (mixed with a little milk—or puréed fruit in an older infant—or followed with a drink). On average, infants and young children require higher doses of pancreatin per kg body weight than do older children and adults. This reflects their higher fat intake (5 g fat/g/day, compared with the average adult intake of 2 g/day).

Box 1 **Age-related definition of nutritional/growth failure**

Child < 5 years	Weight/height < 85% Weight loss or plateau in weight gain over two clinic visits (maximum time 4 months)
Child 5–18 years	Weight/height < 85% Weight loss over two clinic visits (maximum time 6 months) Plateau in weight over two clinic visits
Adult	Body mass index < 19 Weight loss > 5% body weight for > 2 months' duration

(Based on CF Trust Nutrition Consensus Report 2000)

If an infant is failing to thrive despite adequate control of their malabsorption, energy supplements can be prescribed to boost the energy content of foods and fluids. Additional supplementation of infant formulae up to 8% carbohydrate and/or 4% fat will achieve an energy density of approximately 1 kcal/mL. A high-energy infant formula can be used if the infant is bottle-fed, but is perhaps less flexible and more expensive. A breast-fed infant may need to be encouraged to feed more frequently.

There is no evidence to suggest that infants with CF require routine sodium supplementation. However, growth problems may be exacerbated by poor dietary intake of sodium[22]. A standard infant formula provides 1.6 mmol/kg sodium, whereas the same volume of hydrolysed formula supplies 2.8 mmol/kg. Sodium deficiency can be confirmed by a spot urine analysis ($Na^+ < 10$ mmol/L) and corrected with sodium supplementation of 1–2 mmol/kg/day and the response monitored. Cow's milk protein intolerance has been reported in association with CF, with an incidence as high as 8% in the UK[23]. Although soya or hypoallergenic formulae are usually recommended, it may be prudent to use the latter in view of the possibility of coexisting soya intolerance. Lactose intolerance may also be seen, particularly in infants presenting with meconium ileus. Long-term surgical complications (adhesive small bowel obstruction and blind loop syndrome) can be expected in 33% of those managed with resection or enterostomy, compared to those treated by enterotomy and lavage[24].

PRESCHOOL YEARS

Dietary counselling and advice are essential during this period, when long-term feeding habits are developing. Behavioural feeding problems are common in children of this age, as the child begins to assert its individuality. The pressure to maintain growth rates, together with toddler food fads, can often be a source of parental anxiety. Early intervention from members of the CF team (psychologist and/or dietitian) to identify problems and advise and support parents and carers over this period can help minimize these issues and avoid the development of long-term behavioural feeding problems[22,25,26]. The booklet *Nutrition in Cystic Fibrosis—A Guide for Children and Parents* (CF Trust) and the leaflet *Help, My Child Won't Eat* (Paediatric Group of the British Dietetic Association) are useful to provide practical support strategies. The expert involvement of a family psychologist is necessary if behavioural problems have become entrenched.

OPTIMIZATION OF PANCREATIN THERAPY

The aim of pancreatin supplementation is to deliver enough active enzyme to the proximal bowel to hydrolyse the fat content of any meal and promote normal absorption.

Box 2 **Factors affecting pancreatin function**

- The number of capsules consumed
- The strength of the capsules
- Residual endogenous enzyme secretion
- Timing of enzyme dose in relation to meal
- Size and density of the microspheres
- Rate of gastric emptying
- Intestinal transit times
- Composition of meal
- Effect of proteolytic enzymes on lipase
- Dissolution point of the enteric coating
- The pH in the proximal bowel (bicarbonate secretion)
- Bile salt function

However, the effectiveness of enzyme supplements is influenced by several factors (Box 2).

The hydrolysis of fat is complex: to achieve adequate lipolytic activity requires the interaction of several factors, including various enzyme systems—lipase, co-lipase, phospholipase and bile, which is needed to anchor the lipase on to the fatty droplets. This whole process is influenced by bowel motility and the luminal pH. Furthermore, pancreatic dysfunction is not the only gastrointestinal problem in CF. An increasing number of patients have evidence of liver disease, and more than half have a non-functioning gallbladder. The intestinal secretory apparatus, mediated via cystic fibrosis transmembrane regulator, is also defective in CF, causing a lack of fluid secretion throughout the small and large bowel[27]. There are also specific defects in active transport in the terminal ileum. Thus there is a whole spectrum of abnormalities in the CF bowel which inhibit digestion and compromise absorption.

Gelatin pancreatin capsules dissolve rapidly in the stomach, releasing the microspheres or minitablets, which mix with chyme in the gastric antrum and then pass into the duodenum. Here, in healthy individuals there is an outpouring of bile and bicarbonate; the pH rapidly rises, dissolving the thin enteric coating and releasing the lipase into the proximal duodenum, where it is activated.

The smallest dose of pancreatin to control steatorrhoea and achieve a normal pattern of growth and weight gain should be used. The current Committee on Safety of Medicines recommendation is that doses should not exceed 10 000 IU lipase/kg/day (stated dose)[28]. Patients with CF vary in their degree of pancreatic insufficiency and so their enzyme requirements will differ. It should be noted that pancreatin is prepared from animal sources, and so dosages are approximate. Moreover, the stated capsule dose is a minimum, as capsules are overfilled to compensate for enzyme degradation during storage. The actual doses may exceed the stated minimum dose by 20–50%[29].

OTHER ASSOCIATED DISORDERS

Patients with enzyme requirements $>10\,000$ u/lipase/kg/day should be investigated to exclude any associated causes of malabsorption. Possible disorders include lactose intolerance, coeliac disease, Crohn's disease[30] and fibrosing colonopathy[31].

Cystic fibrosis-related diabetes mellitus (CFRD) is becoming increasingly common as the median age of survival of patients with CF continues to rise[32], and may present with growth failure. Criteria for the diagnosis of CFRD (based on British Diabetic Association recommendations, 1999) are: diabetes symptoms (polyuria, polydypsia, unexplained weight loss) plus any one of the following:

. Random venous plasma glucose $\geqslant 11.1$ mmol/L
. Repeated fasting blood glucose levels $\geqslant 7.0$ mmol/L (whole blood $\geqslant 6.1$)
. 2-h glucose levels $\geqslant 11.1$ mmol/L on oral glucose tolerance testing[33].

MANAGEMENT OF NUTRITIONAL FAILURE

Can nutrition be improved? The encouragement of a high-calorie high-protein diet will produce adequate growth in the majority of children and adults with CF. In other cases an improvement in nutrition can be achieved by simple means, including the use of premixed and powdered dietary supplements. In patients with more severe lung disease anorexia is often the chief problem, leading to malnutrition. In such patients oral supplements of varying palatability are frequently rejected. Under these circumstances some form of invasive nutritional intervention is necessary. Significant weight gain and an improvement in pulmonary function have been achieved, in both the short and the long term, by providing supplementary nutrition. Simple techniques such as nasogastric feeding with bolus or overnight feeds should be considered as short-term solutions. Long-term supplementation via both gastrostomy and jejunostomy has also produced either an acceleration in growth velocity or improved weight for height[34]. Endoscopic placement of percutaneous gastrostomy tubes under local anaesthesia makes the former technique particularly attractive.

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