Nutritional management of cystic fibrosis

Anita MacDonald

Nutritional support in cystic fibrosis has achieved a new importance. First, nutritional intervention is associated with better growth and improvement or stabilisation of pulmonary function. Second, malnutrition has many adverse effects on pulmonary function including decreased ventilatory drive, impaired pulmonary muscle function, decreased exercise tolerance, and altered pulmonary immune response. Third, there is evidence from a comparison of two North American clinics with very similar care programmes, differing only in their approach to nutrition, that a high energy and fat diet was associated with better growth and improved survival.

The nutritional problems in cystic fibrosis are multifactorial, and include increases in intestinal losses, energy requirements, and urinary glucose losses. One or more factors almost invariably coexist in combination with an inadequate energy intake. Malabsorption in cystic fibrosis occurs mainly as a result of malabsorption secondary to pancreatic insufficiency, which is rarely normal despite improved pancreatic enzyme preparations. In addition, abnormal bile salt metabolism, liver disease, mucosal absorptive abnormalities and short bowel syndrome, after intestinal resection in the neonatal period, may all contribute. Murphy et al have estimated that stool energy losses account for 10% of gross energy intake in cystic fibrosis patients, three times higher than normal.

Although patients with moderate lung disease may have a comparable total daily energy expenditure to controls, resting energy expenditure has been shown to be increased by between 9% and 30%. This is related to the increased work of breathing, lung infection and inflammation, enteral feeding, and drugs such as salbutamol. A primary defect at a cellular level has been suggested, although this is disputed. Antibiotics have been shown to reduce energy requirements of moderately ill cystic fibrosis patients with chronic Pseudomonas aeruginosa. Diabetes, if undiagnosed or inadequately controlled may increase energy losses due to glycosuria. Further substantial nutrient losses may occur in the sputum, which have been estimated by Wootton et al to be up to 1–5% of gross energy intake and up to 14% of total nitrogen losses. Sodium losses are important, and subclinical salt depletion can result in growth impairment, particularly in infancy.

Dietary assessments show that patients with cystic fibrosis rarely exceed the estimated average energy requirement or daily recommended amount (table 1). Factors associated with reduced appetite include chronic respiratory infection, and other complications of cystic fibrosis such as distal ileal obstruction syndrome, and gastro-oesophageal reflux resulting in oesophagitis, pain, and vomiting. Media pressure to eat a healthy, low fat, low sugar diet, inappropriate concepts regarding body image, poor use of dietary supplements, behavioural feeding problems, particularly in toddlers, lack of financial resources and a dislike of fatty foods all contribute to a reduced food intake.

There is now sufficient evidence to warrant energetic implementation of nutritional treatment in cystic fibrosis, and most centres utilise the skills of a specialist paediatric dietician and nutritional care team to provide nutritional support to their patients. It is known that prognosis in cystic fibrosis is better in large centres, and it is likely that changes in nutritional support and diet have contributed to this.

**Monitoring nutritional status**

**DIETARY ASSESSMENT**

In the cystic fibrosis unit in Birmingham, the dietician conducts an annual assessment of nutritional intake using a three day prospective recorded diet diary, using household measurements with supplementary information collected.

**Table 1 Energy intake of cystic fibrosis patients on a normal diet in the UK**

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>No of patients studied</td>
<td>20</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>5-3-17-3</td>
<td>5-3-16-0</td>
<td>0-75-25</td>
</tr>
<tr>
<td>Energy intake of the respective RDI (%)*</td>
<td>99</td>
<td>92</td>
<td>97</td>
</tr>
<tr>
<td>Range (%)</td>
<td>67-133</td>
<td>76</td>
<td>57-169</td>
</tr>
<tr>
<td>Mean daily intake (g)</td>
<td>73</td>
<td>76</td>
<td>–</td>
</tr>
<tr>
<td>Range (g)</td>
<td>36-133</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>% Fat energy</td>
<td>30</td>
<td>36</td>
<td>34</td>
</tr>
</tbody>
</table>

*RDI=recommended daily intake.
by a 24 hour retrospective recall diet history at the routine clinic visits. Although these methods are not entirely accurate, they give a useful guide to energy intake, nutrient profile, feeding routines, types of foods eaten, and changes in dietary pattern.

ANTHROPOMETRY
Serial data on height and weight, expressed as weight and height for age, weight for height z scores, and head circumference in the first two years, are plotted. Serial measurements of triceps skinfold thickness and mid-arm circumference are used as a way of assessing body fat and lean body mass.

MALABSORPTION
The gold standard to obtain an estimate of the degree of malabsorption is a faecal fat estimation, it is the method of choice, and is successfully used by many cystic fibrosis clinics. Unfortunately, the difficulties in performing this investigation have rendered it impractical for routine use in our clinic. The faecal fat measurement should be conducted in combination with diet diaries to obtain estimates of fat intake and therefore fat absorption. It is also useful for parents to record pancreatic enzyme dosage, method of administration and timing, together with a symptom diary collecting information about abdominal pain and stool frequency. An alternative and simple way of assessing fat malabsorption in young children is the modified steatocrit procedure described by Lloyd and coworkers.19 We have found it particularly helpful for serially monitoring changes in fat malabsorption when adjusting pancreatic enzymes dosage in infants and young children.

Biochemical monitoring
Annual assessment of blood concentrations of vitamins and minerals such as vitamin A, vitamin E, zinc, and iron which have been reported to be low in cystic fibrosis is important. Albumin and prothrombin times are also routinely measured. Although deficiency of trace minerals such as selenium have been documented,20 most recent research would suggest that selenium status is satisfactory, and we do not routinely monitor this.21

Nutritional requirements
The nutritional requirements of cystic fibrosis patients are ill defined. Cystic fibrosis is a syndrome with variable expression and so energy requirements will differ according to the clinical state as well as age, sex, and activity of the individual. Although it is commonly recommended to advocate an energy intake of 120-150% of estimated average requirements, it is our practice to assess and closely monitor energy intake and equate this to the nutritional status of the patient. If weight gain or growth is poor, the usual energy intake is increased by a further 20-30% of total intake by encouraging liberal quantities of fat (35-45% of energy intake) and sugar. Parental concern is often expressed about the effect of dietary fat on blood lipids. It is reassuring to know that adults with cystic fibrosis and pancreatic insufficiency eating a fat intake providing 34-35% of total energy intake have lower mean plasma cholesterol concentrations than controls. It is only pancreatic sufficient patients who have lipid levels in the high normal range.22 Fifteen per cent of the total energy intake is given from protein to compensate for excessive loss of nitrogen in the faeces and sputum.

Nutritional support
It is custom to provide three levels of nutritional support in our cystic fibrosis clinic. These include: (1) a high energy/high protein diet; (2) dietary supplements; and (3) enteral feeding.

(1) HIGH ENERGY/HIGH PROTEIN DIET
We encourage an energy and protein dense diet giving foods such as full cream milk, full fat cheese, meat, eggs, full fat margarine or butter, bread, and cream. Although the principles are simple, it is important that the diet is tailored to the individual and carefully considers lifestyle, clinical condition, nutritional state, family circumstances, dietary beliefs and attitudes, food fads, appetite, and activity levels. Nutritional counselling should always be age appropriate and we develop education programmes with the aid of information booklets, games and other teaching materials for each patient to meet changing dietary needs. Specific attention is focused on involving the child with cystic fibrosis in discussions about food and achievable dietary goals are set and agreed in consultation with the child and parents at each clinic visit.

Parents are encouraged to adopt normal feeding routines, limit meal times to a maximum of 30 minutes, and develop consistent feeding strategies and above all, remain positive if food is refused. It is our experience that excessive focus on food, feeding, and weight gain can lead to abnormal feeding patterns and negative feeding behaviour in cystic fibrosis children.23 McCollum and Gibson reported that 37% of 65 children with cystic fibrosis over 1 year experienced feeding difficulties.24 Many factors may precipitate food refusal, including parental anxiety about food, acute infections, frequent disruptions due to hospital admittance, and vomiting and gagging associated with coughing spasms.25 In practice, reports of prolonged mealtimes, vomiting and gagging, constant parental nagging, and force feeding indicate that additional support on feeding behaviour management is needed. If simple dietary advice and reassurance fails, enlisting the help of a psychologist with an interest in feeding problems is invaluable. There is some evidence to suggest that short term behavioural management programmes result in improvements both in nutritional
Table 2  Useful dietary supplement for children in cystic fibrosis

<table>
<thead>
<tr>
<th>Dietary supplement</th>
<th>Energy/ 100 ml (kcal/ml)</th>
<th>Protein/ 100 ml (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fortified milk shakes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Freesum (Fresenius)</td>
<td>100/420</td>
<td>3.8</td>
</tr>
<tr>
<td>Ensure Plus (Abbott)</td>
<td>150/630</td>
<td>6.3</td>
</tr>
<tr>
<td>Fortiai (Nutricia Clinical Care)</td>
<td>150/630</td>
<td>5.0</td>
</tr>
<tr>
<td>Entera (Fresenius)</td>
<td>150/630</td>
<td>5.6</td>
</tr>
<tr>
<td>Fortified fruit juices</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fortiai (Nutricia Clinical Care)</td>
<td>125/525</td>
<td>2.5</td>
</tr>
<tr>
<td>Provide (Fresenius)</td>
<td>60/252</td>
<td>3.6</td>
</tr>
<tr>
<td>Glucose polymers/drinks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Super Soluble Maxijul (SHS)</td>
<td>360/1512</td>
<td>–</td>
</tr>
<tr>
<td>Caloreen (Clinic Nutrition)</td>
<td>400/1680</td>
<td>–</td>
</tr>
<tr>
<td>Polycal (Nutricia Clinical Care)</td>
<td>380/1596</td>
<td>–</td>
</tr>
<tr>
<td>Liquid Polycal (Nutricia Clinical Care)</td>
<td>246/1033</td>
<td>–</td>
</tr>
<tr>
<td>Hycaal (Beekhams)</td>
<td>243/1021</td>
<td>–</td>
</tr>
<tr>
<td>Liquid Maxijul (SHS)</td>
<td>187/785</td>
<td>–</td>
</tr>
<tr>
<td>Fortified puddings Formance (Abbott)</td>
<td>176/739</td>
<td>4.8</td>
</tr>
</tbody>
</table>

intake and nutritional status both in the short and long term in a small group of children with cystic fibrosis.26 27

(2) DIETARY SUPPLEMENTS

We reserve use of dietary supplements for weight loss, any decline in height or weight z scores (providing weight z score is no more than 1 SD above height), if the quantity of nutrient intake is below dietary reference values, or during acute chest infections. The range and type of Advisory Committee for Borderline Substances prescribable dietary supplements have improved in recent years. Three main types are available: (i) nutritionally fortified milk shakes providing 1-0 kcal/ml and 1-5 kcal/ml, (ii) glucose polymers, and (iii) nutritionally fortified desserts. The suitable supplements we have found most useful for children are summarised in table 2. Unfortunately, there are few published data to demonstrate efficacy of dietary supplements in cystic fibrosis and if excess quantities are used they are likely to reduce the intake of normal food. The quantity recommended is age dependent and the following is a guide of how much we aim to give daily: 1-2 years, 200 kcal (840 kJ); 3-5 years, 400 kcal (1680 kJ); 6-11 years, 600 kcal (2520 kJ); over 12 years, 800 kcal (3360 kJ).

(3) ENTERAL NUTRITION

Enteral feeding is initiated when oral methods of maintaining nutritional status have failed and substantial deviation from normal weight gain or growth occur. Enteral feeding is considered in our clinic if a child is persistently less than 85% expected weight for height, or has failed to gain any weight over a three to six month period. Only 5% of our cystic fibrosis clinic of 360 children need enteral feeding and the majority are teenagers, reflecting the deterioration in nutritional status which occurs in adolescents with cystic fibrosis. Enteral feeding is associated with improvements in body fat, height, lean body mass and muscle mass, increased total body nitrogen, improved strength, and development of secondary sexual characteristics. To produce lasting benefit, numerous studies have demonstrated that enteral feeding should be continued long term.28-30 However, Dalzell and coworkers demonstrated significantly greater height and weight scores in a group of 10 cystic fibrosis children four years after cessation of tube feeding after one year.4

We have experienced occasional failures with enteral feeding and it is not without complications. It may take up to six months before there is an increase in linear growth velocity, weight gain may be disappointing even two to three months after starting feeds, and the weight/height ratio is rarely returned to normal. We have found that adolescent girls who improve their nutritional status on enteral feeds do not necessarily improve their image or self concept.16 Furthermore, daytime appetite is almost always diminished and common complications include vomiting, nasogastric tube dislodgement, gastrostomy tube blockage, leakage around the gastrostomy tube or button site. Gastro-oesophageal reflux is common in cystic fibrosis, and we have found this a problem in a small number of patients on nasogastric or gastrostomy feeding. Scott et al studied eight patients on overnight continuous nasogastric feeds and although episodes of reflux increased significantly, there was no increase in percentage time oesophageal pH was less than 4 and no evidence of aspiration or deterioration in lung function.31

It is our practice to give enteral feeding for 8-10 hours overnight with a 1-2 hour break before the first physiotherapy in a morning. Allowing teenagers to have one or two nights off the feed each week helps compliance. At least 40%-50% of the estimated energy requirement is usually given via the tube, but we review the feeding regimen and anthropometric measurements monthly and the feed composition is adjusted if nutritional status is not improving. Thirty per cent of our patients have developed hyperglycaemia requiring insulin treatment since starting enteral feeds and we have seen hyperglycaemia in a 4 year old child on overnight feeds. It has been reported that up to 64% of adult patients on enteral feeds experience hyperglycaemia which was managed with small doses of short acting insulin.32 Consequently, when starting enteral feeding and on subsequent hospital admissions, or if weight gain is poor, four hourly blood glucose profiles are monitored for 24 hours.

For most cystic fibrosis patients over 20 kg we find an energy dense polymeric feed providing at least 1·5 kcal/ml (6·3 kJ/ml) such as Fortisip (Nutricia) or Ensure Plus (Abbott) is well tolerated. For children weighing less than 20 kg it is better to give a polymeric paediatric feed such as Nutrison Paediatric or Paediasure providing 1·0 kcal/ml as the protein and nutrient profile has been developed especially for the younger age group. Some centres in the UK still prefer to use an elemental chemically defined formulas for enteral feeding in cystic fibrosis. In theory, elemental feeds have a good buffering effect on gastric acidity at night,2 and are better absorbed. Some centres do not give pancreatic enzymes with elemental feeds but
Vitamin and mineral supplements

FAT SOLUBLE VITAMINS

Low serum vitamin A concentrations are commonly reported in cystic fibrosis and documented clinical features of vitamin A deficiency include night blindness, conjunctival and corneal xerosis, dry thickened skin, and abnormalities of bronchial mucosal epithelialisation. For many years we have given supplementation of up to 2400 μg (8000 IU) to 3000 μg (10 000 IU) of vitamin A daily in the form of 1/2 ml Abidec (Paines and Byrne), Dalivit, or two vitamin A and D capsules. However, vitamin A supplemented cystic fibrosis patients are known to have nearly a 3-5-fold hepatic vitamin reserve than normal controls. Hypervitaminosis has been reported in an infant with cystic fibrosis after excessive vitamin A supplementation and in an adult supplemented with 10 000 IU of retinol palmitate. There is some suggestion that accumulation of vitamin A in the liver, despite low serum concentrations may lead to hepatic toxicity with long term high dose vitamin A supplementation. Vitamin A status and supplementation warrants further investigation in cystic fibrosis.

A neuropathy due to vitamin E deficiency has been widely reported in adult cystic fibrosis patients. Symptoms and signs include absent deep tendon reflexes, loss of position sense and vibration sense in the lower limbs, dysarthria, tremor, ataxia and decreased visual activity. Almost all cystic fibrosis centres now give routine vitamin E supplements and the usual recommended daily doses are 50 mg in infancy, 100 mg in 1-10 year children, and 200 mg for teenagers. Both water miscible and fat soluble preparations of vitamin E are effective in achieving normal serum concentrations.

Decreased bone mineral density and osteopenia, associated with low 25-hydroxyvitamin D levels have been described in adult patients with cystic fibrosis. Rickets is rarely seen in childhood, although subclinical concentrations of vitamin D metabolites have been reported. A daily supplement of 20 μg/day (800 IU) of vitamin D is given to all age groups.

MINERALS

Normally there appears no need to recommend additional sodium, but salt depletion can occur in hot weather, through physical exercise causing increasing sweating and in infancy if an infant is on a normal low electrolyte formulas such as SMA Gold (SMA Nutrition) or Nutrilon Premium (Cow and Gate). Anorexia and poor growth may result from chronic salt depletion. Significant hyponatraemia may be accompanied by vomiting. We advocate routine salt supplements during hot weather and in all infants on normal infant formulas. The amount given is arbitrary, but the following is a useful guide: 0-6 months, 2 mmol/kg/day of sodium in the form of sodium chloride solution (1 ml=1 mmol); 7-12 months, 1 mmol/kg/day of sodium; 1-5 years, 10 mmol sodium/day (2×300 mg sodium chloride tablets); 6-10 years, 20 mmol sodium/day (2×600 mg sodium chloride tablets); and 11 years, 30-40 mmol sodium/day (3-4×600 mg sodium chloride tablets).

Pancreatic enzyme supplements

Most cystic fibrosis centres predominantly use enteric coated microspheres (Creon, Duphar; Nutrizym GR, Merck; Pancrease, Cilag) for all infants and children, either administered as granules or in a gelatin capsule. Enteric coated microspheres should be able to achieve at least 90% fat absorption if administered in appropriate dosages. Several studies have demonstrated that enteric coated microspheres are more effective than conventional pancreatic powder and enteric coated capsules. We have found little difference between existing enteric coated microspheres when matched capsule per capsule, despite differing lipase, protease, and amylase content.

Initial results of studies using high lipase enteric coated enzymes looked promising indicating that dosage of enzymes may be able to be reduced by up to 66%. However, high lipase pancreatic enzymes have been
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Implicated as a possible factor in the aetiology of colonic strictures which have occurred in a small group of cystic fibrosis children.\textsuperscript{51-53} As a result of this the Committee on Safety in Medicines have recommended that cystic fibrosis patients are returned to ordinary strengths of enteric coated pancreatic enzymes until a satisfactory explanation for the development of colonic strictures is found.

Administration and dosage of pancreatic enzymes can be difficult, particularly in infants and young children. In infancy it is our experience that enteric coated microspheres are best mixed with a small amount of fruit puree, which holds the granules in a gel, and given from a spoon at the beginning of the feed. Not all infants will accept enzymes this way and the granules may stick between gums which may cause oral irritation, be spat out, or cause gagging and choking. We recommend a starting dose of 0.5 capsule per 90-150 ml of formula feed or breast feed, although it is difficult to measure proportions of capsules with any accuracy. In the toddler age group, pancreatic enzymes still need to be administered in the granule format. Unfortunately, in this age group, the enteric coated granules are particularly unpopular even when mixed with favourite foods and enzyme refusal, coughing, choking, or even vomiting is common. Some toddlers may chew the granules or hold them in their mouths for considerable periods of time releasing the enzyme and predisposing to mouth ulcers. In this age group, it may be better to spread the enzyme dosage throughout the meal, so the dosage can be varied according to the volume and type of food consumed, even though there is evidence to suggest that fat excretion is reduced in younger children when pancreatic enzymes are given before meals.\textsuperscript{54} It is difficult to administer pancreatic enzymes to a toddler and if simple behaviour strategies such as praise, encouragement, and consistency are ineffective, it may be helpful to enrol the help of a behavioural psychologist.

Unfortunately, if there is no objective measure of fat excretion, arbitrary assessment of enzyme dosage based on abdominal pain and stool description can lead to overdosage of pancreatic enzymes as it is assumed that all abdominal symptoms are invariably due to pancreatic insufficiency. Firm guidelines are needed in the UK on the daily upper limit of pancreatic enzymes in relation to body weight and age. In the USA, Lenbenthal suggests the following upper limits for lipase pancreatic enzyme dosage: 3000 units/kg/dose.\textsuperscript{55} A Committee on Safety of Medicines Working Party investigating the use of pancreatic enzyme supplements and colonic strictures have issued a preliminary recommendation that doses in excess of 10,000 units of lipase/kg/day, irrespective of the preparation, should be avoided (M D Rawlins, personal communication).

Infant feeding in cystic fibrosis

Screened and non-screened infants have been shown to have nutritional problems at the time of diagnosis. Failure to thrive, hypoalbuminaemia\textsuperscript{56} and even kwashiorkor\textsuperscript{57} are seen in unscreened infants, whereas nutritional deficits in screened infants are more subtle, but include reduced body mass, length, total body fat, total body potassium\textsuperscript{58} and low levels of tocopherol, linoleic acid, vitamin C, vitamin D,\textsuperscript{59} and plasma carnitine.\textsuperscript{61} We find most infants with pancreatic insufficiency will thrive on a normal energy intake of 100-130 kcal/kg in adjunct with pancreatic enzymes. If weight gain is less than expected or if a meconium ileus has resulted in surgery and bowel resection, the energy requirements may be as high as 150-200 kcal/kg.

We encourage breast milk for infants with cystic fibrosis. It contains lipase, long chain polyunsaturated fatty acids, provides some immunological protection against infection, and may be psychologically better for the mother. Infants on breast milk and pancreatic enzymes grow and gain weight appropriately with near zero Z scores.\textsuperscript{62} One possible concern is the possibility of electrolyte depletion\textsuperscript{63} on this low sodium milk and we administer routine sodium supplements to all breast fed babies (see mineral section), and monitor urinary electrolytes if weight gain is poor. Alternatively, infants with cystic fibrosis thrive satisfactorily on normal infant formulas,\textsuperscript{64} although like breast milk, electrolyte depletion is a possibility\textsuperscript{65} and we supplement routinely with sodium supplements. Energy supplementation of formula is only necessary if there is lack of catch-up weight gain, weight loss, or decline in weight Z score. Glucose polymer together with a long chain 50% fat emulsion, for example, Calogen (SHS) are used. The addition of 5 g glucose polymer and 3 ml of a 50% fat emulsion/100 ml of normal infant formula provides approximately 100 kcal/100 ml.

Although protein hydrolysates are favoured for infants with cystic fibrosis in the USA,\textsuperscript{66} we would only use these formulas if an infant develops a temporary disaccharide intolerance after surgery for meconium ileus. These formulas appear to have no advantages in cystic fibrosis, are expensive, and should still have pancreatic enzymes administered with them.\textsuperscript{66}

Diabetes and cystic fibrosis

Glucose intolerance and diabetes mellitus is common in cystic fibrosis. The incidence of diabetes mellitus may be as high as 8%-15% and this increases with age,\textsuperscript{67} although it has been reported in children as young as 2 years.\textsuperscript{68} The diabetes is non-ketotic, has a slow onset, but is usually insulin dependent. An insidious decline in overall clinical status often occurs before diagnosis of diabetes is made.\textsuperscript{69}

No clear guidelines have been issued on ideal dietary management for patients with both cystic fibrosis and diabetes, although advice should be tailored according to the severity of the cystic fibrosis. Providing optimal nutrition for the cystic fibrosis patient is still of paramount importance and any dietary restriction should be...
minimised. We still advise a high fat and carbohydrate intake. However, we do if possible encourage sugar free soft drinks, exchange glucose polymer supplements for fortified milk supplements, and some unrefined carbohydrate is given at regular meals, snacks, and bedtime. With the exception of drinks, simple sugars are not prohibited, but intake is encouraged alongside the refined carbohydrate. Diabetic control is improved by alterations in insulin treatment rather than imposing dietary restrictions which may adversely affect nutritional status.

Conclusion
Nutritional support is an integral part of the management of cystic fibrosis patients. It is arguably best provided by a qualified dietician and nutritional care sister working in conjunction with the rest of the cystic fibrosis team. The patient’s nutritional needs should be assessed, regularly reviewed, and nutritional treatment tailored to meet the changing clinical and psychosocial needs of the patient. Nutritional intervention is not without complications, and in particular attention to normal feeding behaviour and vigilance when instituting supplementary nutrition may prevent many feeding difficulties.

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