7. Gastrointestinal & nutritional care

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7.1 Nutritional care & assessment

The aim of nutrition intervention is to promote normal growth and development throughout life. Although patients with CF can have widely varying energy requirements, an intake of 120% to 150% of the Estimated Average Requirement (EAR) for energy is considered suitable for most patients.

It is expected that generally children eat well and should be able to meet their nutritional requirements with regular meals and snacks; however poor appetite (and the resulting poor intake) is sometimes a challenge. This may be a consequence of a variety of factors, including poor lung function or recurrent exacerbations, chronic underlying infection, excessive cough, untreated gastro-oesophageal reflux, low mood/depression, gastrointestinal disturbances (*i.e.* constipation, DIOS, abdominal distension or pain), a dislike of high-energy foods, and/or some psychological/behavioural factors.

Children and families should be encouraged to follow a balanced and varied diet, but with added energy. This helps to promote normal eating behaviour and avoids eating difficulties at a later stage. Nutritional care plans are individually tailored and include practical suggestions on how to increase energy intake and meet these high requirements. This may include food fortification advice with the addition of fats (aiming for healthy fats as much as possible *e.g.* oil, avocado, nut butters etc.) or encouraging additional protein. This will help to increase the caloric density of meals. Use of prescribed oral supplements can be used if required.

As well as a high calorie diet, it is important to consider the need for additional fat-soluble vitamins, fluid and salt.

Malabsorption of fat-soluble vitamins (A, D, E & K) is common in CF.

- **All** children are supplemented from diagnosis, with the aim of achieving normal fat-soluble vitamin status.
- Pancreatic insufficient patients will always require fat soluble vitamins and remain on them life-long.
- Pancreatic sufficient patients will remain on fat soluble vitamins until the age of 5; after this they will still require vitamin D and K, due to the effect on bone metabolism. This is easiest done by using DEKAs from birth and continuing on it.

Vitamin levels are tested at annual assessment and dosages adjusted as necessary. (See section 11.2b on vitamin preparations). Be sure that pancreatic sufficient patients do not have high levels of vitamins A&E.

It is essential for all CF patients to remain well hydrated, so they are encouraged to drink at least their requirement of fluid, if not more, each day. This is particularly important during periods of hot weather in the UK, on holidays abroad in hot climates, and during exercise. It is recommended that salt is added to food routinely which is usually sufficient to replace additional losses. In some cases, salt supplements can be prescribed for patients with particularly high needs or those who dislike salty foods.

Nutritional Assessment

A specialist Dietitian is available in CF clinic and children are reviewed on a regular basis. At each review the Dietitian will assess growth, calorie intake, enzyme dosage, and education will be provided as needed. All children must be weighed and measured at every clinic visit. Children under 1 are weighed naked and children over 1 are weighed in light clothing *i.e.* removing jackets, jumpers and shoes. In addition, infants under 1 year should have their head circumference measured. This data should then be plotted on appropriate weight, height and BMI growth charts.

The aim should be for infants and children with CF to grow normally, with infants achieving weight and height centiles like the non- CF population by 2 years of age. For adolescents the aim should be a BMI at the 50^{th} centile. Please note BMI should not be used as a one off in isolation in growing children, height and weight centiles trends should be assessed, as stunting can be masked.

Although nutritional screening of CF patients is similar throughout the UK, there is no recent consensus of how best to assess or identify faltering growth or nutritional failure in children with CF. Previously % weight/height has been widely used, however in our practice we aim to identify children who fall into the following categories:

- Infants who have had difficulty regaining their birth weight, who are drifting across centiles in the early stages, and those who suffer with ongoing gastrointestinal issues.
- Children that cross centile lines in a downward trend. This can be an acute picture or a longer, and potentially less noticeable, chronic change.
- Children with a BMI of $<25^{th}$ centile should be considered ‘at risk’ of nutritional failure, with attention paid to height and weight trends.

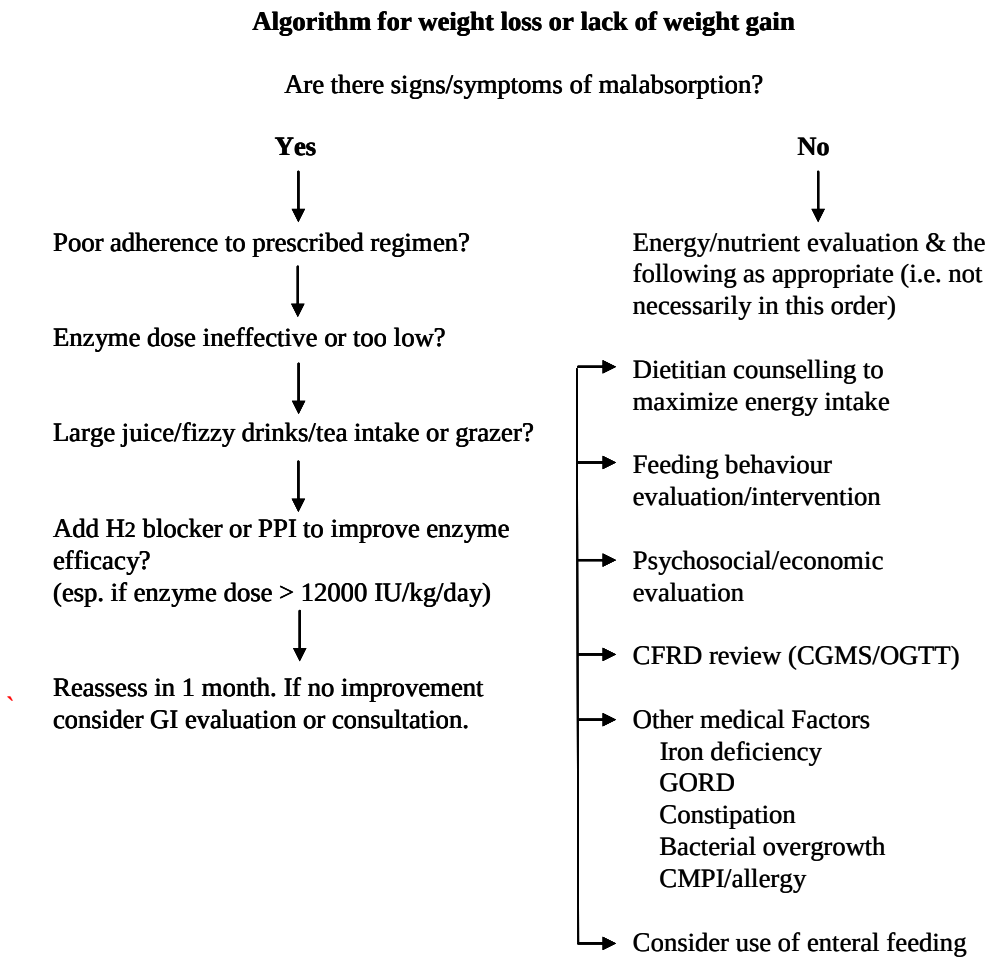
Clinical assessment of both height and weight centiles are analysed using UK WHO Growth Charts. This is monitored closely on at least a 1-2 monthly basis for infants and 2-3 monthly for older children and adolescents.

Nowadays malnutrition rarely presents as poor linear growth alone, therefore if children are identified with faltering growth on their height centile, they are referred to our endocrinologists Nicola Bridges or Saji Alexander for further investigation.

Children with unexplained faltering growth should have the following considered –

- Check for malabsorption *e.g.* enzyme dosing, stool microscopy for fat (fat globules). Any child labelled ‘pancreatic sufficient’ should have faecal elastase checked again.
- Check calorie intake with food diary.
- Serum vitamins A, D & E.
- Urinary & serum electrolytes. A spot urine sodium of <20 mmol/L indicates a low total body sodium and requires correcting in order for weight gain to occur. This is not measured routinely in newborn infants up to 3 months of age as their urine sodium is often low. In this case if growth is a concern in infants, sodium supplements are started automatically.
- CF-related diabetes must be considered.
- Gastrointestinal causes such as lactose intolerance, coeliac disease, inflammatory bowel disease, giardiasis, or short gut syndrome (in those with previous gut surgery) must be excluded.
- Cow’s milk allergy should also be considered in infants.
- Check psychological well-being.

Refeeding syndrome. If a child is admitted with very poor nutrition, care must be taken that once they start to feel better with treatment of their chest or abdominal symptoms, they do not overeat, as ‘refeeding syndrome’ can occur. This can also occur if they are enterally fed too quickly. The syndrome is seen when refeeding patients with anorexia nervosa and can include breathlessness due to impaired diaphragmatic contractility, oedema, ascites and heart failure; it is accompanied by hypophosphataemia, hypomagnesaemia and hypokalaemia. Good reference for refeeding is Sachs et al, Eating Disorders 2015;23:411-21.



Adapted from Borowitz et al J Pediatr Gastroenterology Nutrition (2002)

7.2 Pancreatic enzyme replacement therapy (PERT)

Approximately 90% of CF patients in northern Europe are pancreatic insufficient. The most effective test to confirm the diagnosis is to measure **faecal elastase**, which is low in people with pancreatic insufficiency. This test is not affected if the children are already taking pancreatic enzymes. The sample should be sent to Biochemistry who will have it assayed in the Biochemistry Department of Sandwell and West Birmingham City Hospital.

Normal	>200 mcg/g stool (usually >500)
Mild/moderate pancreatic insufficiency	100-200 mcg/g stool
Severe pancreatic insufficiency	<100 mcg/g stool
CF pancreatic insufficiency (typically)	<15 mcg/g stool

Levels of <15 mcg/g stool are usually seen in CF patients who are pancreatic insufficient. Normal faecal elastase levels are expected by day 3 in term infants and by 2 weeks of age in those born at less than 28 weeks gestation, so tests should not be performed before this time. Due to the delay in receiving test results for faecal elastase, requesting faecal fat globules by microscopy may be useful as an early indicator for the need to commence enzyme therapy.

Whilst some infants may initially be pancreatic sufficient, they may become insufficient over time. 90% of children with CF are likely to exhibit pancreatic insufficiency by 12 months of age. As pancreatic sufficient (PS) children can become insufficient when older, this must be considered should they present with symptoms of fat malabsorption or poor weight gain.

If a newborn screened baby is found to be pancreatic sufficient, the stool elastase should be repeated at 3 months of age then at the 1st annual review. This may be repeated sooner if results are in mild to moderate range (*e.g.*100-250) or if symptomatic. After one year, further repeats will only be done when necessary, rather than routinely.

Requirement of PERT varies widely and should be assessed on an individual basis following dietary or symptom analysis. Abdominal symptoms and stool characteristics such as oily, floating, pale/grey or yellow, loose stools are indicators that PERT is not optimal. Performing a test for faecal fat globules may be useful if symptoms are present or a child is demonstrating faltering growth.

There are several enzymes available on prescription, but the most commonly used brand is called Creon. Creon contains three digestive enzymes - lipase, protease and amylase. These help digest the different component of foods: fat, protein and carbohydrates respectively. The enzymes come in various strengths including enteric-coated microspheres (Creon Micro), and capsule forms of 10,000 and 25,000 units.

Pancreatic enzymes should be taken with all meals, snacks and drinks containing fat and protein. Education on the amount of Creon taken with different foods is provided by the Dietitian. Some foods do not require enzyme supplementation. These are sugars/carbohydrate only foods:

- Fruit (except avocado) and vegetables
- Sugar, jam, honey, syrup
- Fruit juice, fizzy drinks, and squash
- Sorbet or fruit lollies
- Jelly and boiled sweets
- Juice-based supplements

Infants and children under the age of 3 are started on enteric-coated microspheres (Creon Micro). Creon Micro contains 5000IU lipase per Creon scoop. These are currently only available as a porcine base and hence there may need to be a discussion with families of certain cultures and religions. The granules are given on a spoon in a small amount of apple puree (just enough to suspend the granules in) at the start of feeding. Enzyme granules ***must not*** be mixed into a bottle formula or into a meal as the enzymes will be activated before they reach the small intestine. The enzymes can be denatured within the acidic stomach so become ineffective. In addition, enzyme granules are unpleasant to chew, can cause ulceration of the mouth and gums, and can deter children from eating. Parents are offered the switch to Creon 10000 IU capsules at the 1st annual assessment for practical reasons. In this case parents open the capsules onto the apple puree. One capsule is the equivalent to 2 scoops of Creon Micro.

It is recommended that parents follow the Department of Health guidelines when infants are commenced on solids. The Dietitian will offer individualised advice to parents to ensure that PERT doses are calculated correctly depending on what foods are offered. Parents will often require more frequent advice at this stage.

Between the ages of 2-5 years old children should be encouraged to learn to swallow capsules. They should be swallowed whole and are generally taken at the start of a meal. Although there is a lot of research into optimal timing of PERT none is conclusive. Enzymes can be taken at the beginning, during, or at the end of a meal. Enzymes are most effective for 20-30 minutes once taken, so ideally meals should be finished within this time. This is not practical for all children so splitting the dose of enzymes between the main course and the pudding can be more effective. It is important to have quick and easy access to enzymes for better adherence. For any children who are having difficulty swallowing capsules after the recommended age, clinical psychology referral for pill school may be useful, usually from the age of around 3 years.

There are no specific guidelines for enzyme dosing and the **starting** doses tend to be as described below. Doses are increased on an individual basis until symptoms of malabsorption are resolved and normal growth is achieved.

- Babies: ½ scoop increasing to 1 scoop of Creon micro granules per breast feed or equivalent formula feed (of 120ml). 1 scoop per 4g fat.
- Toddlers: 2 Creon capsules with meals, 1 with snacks
- Pre-school: 2-3 Creon with meals, 1-2 with snacks
- School age: 4-6 Creon with meals, 2-3 with snacks
- Adolescents: 5-8 Creon with meals, 2-3 with snacks

Some infants may become constipated, when commencing creon therefore may require Dioralyte on a daily basis whilst establishing creon dose to support bowel motions.

The majority of our patients use the Creon 10,000 preparation. Higher strength enzymes are available but are only occasionally prescribed to older children and adolescents taking large numbers of capsules.

National guidelines advise against doses exceeding 10,000 IU lipase/kg. However, it is frequently observed that many infants and children require doses higher than this to control symptoms of malabsorption, especially during stages of accelerated growth *e.g*. infancy and adolescence. When a child is on a particularly high dose, (*e.g*. >15,000 IU lipase/kg/day) the Creon prescription and other routine clinical investigations should be reviewed to ensure there is not an additional underlying reason for malabsorption.

Excessive doses can cause perianal irritation and barrier nappy cream is useful in babies with a sore perianal area to prevent excoriation. In very high doses, hyperuricaemia and hyperuricosuria can occur, although this is rare. If excessively high doses appear necessary, enzyme efficacy can be improved by using a proton pump inhibitor or H_2 antagonist to reduce gastric acid output.

In the case of patients who are solely tube fed, although not licenced, Creon Micro can be flushed down their feeding tube. The tube must be well flushed to avoid blocking and degradation. Only tubes of 14FR or larger are suitable as granules will not pass easily through a smaller tube. If necessary, Creon micro can be dissolved in water and/or sodium bicarbonate (to be discussed with Doctor and Pharmacist). Pancrex powder can also be considered.

7.3 Salt & its supplementation

Patients with CF have a higher sodium requirement due to additional losses through sweat, especially in hot weather, exercise, periods of ill health and additional fluid loses such as diarrhoea and a high output stoma. They are susceptible to more rapidly depleting stores and therefore should be encouraged to include extra salt in their diet. Sodium is essential for growth and maintaining hydration. The current guidelines for Europe and the UK do not advise routine supplementation but encourage an individualised approach. The current recommendation is to give additional sodium during hot weather and exercise and should be considered for infants where growth is a concern. However, it is becoming more evident that some centres are using supplements as routine, including Australia and the USA. There is currently no evidence to support this although it has recently been shown to have a positive effect on catch up growth in young infants.

Infants are more susceptible to becoming sodium depleted due to the low sodium level in both breast milk (15mg/100ml, or 0.65mmol/100ml) and standard infant formula (17-24mg/100ml, 0.7-1mmol/100ml). It has been shown that young infants have a low clearance rate for sodium irrespective of their total body sodium or serum level and therefore testing urine sodium at an early age is a poor indicator of sodium status. Therefore, if growth becomes a concern then sodium should be supplemented regardless of urinary sodium level.

Supplementation

The current recommendation for sodium supplementation is 1-2mmol/kg in paediatrics when required.

Breastfed infants

For breastfed babies it is preferable to give sodium supplements. This comes in the form of 1mmol/ml or 5mmol/ml solutions. It is *preferable* for the GP to prescribe the 5mmol/ml solution, but it is essential parents are given the correct instructions for dilution as this can be very potent. It can be given via a syringe or mixed into milk/apple puree just before a feed.

Bottle fed infants

As the baby is used to drinking from a bottle then Dioralyte can be used as first line. This is easier than giving sodium solution, more palatable, and gives the baby additional fluid. One sachet of Dioralyte makes up 200ml. This can be easier to achieve by giving 100ml twice a day in younger babies (reconstituted solution can be kept for up to 24 hours in the fridge). This provides 12mmol sodium chloride which is usually sufficient in meeting the recommended dose in a young infant weighing around 3-5kg. It is often a concern that if a baby is drinking Dioralyte the milk consumption may reduce however this is rarely seen in practise and they will drink this in addition. Sodium solution can be used if Dioralyte is not tolerated.

Older infants

If a baby is weaning or eating small meals, then salt can be added to food. The amount of salt can be guided by the Dietitian but ~one sixth teaspoon salt is equivalent to 15mmol NaCl. If

growth is a concern, then prescribing Dioralyte or sodium solution is a better option to ensure the intake is sufficient and consistent.

Children

Children should be encouraged to follow a salty diet as a part of their regular daily intake. This should include *naturally* salty foods within a healthy diet for example, ham, cheese, olives, bread, baked beans, tomato ketchup, marmite etc. and then foods with added salt *e.g.* soups, crisps, pizza. As soon as children can swallow tablets then these can be used as well, for example Slow Sodium, which provide 10mmol sodium chloride per tablet. However, Dioralyte can be a better option as it also provides additional fluids.

For children who are particularly active, are very sweaty or simply dislike salty foods then routine salt supplements should be considered. Fluids should always be encouraged in tandem.

Holidays to a hot country or particularly hot weather in UK
Adding extra salt to the food is usually sufficient. However, if going to a very hot & dry country, salt supplements may be necessary (Slow sodium (sodium chloride MR) 600mg (10mmol) tablets; 1-4 / day, age dependent). This is also necessary in very hot weather in the UK. See Appendix 12 for more information.

7.4 Oral nutritional support

There is a wide range of prescribable products available - largely drinks and fortifiers - for children with faltering growth. Following appropriate dietetic counselling children may be commenced on supplements.

Generally, no more than 20% of the EAR should be provided by dietary supplements except during cases of acute infection or if the patient is being considered for enteral feeding. Excessive consumption may impair appetite and decrease nutrient intake from normal foods. Supplements should be given in between mealtimes, or in the evening. Parents can use supplements creatively (*e.g.* in cooking) to encourage intake and avoid taste fatigue. In our experience, short term use of supplements, with good adherence to the recommendations in regard to these supplements maximises their effectiveness. These are available in a variety of different flavours and presentations, an outline of which is given below:

Milk Based Supplements	Infant (Birth to 18 months)	• SMA Pro High Energy (SMA) • Infatrini (Nutricia) • Similac High Energy (Abbott) • Concentrated Standard infant formula – *must* be supervised by the Dietitian
	Paediatric	• Paediasure Plus & Paediasure Compact (Abbott) • Fortini & Fortini smoothies (Nutricia) • Frebini Energy (Fresenius Kabi)

	Adolescent	• Ensure Plus (Abbott) • Ensure TwoCal (Abbott) • Ensure Compact (Abbott) • Scandishake (Nutricia) • Calshake (Fresenius Kabi) • Enshake (Abbott) • Fortisip (Nutricia) • Fortisip Compact & Fortisip Compact Protein (Nutricia) • Fresubin Energy (Fresenius Kabi)
Juice Based Supplements	Paediatric	• Paediasure Plus Juce [spelt correctly!] (Abbott)*
	Adolescents	• Ensure Plus Juice (Abbott)* • Fortijuice (Nutricia)*
Powder and liquid polymers to add to foods	Carbohydrate	• Maxijul (SHS)* • Polycal (Nutricia)*
	Fat emulsions	• Calogen (Nutricia) • Liquigen – MCT fat (Nutricia) * • Fresubin 5kcal shot (Fresenius)
	Mixed macronutrients	• Duocal (Nutricia) • Calogen Extra (Nutricia) • Procal Powder (Vitaflo) • Procal Shot (Vitaflo)

** DO NOT NEED ENZYMES*

7.5 Enteral nutritional support

Only a small number of patients will require supplementary feeding which will provide long term "intensive" nutritional support. Gastrostomies can be beneficial in stabilising and promoting weight recovery and preventing ongoing weight loss affecting linear growth. Discussions about the potential need and benefits of gastrostomy feeding should commence early to avoid the stigma of insertion being associated with nutritional failure. We have found that the need for gastrostomies has fallen over the last decade. This is likely due to increased awareness of the importance of nutrition at diagnosis, and the implementation of the new born screening programme.

A gastrostomy should be considered if there has been a progressive fall in weight on the growth chart despite the following:

- Intensive dietetic support with repeated attempts to improve dietary intake. This includes appropriate dietary modification and trials of high-energy nutritional supplements.
- Control of malabsorption (consider causes other than pancreatic exocrine deficiency)
- Co-operation with treatment
- Optimal control of respiratory disease
- Involvement of clinical psychologist
- Exclusion of other conditions, especially CFRD and Pseudo-Bartter's syndrome.

Do not leave the decision over a gastrostomy too late in someone with poor nutrition and deteriorating lung function, otherwise the risk of the operation may become too high.

The following investigations should be carried out:

- CGMS
- Urinary sodium
- Serum electrolytes
- Thyroid function
- Coeliac screen: TTG (anti tissue transglutaminase) IgG & IgA; endomysial antibody. Ensure that the total serum IgG/IgA is known as well
- ESR
- Faecal calprotectin (plain container) *

*__Faecal calprotectin__ can indicate inflammatory bowel disease when significantly raised; if it is normal it is not IBD which is its main use. Levels can be raised in CF anyway, associated with pancreatic insufficiency, CFRD, and PPI use, but also due to CF enteropathy.

<50-75 mcg/g	definitely normal
<200	likely to be normal
>500 (esp. >1000)	could be IBD

Caution should be used before placing a gastrostomy in a child with behavioural feeding difficulties. The team may wish to seek psychology input for the family and child, and recognise that gastrostomy placement may not be relied on to solve feeding issues. Existing behavioural feeding difficulties, which are not addressed, may continue to impact on the young person's feeding even after a gastrostomy is placed.

Patients and parents should be introduced to the concept of a gastrostomy as a part of general nutrition support education in the early years. When the decision has been made to progress towards a gastrostomy it is important that families are educated on the potential effects. This includes the effect on growth, timely initiation of puberty, family stress levels, and overall health. Some children and parents find it useful to speak to a patient who already has a tube in place. The play therapy team have access to gastrostomy models which can be a helpful visual aid along with other written information. Body image can be a concern after placement of a gastrostomy, particularly in teenage girls. Early recognition of a distorted body image is essential, so that counselling can be arranged. It is critical however that a procedure for a gastrostomy is not left too late due to parental or professional procrastination, as the operation and general anaesthetic risk is increased markedly if the child is malnourished with a poor respiratory status.

Concomitant gastro-oesophageal reflux must be considered, possibly with a pH study, as a Nissen's fundoplication may be necessary as a gastrostomy can worsen reflux.

The procedure is either carried out at the Royal Brompton or at Chelsea & Westminster Hospital. This is by a Consultant Paediatric Gastroenterologist, Dr Krishna Soondrum or Dr John Fell, together with Mr Muhammad Choudhry or Mr Simon Clarke (Consultant Paediatric Surgeons).

- To **organise** a gastrostomy, please contact the Gastroenterology Dept. secretary on 0203 315 8628 or paediatric surgery secretary on 0203 315 8885.

- Also liaise with the Surgical Clinical Nurse Specialist at C&W on 0203 315 8627 or 0203 315 8000 bleep 4988; or via cw.gastrostomy@nhs.net who will assist with parent education.

Our Dietitian and CF Nurse Specialist must also be aware of the arrangements as the setting up of home enteral feeds usually takes at least 5 days. The child is admitted for the peri-operative antibiotic regimen (**see section 10.1**). Children with poor nutrition and suboptimal lung function will need 7-10 days of IV antibiotics pre-PEG insertion, which is provided at the Royal Brompton Hospital or the local hospital. After placement, feed initiation and post-gastrostomy care should be followed according to the advice from the surgeon, or as per the Royal Brompton Hospital 'Policy for the use of gastrostomy devices (adult and paediatric)' which is available on the intranet.

For problem solving with gastrostomies first refer to the link nurse on Rose Ward. For any further complications contact the Paediatric Gastroenterology Nurse at Chelsea & Westminster Hospital on 0203 315 8627 or 0203 315 8000 Bleep 4988.

PEG tube care (see appendix 10)

- Clean around the exit site of the stoma daily using water and a soft cloth. It is important that the area is dried gently but thoroughly.
- For the first 3 weeks you should not fully immerse the stoma in water, so a shower or very shallow bath is best.
- Check the area around the tube for redness, inflammation, swelling, irritation, skin breakdown, soreness or excessive movement of the tube. If you are concerned about any of these or there is a temperature or smelly discharge present, please contact the hospital.
- Change the position of the clamp on the tube regularly.
- Flush the tube before and after all feeds and medications with at least 10mls of water.
- Ensure all medications are in liquid form.
- Maintain oral hygiene with regular teeth brushing.

Types of feed

Each child is individually assessed, and the most appropriate feed is chosen to match their nutritional requirements. Only around 20-30% of the EAR should be given via the tube. Feeding regimens are frequently reviewed to ensure these fit within a patient's lifestyle. Gastrostomy feeds are usually given as a continuous infusion by a feeding pump for 8-10 hours overnight, aiming for a 1-2 hour break before physiotherapy in the morning. Oral intake is encouraged during the day. Occasionally additional feeds are used to supplement daytime intake, particularly during acute illness. Allowing a night off each week can help with compliance, especially in teenagers.

Most children with CF who are pancreatic insufficient will gain weight well if given a standard polymeric feed. The Dietitian will advise on appropriate enzyme doses to give with feeds. Patients are usually advised to take half to two-thirds of the enzyme dose pre-feed and the remainder afterwards. Waking children during the night to provide enzymes while a feed is running is strongly discouraged.

If there continues to be ongoing issues with malabsorption and poor weight gain, then a feed containing hydrolysed protein and a fat source from medium chain triglycerides (MCT) will be considered. Due to the nature of these feeds, it is possible that patients will require a lower

dose of enzymes but is not always the case. The Dietitian will advise on enzyme dosing for these feeds. Fibre containing feeds are not frequently used in CF patients.

Most feeds come in 'ready to hang' bottles and are therefore a closed system. These feeds are easy to use at home and reduce the risk of microbial infection. Powdered feeds such as Emsogen need to be made up with water; they can be inconvenient but are more flexible when it comes to adjusting the calorie content of the feed.

	Feed Name	Enzymes			Comments
		Yes	No	Reduced dose	
Infant feeds (Birth – 12 months/8kg)	Expressed Breast milk (Follow RBH guidelines on storage and use)	✓			0.67 kcal/ml (Can be fortified under Dietetic supervision)
	Standard Infant formula	✓			0.67 kcal/ml
	Neocate (Nutricia)	✓			0.68 kcal/ml
	Pepti- Junior (Cow & Gate)			✓	0.66 kcal/ml
	SMA High Energy (SMA)	✓			0.91 kcal/ml
	Infatrini (Nutricia) / Similac High Energy (Abbott)	✓			1.0 kcal/ml
Paediatric Feeds (8-20 kg or >1 yr of age)	Paediasure (Abbott)	✓			1.0 kcal/ml
	Paediasure Plus (Abbott)	✓			1.5 kcal/ml
	Nutrini Energy (Nutricia)	✓			1.5 kcal/ml
	Peptamen Junior Advance (Nestle)			✓	1.5 kcal/ml
	Nutrini Peptisorb			✓	1.0 kcal/ml
Adolescents feeds Adult feeds (>20kg)	Tentrini Energy	✓			1.5 kcal/ml (7-12 years / 21-45 kg)
	Osmolite 1.5 (Abbott)	✓			1.5 kcal/ml
	Ensure TwoCal (2 kcal/ml) (Abbott)	✓			2 kcal/ml
	Nutrison Energy (Nutricia)	✓			1.5 kcal/ml
	Fortisip Compact (Nutricia) / Ensure Compact (Abbott)	✓			2.4 kcal/ml
	Peptamen (Nestle)			✓	1.0 kcal/ml
	Emsogen (SHS)			✓	0.88 kcal/ml (Can be made-up more concentrated)

The Dietitian will educate the family about the feed preparation and administration, and work with the community team and enteral feeding companies to provide equipment and training for parents and caregivers. Home enteral feeding companies loan feed pumps to the patient at home and will also deliver feeds directly to the patient. Ancillaries (*e.g.* giving sets, feed reservoirs) are funded from the local GP and CCGs and the Dietitian will make arrangements for these to be supplied at home.

7.6 Promoting healthy feeding behaviour

It is acknowledged that a quick survey of any group of parents will reveal many differences in the feeding habits and preferences of their children. For children with CF and their parents the team at RBH recognises that, due to the nature of the condition, the challenges of ensuring adequate nutrition for their child with CF can be greater. Reasons for this are manifold but include: experience of discomfort for the child during or following eating; the higher incidence of gastro-oesophageal reflux in early infancy; taking prescribed medications (including creon) prior to or after feeding; and the emphasis often put on increasing nutrition and fluid intake by the CF Team. Feeding difficulties can be common in patients with CF although, since new born screening, evidence suggests that these are becoming less prevalent

in those children diagnosed after 2007. Given the above, the CF team at RBH would like to suggest that it is important for all children and their parents to develop as relaxed and positive attitude towards food and nutrition as possible.

For most parents weaning infants onto solid food is a challenging but enjoyable experience; however, they can often require extra help and advice at this stage. The Department of Health guidelines regarding types and textures of foods when weaning are appropriate for children with CF. The dietitian should be available at this time to offer individualised advice to ensure that PERT doses (if applicable) are judged correctly, depending on what foods are offered.

At any time of their lives, most children's appetite and intake can vary from time to time. This is typical in a child's development and we advise the same parental guidance about managing mealtimes and snacks as for any other child. While nutrition is very important, families are encouraged to make meal times as ordinary as possible without focusing on the type or amount of food consumed. If a parent is concerned for any reason, the team can give individualised suggestions as to how to minimise stress at mealtimes for them and their child. We encourage families to discuss this with their child's dietitian, clinical nurse specialist or paediatrician as soon as possible so as to ensure behaviours do not become a long term problem. Suggestions will be implemented and if the challenges persist a referral to the paediatric clinical psychology or other (*e.g.* feeding) team may be discussed and/or advised. The following principles are encouraged to promote healthy feeding behaviour. However, if parents have a style of parenting which does not follow the below, this is fine unless nutrition of their child with CF presents as a problem to their general health and/or well-being:

- Adults and other family members modelling healthy eating and enjoyment of food, including eating socially - as a family or with peers/friends.
- Having a consistent approach from all adults involved with feeding a child.
- Creating a relaxed and enjoyable feeding environment *e.g*. avoiding distractions such as the television - if this appears to interfere with the child's feeding behaviour.
- Offer age appropriate portions and offering second helpings if desired.
- Giving *gentle* encouragement to eat and positive feedback for good behaviour.
- Try to ignore feeding behaviour that is not acceptable.
- Creating a structured meal and snack pattern appropriate to the child's age and lifestyle.
- Limiting mealtimes to a maximum of 30 minutes (meals that last longer than this rarely result in higher calorie consumption in the long run).
- Not offering alternative meals or snacks if that chosen (out of two options) is then refused, having been agreed on, prepared and presented.
- Engaging children at meal times (for example 'messy play', self-feeding and simple food preparation).

7.7 Management of feeding difficulties

Feeding difficulties are common in patients with CF. This can be challenging from a physical health perspective and for families to manage. It is important for children and their parents to develop a relaxed and positive attitude towards food and nutrition despite the strong emphasis from CF team on the importance of growth.

Most children's appetite and intake can vary from time to time. This is a typical in a child's development and we advise normal parental guidance as for any child. While nutrition is very important, families are encouraged to make meal times as normal as possible without focusing on the volume of food consumed. If a parent is concerned, the team can give suggestions on how to minimise stress at mealtimes (see below). We encourage families to discuss this as soon as possible so as to ensure behaviours do not become a long term problem.

7.8 Gastro-oesophageal reflux & unsafe swallow

Gastro-oesophageal reflux (GOR) is common in infants with and without cystic fibrosis. It has a range of severities and most children will have fully grown out of it by 18 months of age; although symptoms will often have gone before this age, lessening from about 6 months. From our own data about 50% of infants will have GOR when measured by a dual probe 24-hour pH study at 4 months of age. Most will display some symptoms such as colic, posseting and effortless vomiting characteristically being able to feed straight afterwards, although reflux can be silent. In an infant without CF who is thriving, these symptoms may not be treated, or a simple milk thickener may be used. In CF there is some concern that GOR may have a negative impact on lung health, with possible aspiration so we have a low threshold to treat with an antacid either a proton pump inhibitor (PPI) or H_2 antagonist as a first line rather than thickeners. Infants that have evidence of discomfort especially with back arching should definitely be treated. Cow's milk protein intolerance or allergy can be associated with GOR in infancy and must not be forgotten in the face of severe symptoms, refusal to feed or faltering growth.

Some children with CF do not grow out of their GOR or may develop it again later in life especially if they have worsening of their lung symptoms. It should also be considered as a potential reason for unexplained deterioration in lung function. Some children will complain of "sicky burps" or heartburn, a month of high dose PPI is recommended before dropping down to a maintenance dose, usually in the morning to allow for some natural acidity to return to the gut overnight.

We try and avoid long term PPIs as there is an association (not necessarily causal) with hospitalisations and pulmonary exacerbations.

There are no research proven motility drugs for use in GOR, but we occasionally use erythromycin if a PPI is not working for its prokinetic action.

In the face of continued symptoms despite treatment, further investigation may include a milk scan to look for aspiration and/or a barium meal to check the anatomy of the stomach outlet prior to considering a fundoplication. A pH study or impedance study are also useful and maybe a useful opportunistic investigation to do in conjunction with bronchoscopy.

We no longer screen all newly diagnosed infants with a pH study at 3 months. However, if we repeatedly grow coliforms (*e.g. Enterobacter, Escherichia, Klebsiella, Citrobacter*), we will assume the child has reflux, treat accordingly and consider a pH study.

Unsafe swallow – we have a few infants with obvious symptoms on drinking (cough, splutter, choking), and some with silent aspiration (asymptomatic on drinking). Unsafe swallow with aspiration of fluids is something to be considered in an infant with frequent

symptoms or infections. When indicated we refer to our Speech & Language Team for a clinical assessment, and some will have a video fluoroscopy. Management is with thickened fluids and other techniques *e.g*. pacing (slowing down feeding), position etc.

7.9 DIOS and constipation

Distal Intestinal Obstructive Syndrome (DIOS) is a common complication in CF (paediatric lifetime prevalence of ~8%). The incidence varies widely but it mostly affects those with pancreatic insufficiency. The pathophysiology is not fully understood, but there are often multiple contributory factors including:

- Severe CF genotype
- Pancreatic insufficiency
- Inadequate salt intake
- Dehydration
- Poorly controlled fat malabsorption
- History of meconium ileus as neonate or DIOS
- Post organ transplantation

Viscid muco-faeculent material accumulates in the terminal ileum / caecum usually leading to partial obstruction (now called "incomplete or impending" DIOS) with pain often in the right lower quadrant, abdominal fullness and a palpable mass in the right iliac fossa. Children often report having their bowels open as usual, or sometimes diarrhoea (from overflow). Bowel motion history can be inaccurate or misleading.

Important features that increase suspicion of DIOS are:

- Acute periumbilical or right lower quadrant abdominal pain
- Vomiting
- Palpable faecal mass in right lower quadrant
- Previous DIOS

Complete DIOS is when there is total bowel obstruction characterised by abdominal distension, pain (often colicky), fluid levels on AXR and vomiting, usually bilious.

Differential diagnosis

Constipation (commonest), adhesions post abdominal surgery, appendicitis, intussusception, volvulus, fibrosing colonopathy (extremely rare), biliary tract or gallbladder disease, acute pancreatitis, urinary tract infection.

Complete DIOS is rare in children, but a surgical opinion should be sought early if there is any doubt about the differential (*e.g*. risk of adhesions if previous surgery).

Investigations

- A good history and abdominal examination is often sufficient to diagnose DIOS.
- A plain abdominal x-ray (AXR) may be needed to diagnose DIOS or constipation, radiation dose is up to 20x that of a CXR and they should be used sparingly. Faecal loading throughout the colon, especially in the right iliac fossa suggest DIOS.

Intestinal fluid levels confirm severe DIOS with obstruction; the differential diagnosis of a surgical cause of obstruction must always be considered.

If there if are doubts over the cause of abdominal pain, the following may be helpful:

- WBC, amylase, liver function tests, ESR, CRP.
- Urinalysis
- Abdominal ultrasound.
- Barium /gastrografin enema - by specialist radiologist can diagnose and help treatment at same time.

Management of DIOS

1. <u>Acute management</u>

A stepwise process will always include adequate hydration.

Incomplete or Impending DIOS – Mild

i. Ensure:

- ***Rehydration*** - patient must be **well hydrated** before and during treatment.
- Adequate salt replacement to help terminal ileum absorption of bile acids and correct any bowel CFTR electrolyte imbalance that may be implicated in DIOS.
- PERT therapy is reviewed and adjusted if needed.

ii. **Movicol**
The paediatric preparation is used up to 12 years old.
Doses are age dependent, usually starting at 1-2 sachets daily. See formulary 11.2e.

iii. **Oral N-acetylcysteine**- a disulphide bond breaker, comes in sachets containing granules (200mg – dissolved in water, orange flavoured). There is also a 600mg tablet available. The 200mg/ml injection can be given orally but is usually only used in the neonatal setting and should be mixed with water to a concentration of 50mg/ml (orange or blackcurrant juice or cola may be used as diluent to mask the taste).

iv. **Oral gastrografin**
Hydration is very important if gastrografin is used as it is highly osmotic. This is often done as an in-patient – for first doses and especially in the more severe cases when IV fluids may be required. Be particularly careful in babies & infants who can easily become dehydrated. See formulary 11.2e.

- Use for up to 3 days if no response in first 24 hours but not if symptoms worsen.
- Follow up with Movicol (paediatric if <12 yrs) for several weeks and review chronic management below.
- ***Contraindicated if complete bowel obstruction.***

Incomplete or Impending DIOS – Severe

- **Klean-prep**
  - Admit patient.
  - Aim is to take solution until clear fluid is passed PR. See formulary 11.2e.

- NG tube is usually required as volume is so large but occasionally some patients will prefer to drink it (more palatable if cool).
- No food in 2 hours before the treatment and during the 4 hours of clean prep to be able to assess for clear fluid being passed.
- Beware hypoglycaemia and electrolyte imbalance

Complete DIOS – severe

If there is complete obstruction (*e.g.* bilious vomiting) an NG tube is needed to empty the stomach and prevent bilious

aspiration, and IV fluids are given ('drip and suck'). An early specialist opinion from gastroenterologist or surgeon may be needed, always beware of other causes of bowel obstruction or an acute abdomen.

- **Rectal gastrografin**
  - Same dose as oral, diluted as per formulary 11.2e. Consider rectal gastrografin if oral administration is not possible or if there is vomiting due to obstruction. This is rarely used and is a last resort. It can be administered **under radiological guidance to achieve a guided approach.** Watch for dehydration, a plain AXR at 1 hour may be required to exclude massive dilation. If the latter is present, urgent referral to a paediatric surgeon is required.

Other treatments

- **Picolax** may be used as a first line instead of gastrografin

- Colonoscopy or surgery is rarely required although is indicated where above medical management has failed. May involve laparotomy and enterostomy or even bowel resection.

2. Chronic (management after an acute event)

The onset of DIOS may be indolent with just intermittent abdominal colicky pain, some anorexia and palpable right iliac fossa mass. Laxatives *e.g.* Movicol or occasionally lactulose in a young child should be continued for several months post DIOS. See Formulary 11.2f. Make sure child has been reviewed by a dietitian.

- Avoid dehydration - ensure adequate fluid & salt intake.
- Check dose / compliance / timing of enzyme supplements.
- If ongoing malabsorption is documented, consider starting ranitidine or omeprazole.
- Diet – ensure adequate dietary roughage.
- Ensure patient has well established toilet routine (try to go after meals), even at school.
- Movicol (Paediatric if < 12 yrs) is first line treatment, lactulose may help.
- In some children, oral N-acetylcysteine may help, especially in settling abdominal pain.

If continuing problems refer to Dr Krish Soondrum (who does a ward round on alternate Wednesday mornings on Rose Ward) or Dr Anthi Thangarajah who comes on alternate

Thursday mornings; or one of the GI consultants at Chelsea and Westminster Hospital in clinic.

Constipation

If severe should be considered as part of DIOS spectrum. However, beware of increasing enzyme doses when all that is needed is simple childhood constipation treatment. The main difference from DIOS is that constipation tends to be limited to rectum, so faecal masses are only felt in the left iliac fossa. Stool is more likely to be hard and pellet like or even painful to pass.

Treatment:

- Ensure adequate fluid intake.
- Movicol (Paediatric if <12 yrs) or Lactulose may be used (see formulary 11.2f).
- Movicol dose can be adjusted up and down to produce regular soft stools.
- Lactulose can cause stomach cramps and flatulence in large doses.

7.10 Liver disease

The reported prevalence of liver disease in CF varies according to the definitions used. Liver involvement in CF is very common, but clinically important cirrhosis affects between 20-30% of adult CF patients and associated portal hypertension affects 5-10%. Symptomatic liver disease is reported as the cause of death in only 2.5% of CF patients. Incidence does not rise progressively but seems to peak during the second decade and is more common in males (3:1). There is no known genotype-phenotype correlation but there is a high familial concordance and strong association with certain polymorphisms that may be predictive of future disease, for example α1-antitrypsin Z allele heterozygotes have a 7-fold increased risk of cirrhosis.

There is a wide spectrum of hepatobiliary complications arising in CF patients. This includes steatosis and focal or multilobular biliary cirrhosis, neonatal cholestasis in infancy (conjugated hyperbilirubinaemia secondary to bile duct obstruction), gallstones and cholecystitis in later childhood and abnormally raised transaminases. Intermittently raised liver transaminases are extremely common, this is observed in nearly all children with CF by the time they reach adulthood and doesn't always correlate with the presence or severity of CF related liver disease.

Steatosis (Fatty liver)

This is a relatively common CF finding, detected in 23-75% of patients on liver ultrasound. The pathogenesis is unclear, although it has been suggested that it arises secondary to fatty acid, choline or carnitine deficiency, or insulin resistance. Its natural history is still uncertain and the frequency of progression to cirrhosis is unknown. Guidance from King's College Hospital (Specialist paediatric liver unit) is that in the absence of hepato- or splenomegaly, and with normal liver function, they would not start ursodeoxycholic acid for steatosis alone but would repeat the ultrasound in 1 year.

Detection of liver disease

There is no single gold standard for the diagnosis of liver disease, but careful attention should be given to the following:

- Palpation of an enlarged liver and/or spleen.
- Routine annual assessment ultrasound on alternate years from aged 5 years and above. It will be repeated in 1 year if abnormal. Other indications for ultrasound are persistently raised transaminases on 3 consecutive measures over 12 months, clinical hepatomegaly or clinical splenomegaly.
- Liver function tests (transaminases) have a poor sensitivity and specificity. Consider drug causes – discuss with the pharmacy team at the earliest opportunity.
- Prolonged prothrombin time (although more likely to be due to malabsorption of vitamin K than liver disease).

The liver ultrasound scan at annual assessment is now reported in a standardised manner and includes a measure of liver elastography (the **ISHAK score**). This score has been developed to quantify the degree of hepatic fibrosis using ultrasound sheer wave elastography. This has not yet been validated in children but may be useful to monitor for longitudinal change in the degree of hepatic fibrosis where a trend of increasing ISHAK score may trigger consideration of increasing hepatic fibrosis. It has been shown to have less intra- and inter-observer variability when compared to ultrasound alone. The score is a non-linear scale (from 0-6) and the difference between ISHAK stage 1 and 2 may not be comparable to the difference between stage 3 and 4. If ISHAK score is elevated above 2, ultrasound scan should be repeated sooner than it would normally, even if no other abnormalities are seen.

Standard treatment

In children with hepatomegaly, significantly elevated liver function tests, abnormal clotting or evidence of cirrhotic changes on liver USS:

- Ursodeoxycholic acid. This increases bile flow. It is well tolerated with main side effect of diarrhoea, in which case the dose is reduced. Ursodeoxycholic acid reverses markers of CF liver disease but it is unclear whether it can delay or reverse fibrosis. Doses should be reviewed regularly and optimised to 10-15mg/kg twice daily, particularly in cases where there is significant CF liver disease.
- We use Paravit-CF routinely for anyone with significant liver disease (which for these purposes we define as anyone on ursodeoxycholic acid) instead of DEKAs, as it contains enough vitamin K so we do not need to prescribe extra vitamin K on its own (see section 11.2b).
- If there is significant abnormal clotting with a prolonged prothrombin time, extra vitamin K (menadiol or phytomenadione) may be needed. Occasionally 2 IV stat doses are required, and additional IV cover might be necessary at the time of surgical procedures.
- Platelet transfusion may be required to cover a surgical procedure if significant thrombocytopaenia. General guide is not needed >30-50 $x10^9$/L but consult with haematologist on each individual basis.
- Avoid aspirin and NSAIDs in those with documented cirrhosis.
- Care with drug therapy, including fusidic acid, minocycline, rifampicin, azithromycin, itraconazole, voriconazole, posaconazole and CFTR modulators (e.g. ivacaftor, Orkambi). If in doubt consult with BNFc and a pharmacist.

Referral to hepatologist

- Refer patients with cirrhosis or evidence of portal hypertension.
- Also refer anyone with atypical abdominal pain or abdominal sepsis or sudden changes in liver function tests.
- Dr Marianne Samyn or Dr Sanjay Bansal at King's College Hospital for children with significant liver disease - 020 3299 5614 (or secretary 020 3299 1162).
- Dr Alan Steel is the adult CF gastroenterology specialist who does a joint clinic once monthly at Chelsea and Westminster Hospital. Patients who are about to transition to our adult team may be referred to him for continuity.

Treatment of complications - (All management of complications should be discussed with the child's hepatologist)

- Portal Hypertension
  - Splenomegaly - Avoid contact sports.
  - Varices (oesophageal and gastric) -
    - **Acute management**: Initial volume resuscitation with blood. Advice for further management should be from hepatology team but may include: intravenous octreotide, terlipressin (splanchnic vasoconstrictor), endoscopic sclerotherapy. Octreotide can be started on Rose ward prior to transfer but does have implications for nursing care.
    - **Chronic management**: As directed by hepatologist: examples include endoscopic sclerotherapy, non-selective β-blockers (beware if child has airflow obstruction) or surgical shunts *e.g.* Transjugular intrahepatic portosystemic shunts.
  - Ascites – Standard treatment includes: sodium restriction and diuretics.
  - Hepatorenal syndrome - rare in CF but consider in cases of severe liver disease.
  - Spontaneous bacterial peritonitis - rare in CF.
  - Hepatic encephalopathy - rare in CF.
  - Hepatocellular failure is rare but ominous.

- Jaundice - uncommon. Exclude other causes (sepsis, drug reaction, and haemolysis). Mildly elevated bilirubin on annual review bloods might be a sign of Gilbert's syndrome; if this is persistent, genetic testing is now available and can be undertaken if there are concerns.
- Gallstones - high prevalence but not always symptomatic in CF. If symptomatic, refer to surgeon for consideration of cholecystectomy.

7.11 Iron status

The quoted incidence of iron deficiency anaemia in CF patients varies markedly. Iron deficiency anaemia (hypochromic microcytic anaemia with low ferritin) is the extreme end of a spectrum of iron deficiency. The earliest features are low/deficient iron stores, *i.e.* low ferritin, which progresses to iron deficient erythropoiesis *i.e.* low ferritin, raised TIBC, reduced transferring saturation and hypochromic red cells. This will progress to anaemia if the iron stores are not restored.

We have been cautious about supplemental iron in CF patients, especially those infected with *P aeruginosa*, as the organism requires iron for its growth and has developed iron scavenging mechanisms. It has also been shown that free iron *i.e.* that unbound to ferritin, catalyses the

generation of highly reactive hydroxyl radicals and promotes oxidative cell injury. Increased concentrations of iron, ferritin and isoferritins have been found in the sputum of adults with stable CF. However, it seems that airway iron levels are not a function of serum iron, rather the leaky epithelium.

We therefore lowered our threshold for starting iron therapy**. We prescribe it if the MCV is low rather than just if Hb is reduced**. We still do not prescribe it at the earliest stages *i.e.* when only the ferritin is reduced.

Another important cause of hypochromic microcytic anaemia is anaemia of chronic disease, where iron is poorly utilised due to the increase in certain cytokines. Here the major differentiator from iron deficiency anaemia is a normal or raised ferritin. These patients would not benefit from oral iron supplementation. When iron deficiency anaemia and anaemia of chronic inflammation coexist, the conditions can have opposing influences and the ferritin and total iron binding capacity can be high, low or normal.

It must also be remembered that ferritin is also an acute phase reactant and can go up in acute infection/inflammation (although this is rarely seen in practice). If ferritin is high, check what the CRP was to see if it is likely to be an inflammatory response.

We only measure Hb, MCV and ferritin to assess iron status at annual review.

Iron is often poorly tolerated with gastrointestinal side effects. When necessary, we use sodium feredetate (Sytron liquid) or if not tolerated ferrous fumarate liquid, whilst in older children 1st line is ferrous sulphate tablets (see BNFc for dosage). Bloods should be checked after 3 months of treatment. For low iron stores we recommend increasing the iron content of the diet, in the form of red meat, green vegetables, lentils, beans, fortified cereals and eggs. Some parents may choose also to buy food supplements such as Spatone (iron rich water from Snowdonia). It is worth eating these with food rich in vitamin C as that can help iron absorption.

	Iron deficiency			**Mixed**	**Iron malutilisation**
	Storage depletion	Iron deficient erythropoiesis	Iron deficiency anaemia	Iron deficiency anaemia and anaemia of chronic disease	Anaemia of chronic disease
Iron stores					
Serum ferritin	↓	↓	↓	↓↑ or N	N or ↑
Transport iron / iron supply					
Hypochromic red cells	N	↑	↑	N or ↑	N or ↑
Functional iron					
Hb	N	N	↓	↓	↓
MCV	N	↓	↓	N or ↓	N or ↓
Approach to management	Increase dietary iron	Iron supplementation	Iron supplementation	Address underlying inflammation	