

# **Clinical Guidelines: Care of Children with Cystic Fibrosis**

**Royal Brompton Hospital**

**Royal Brompton & Harefield**



NHS Foundation Trust

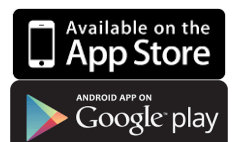
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**2017**

**7<sup>th</sup> edition**



A lifetime of specialist care



The 7<sup>th</sup> edition of these guidelines has been written by members of the Royal Brompton Hospital Paediatric Cystic Fibrosis Team. Contributors over the years include:

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2<sup>nd</sup> to 7<sup>th</sup> editions were edited by Dr Ian Balfour-Lynn.  
1st edition (1994) was edited by Dr Pat Oades.

*These guidelines are based on published evidence as well as the extensive clinical experience of our Paediatric CF Team. This is how we do things, but it does not mean that other regimens are necessarily wrong just because they are different. We are delighted for other centres and other countries to use them with the above proviso. Patients who come to the Royal Brompton Hospital, either for full or shared care, will all be looked after using these guidelines.*

These guidelines have been endorsed by the New Drugs & Clinical Guidelines Group of the Royal Brompton & Harefield NHS Foundation Trust in November 2016.

This year the guideline can now be downloaded as an APP.

If there are any comments, queries or errors noticed, please contact Ian Balfour-Lynn on [i.balfourlynn@ic.ac.uk](mailto:i.balfourlynn@ic.ac.uk).

**Next revision will be published in 2020 so this edition should not be used after that date. Please destroy all 2014 editions.**



## What's new in the 7<sup>th</sup> edition?

There are several changes and updates throughout this guideline but these are the principal ones (section numbers in brackets).

### New personnel & contact numbers (2, & appendix 20)

#### New sections

- 3.6 Safeguarding Children Team
- 5.5 CF Screen-Positive, Inconclusive Diagnosis (CFSPID)
- 6.2c 3-monthly IV antibiotics
- 6.9b *Scedosporium apiospermum* & *Lomentospora prolificans*
- 7.3 Salt & its supplementation
- 7.8 Gastro-oesophageal reflux
- 8.5c Hearing & tinnitus

#### New appendices

- Appx 3. Risks of getting *P aeruginosa* from the environment
- Appx 4. Paediatric CF intravenous aminoglycosides consent form
- Appx 7. Drug Response Assessment testing
- Appx 9. Gastrostomy care
- Appx 10. Consensus statements for management of CFSPID
- Appx 12. Hot weather advice
- Appx 14. Safeguarding children pathway

#### Additional information

- N-acetylcysteine (6.2a 6 IIIe)
- Orkambi (6.8)
- Physiotherapy management of haemoptysis (6.10)
- Table of which nebulisers are needed for which drugs (6.15c, further information in formulary 11)
- Refeeding syndrome (7.1)
- Faecal calprotectin (7.5)
- Liver ultrasound ISHAK score (7.10)

#### New drugs

- Clofazamine (oral)
- Co-trimoxazole (intravenous)
- Ivacaftor granules
- Moxifloxacin (oral)
- N-acetylcysteine (oral)
- Terbinafine (oral)
- Vancomycin (nebulised)

### Policy changes / additions: (section number in brackets)

### Chapter 3 - How the service runs

- Urinalysis for glucose to be tested at annual review for all those with CFRD and on oral corticosteroids (3.1)

- Annual reviews to be moved away from birthdays (3.2)

#### **Chapter 4 - Admission to hospital**

- When having Entonox for procedures, child needs only be nil by mouth for 1-2 hours, instead of 6 hours (4.3).
- After building new bathrooms and an extra cubicle there are now 9 ensuite cubicles, and the playroom can take 2 children with CF at a time after its rebuild (4.7).

#### **Chapter 5 - Making the diagnosis**

- If there is doubt whether to start a newly diagnosed baby on creon (on the day of sweat test) the baby is to be seen by a dietitian that day (5.1).
- We no longer routinely admit newly diagnosed babies at 3 months of age for a surveillance bronchoscopy, but maintain a low threshold for collecting induced sputum (when older) or bronchoalveolar lavage (5.9).
- We no longer perform a routine pH study in newly diagnosed babies at 3 months but continue to have a low threshold for treating symptoms. We assume reflux is likely in those with recurrent cough swab growths of coliforms, and will consider a pH study (5.9).
- Bloods are no longer routinely taken from newly diagnosed babies; and first bloods are taken at annual review. The exception is if the child's genotype is unknown, unless the screening lab still holds some DNA for further testing (5.9).

#### **Chapter 6 - Respiratory care**

- During admissions for chest exacerbations, a formal review of the clinical progress will take place on day 6-9 if there has been no improvement in lung function (6.1).
- During a mild exacerbation being treated at home with oral antibiotics, the nurse specialists contact the parents at 2 weeks to ensure the child is improving, rather than wait for a possible phone call from the parents.(6.2a 4).
- When using intravenous antibiotics in someone with chronic *P aeruginosa* infection, if they have grown *Staph aureus* in the last year, in addition to the first line antipseudomonal IV ceftazidime + tobramycin, we add in IV teicoplanin. We no longer use high dose oral flucloxacillin (6.2a 5).
- In an unwell child with their first growth of *Staph aureus* requiring IV antibiotics, we use IV meropenem + teicoplanin + tobramycin. We no longer use high dose oral flucloxacillin (6.2a 6 I).
- For eradication & re-eradication of new *P aeruginosa*, we give 3 weeks oral ciprofloxacin + 1 month nebulised tobramycin. We no longer use 3 months nebulised colistin. We re-culture 1-2 weeks after completion of nebulised therapy to ensure successful eradication (6.2a 6 IIIa).

- After eradication therapy for new *P aeruginosa*, patients will all have an induced or spontaneous sputum culture. If they remain symptomatic and sputum culture was negative, they will have a BAL. We will not rely on a cough swab to prove successful eradication (6.2a 6 IIIa, 6.14, 6.15e).
- If we have failed 1<sup>st</sup> attempt at *P aeruginosa* eradication (on the post therapy culture), the child will have IV antibiotics (if unwell) or another course of 3 weeks oral ciprofloxacin + 3 months nebulised antibiotics (monthly courses of colistin then tobramycin then colistin) (6.2a 6 IIIb).
- Later regrowths of *P aeruginosa* - re-eradicate with 3 weeks oral ciprofloxacin + 1 month nebulised tobramycin (6.2a 6 IIIc).  
Then regarding further nebulised antibiotics:
  - Long term nebulisers are used if the regrowth occurred within 1 year from the previous growth. If however the new growth occurred after more than 1 year, we do not automatically start long term nebulised antibiotics.
  - If the regrowth occurred whilst already on nebulised colistin, we use monthly alternating colistin and tobramycin.
  - If the regrowth occurred whilst already on alternating on colistin and tobramycin, consider using nebulised aztreonam as one of the alternating antibiotics.
  - Consider stopping long term nebulised antibiotics if there have been no *P aeruginosa* growths for 2 years.
- Parents/carers and the child (if age appropriate) will be given the Information sheet on adverse effects (ototoxicity, nephrotoxicity) when a child is to start IV aminoglycosides. A formal consent form is signed if someone is to start regular 3 monthly IV antibiotics (that include aminoglycosides), or starting IV amikacin (usually for *M abscessus* therapy) (6.2a 6 IIIe, 8.5c).
- Oral N-acetylcysteine is to be given to children during their courses of IV aminoglycosides, when having regular 3 monthly IV antibiotics, or IV amikacin (usually for *M abscessus* therapy) for protection of hearing (6.2a 6 IIIe, 8.5c).
- Co-trimoxazole can be used as one of the oral antibiotics for MRSA eradication (6.2a 6 IV).
- MRSA oral antibiotic eradication is now for 1 month rather than 3 months (6.2a 6 IV).
- Consider IV co-trimoxazole for *S.maltophilia* treatment when IV antibiotics are necessary (6.2a 6 VI).
- NTM cultures additionally requested for all induced sputum samples, and all sputum samples taken on admission for chest exacerbations (6.2a 6 VII).
- *M abscessus* (6.2a 6 VII & appendix 2).
  - Intensive phase intravenous therapy is given for 3 weeks, no longer 2 weeks.
  - Oral azithromycin is used instead of clarithromycin for intensive phase & continuation therapy.

- Oral Co-trimoxazole is used for instead of minocycline for continuation therapy in those aged 12 and less (unless dentists say the child's 2° dentition is complete).
- Moxifloxacin is used instead of ciprofloxacin for continuation therapy.
- *Mycobacterium avium* Complex (6.2a 6 VII & appendix 2).
  - Oral azithromycin is used instead of clarithromycin for intensive phase & continuation therapy.
- Consider IV co-trimoxazole for *Achromobacter xylosoxidans* treatment (6.2a 6 VIII).
- In children having regular 3-monthly IV antibiotics, we will try to use aminoglycosides only on alternate courses (6.2c).
- For a child already on regular once daily DNase who is in hospital for IV antibiotics due to an exacerbation, if the physiotherapists feel increasing the mucoactive drugs may help, we add in 7% hypertonic saline once daily (to the daily DNase) first; before considering double dose DNase, either as 5 mg once daily or 2.5 mg twice daily (6. 4).
- Ivacaftor granules are licensed and NHSE have agreed funding so will be used for all 2-5 year olds with gating mutations. Baseline and follow-up ophthalmological examinations (annually in those under 12 years) are done for all children starting ivacaftor. Stool elastase before starting and 6 months later (6.8).
- Oral posaconazole is 2nd line antifungal therapy, we no longer use oral voriconazole. For the rare occasions intravenous antifungal therapy is needed, IV caspofungin is 1st line, whilst IV liposomal amphotericin is 2nd line (6.9).
- During bronchoscopy for microbiological sampling – lavage will be taken from 3 lobes to maximise microbiological return, without causing respiratory compromise (6.14).
- DNase timing is decided on an individual basis although in most cases it is given at least 30 mins pre-physiotherapy (6.15a).
- We use inhaled salbutamol before all doses of 7% hypertonic saline, which can be given by a spacer device. We only use salbutamol prior to nebulised antibiotics if the child failed the bronchoconstrictor challenge, in which case nebulised salbutamol can be added to the antibiotic, or given beforehand via a spacer (6.15b).

## Chapter 7 - Gastrointestinal & nutritional care

- We will not measure urine sodium routinely in babies under 3 months old (7.1).
- Gastrografin doses have increased to twice daily for treatment of DIOS (7.9).
- We have lowered our threshold for starting iron therapy. We now prescribe it if the MCV is low rather than just if Hb is reduced. We still do not prescribe it at the earliest stages of low iron stores, when only the ferritin is reduced (7.11).

## Chapter 8 - Other non-pulmonary complications of CF

- Routine CGMS screening for impaired glucose metabolism is now done at 10 & 14 years of age at annual review, no longer at 12 & 15 years (8.1).
- For treatment of Vitamin D deficiency, high dose stoss replacement therapy which involves a single high dose of oral vitamin D is now given in preference to a 3 month course (8.4).
- Audiometry should be performed in a local audiology clinic (8.5c):
  - as a baseline at the start of commencing treatment with IV amikacin for *M abscessus* and repeated after 1 year.
  - in all children starting on regular 3 monthly IV antibiotics (that include aminoglycosides) and will be repeated yearly.
  - if a child ever has a high aminoglycoside trough level.
- If there is a family history of deafness, genetic mutation screening for m.1555A>G, which predisposes to aminoglycoside ototoxicity is recommended (8.5c).

## Chapter 9 Transplant assessment

- Infection with *M abscessus* subspecies *abscessus* is now a major contraindication for lung transplantation (9).

## Chapter 10 - Miscellaneous

- Live attenuated influenza nasal spray vaccine (Fluenz®) is now allowed for children with CF above 2 years old, unless they have large bilateral nasal polyps or are severely wheezy (10.2).

## Chapter 11 - Drug formulary

<i>Additions</i>	<i>Changes</i>
<ul style="list-style-type: none"> <li>• Clofazamine (oral)</li> <li>• Co-trimoxazole (IV)</li> <li>• DEKAs vitamins (oral)</li> <li>• Ivacaftor granules</li> <li>• Moxifloxacin (oral)</li> <li>• N-acetylcysteine (oral)</li> <li>• Terbinafine (oral)</li> <li>• Vancomycin (nebulised)</li> </ul>	<ul style="list-style-type: none"> <li>• Cefoxitin – dose changed to 50mg/kg tds</li> <li>• CIVAS dose bands removed</li> <li>• Clofazamine - new drug included for <i>M abscessus</i></li> <li>• Co-trimoxazole – IV dose included</li> <li>• Domperidone – removed from formulary</li> <li>• Fusidic acid – change in dose banding</li> <li>• Gastrografin – now given twice a day</li> <li>• Gentamicin nebulisers – removed from formulary</li> <li>• Inhaled antibiotics – administration information updated <i>e.g.</i> which nebuliser to use</li> <li>• Ivacaftor - dose included for 2-5 years olds (granules)</li> <li>• Moxifloxacin – new drug included for <i>M abscessus</i></li> <li>• N-acetylcysteine (NAC) – new drug included for</li> </ul>

	<p>protection from ototoxicity, and prevention of DIOS</p> <ul style="list-style-type: none"><li>• Omeprazole – dose bands added</li><li>• Posaconazole – dosing information for tablets included and therapeutic drug monitoring information revised</li><li>• Rifampicin – dose included for <i>M abscessus</i></li><li>• Terbinafine - new drug included for <i>Lomentospora prolificans</i></li><li>• Tigecycline – dose included for 8-11 year olds, and <math>\geq 12</math> year olds dose revised</li><li>• Timentin – removed from formulary</li><li>• Vancomycin nebulisers – included for MRSA</li><li>• Vitamin D – inclusion of doses for high dose stoss therapy</li><li>• Voriconazole – inclusion of important safety information and revised monitoring requirements</li></ul>
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## 1. Introduction


The purpose of this document is to set out guidelines to ensure standardised care for children with cystic fibrosis looked after at the Royal Brompton & Harefield NHS Foundation Trust and District General Hospitals on a network care basis. They should be used as a guide only. The Royal Brompton Hospital is a Specialist CF Centre as defined by the Specialist Commissioners, NHS England.

Our philosophy of care for patients with cystic fibrosis is based on current guidelines laid down by the Royal College of Physicians, Royal College of Paediatrics & Child Health (formerly British Paediatric Association), CF Trust, British Thoracic Society, and NHSE Service Specifications. These have identified significant advantages in terms of survival and morbidity for patients receiving care from specialist centres. Specialist centres offer access to comprehensive care from a multidisciplinary team consisting of consultants with a special interest in CF, trainee doctors, nurse specialists, dietitians, physiotherapists, clinical psychologists, pharmacists and social workers. The team is also responsible for producing and distributing educational material and carrying out research to improve knowledge about this disease. Special procedures and investigations are provided that may not be available at District General Hospital level (such as formal lung function and bronchoscopy). We are happy to continue with a shared care policy, as long as the NHSE National Service Specification and our signed Service Level Agreement are adhered to. We also run a number of out-reach clinics whereby our MDT see CF patients in their local hospitals.

Death in childhood from CF is now rare, and children born today are likely to have a mean life expectancy of over 40-50 years. There are approximately 10,500 people with CF in the UK and just under half are children. On average, large District General Hospitals will have a local CF population of between 10 and 20 patients (it may be less in the London region which has a higher density of hospitals); and General Practitioners between 0 and 2 patients. The Paediatric CF Service at the Royal Brompton Hospital has around 340 children under its care whilst there are about 650 patients in the Adult Service. The paediatric team normally sees children and adolescents until they finish their GCSEs and they will have made the transition to an Adult CF Service at the Royal Brompton Hospital or another Specialist Adult CF Centre of their choice by their 17<sup>th</sup> birthday.

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The above can usually be contacted between 9am and 6 pm. Non-urgent messages can be left on the answerphone of the CF Nurse Specialist (0207-351 8755) or the CF secretaries.

For urgent problems, please phone hospital switchboard (0207-352 8121) and ask for the on-call paediatric respiratory SpR.

## Referrals to other specialists

At times we request other consultants to see the children, and this is often done in conjunction with the shared-care consultants. SpRs must not make referrals without prior discussion with Brompton consultant. Our own practice is to use the following:

Adult CF Unit - RBH	Prof Stuart Elborn Dr Khin Gyi Dr Andrew Jones Dr Nick Simmonds	0207 351 8997
Dermatology – C&W	Dr Nerys Roberts	0203 315 8657
Diabetes / Growth / puberty – C&W	Dr Nicola Bridges Dr Saji Alexander	0203 315 8695
Ear Nose and Throat – C&W	Mr Jonny Harcourt Mr Will Grant Mr Guri Sandhu Mr Elliot Benjamin	0203 315 7972
Gastroenterology – C&W	Dr Krish Soondrum Dr John Fell Dr Jenny Epstein	0203 315 8628
Genetics – Kennedy Galton Centre	Dr Sue Holder Manchester lab.	0208 869 3171 0161 276 6506
Gynaecology – C&W	Mr Guy Thorpe-Beeston Ms Jane Bridges	0203 315 7926 0203 315 8191
Heart-lung Transplant - GOSH	Dr Helen Spencer	0207 405 9200
Hepatology – King's	Dr Marianne Samyn Dr Alan Steel (adults C&W)	0203 299 1162/3214 0203 315 8000
Paediatric Surgery – C&W	Mr Simon Clarke Mr Muntha Haddad Mr Muhammad Choudhry	0203 315 8885
Palliative care - Royal Marsden	Dr Anna-Karenia Anderson	0208 661 3625
Radiology - RBH	Prof David Hansell Dr Simon Padley Dr Anand Devaraj	0207 351 8034 0207 352 8121 ext. 2943 0207 351 8964
Rheumatology - GOSH	Dr Clarissa Pilkington	0207 829 7887
Thoracic Surgery - RBH	Mr Simon Jordan Mr Mike Dusmet Mr Eric Lim	0207 351 8559 0207 351 8228 0207 351 8591

*RBH = Royal Brompton Hospital; C&W = Chelsea & Westminster Hospital; GOSH = Great Ormond St. Hospital*

### 3. How the service runs

#### 3.1 Clinics

The clinics are run in a segregation format (see section 4.7). There are 2 clinics per week, Monday and Friday – appointments are in 2 waves - 1.45pm and 3.15pm, with a 4.15pm urgent slot. In addition, new referrals of older patients are occasionally seen for the first time in a general respiratory clinic on Tuesdays am or Wednesday pm.

Children with *Burkholderia* species and MRSA do not attend the routine CF clinics. These patients will attend clinic on the 2<sup>nd</sup> Friday of the month. Patients with MRSA will be booked into earlier time slots and those with *B cepacia* having later time slots. Due to the adult *B cepacia* clinic being held downstairs, patients will be advised to come in via Fulham Road entrance and go straight up the stairs and through physiotherapy into clinic. The HCA/Nurse will take prescriptions down to pharmacy so they do not mix with patients waiting downstairs.

Patients with non-tuberculous *Mycobacteria* (NTM) complex will come to the END of a clinic and will be the last ones in their room. No-one can use the room afterwards for at least 1 hour.

*When can patients rejoin the usual CF clinic?*

- *B cepacia*: when they have been free of the organism for 1 year, with at least 3 negative sputum or cough swabs or BAL samples in that year. Caution though if the original isolation was on sputum or BAL, and subsequent samples are cough swabs only.

MRSA: when they have had 3 negative swabs (see hospital policy

<http://www.rbht.nhs.uk/about/policy-and-performance/mrsa-screening/> (updated Apr 2016).

- If MRSA on skin swabs only – follow Brompton hospital policy.
- If MRSA on sputum/cough swab/BAL – 3 negative respiratory samples, each one taken at least 1 week apart. Caution again as for *B.cepacia* re type of respiratory sample obtained.
- *M abscessus* complex: considered free when they have had 4 negative samples over 1 year since their 1<sup>st</sup> negative sample See also sections 4.7 and 6.2a 6.VII.

There is a joint CF diabetes clinic on the 3<sup>rd</sup> Friday of the month at RBH.

Patients may attend either clinic at their convenience although we encourage continuity where possible. Most children are seen in a CF clinic every 2 months, or every 3 months for those recognised to have very mild disease. Infants diagnosed by newborn screening are often seen monthly in the first year and sometimes more frequently in the first months following diagnosis. For some, all clinic visits are at the Royal Brompton Hospital, whilst others are seen on a shared-care basis with a local District General Hospital, usually on alternate visits. We aim for all patients to be seen at by the full RBH MDT 6 monthly minimum but there are a few patients who are seen yearly only at RBH for annual review (they live abroad). All out-patient visits are discussed at a weekly multi-disciplinary meeting which the consultants attend. After every clinic visit, a letter is sent to the GP, shared-care consultant and parents, which is countersigned by the patient's named consultant. A list of the named consultant for each patient is maintained by the CF nurses and CF secretary and is available on the paediatric T drive.

The families see the following:

**Doctor.** This may be a consultant (Mondays –Bush, Davies, Carr, Chavasse, Greenaway; and Fridays –Rosenthal, Balfour-Lynn, Carr & Charlton, a specialist registrar (usually a national grid respiratory trainee), or a respiratory clinical/research fellow. Parents may request which doctor they wish to see, and this is usually possible although may lead to a longer waiting time. We aim to have patients seen by a consultant alternate visits as a minimum, and a consultant will often speak to the parents in clinic if they have been seen by a trainee.

All patients are allocated a **named consultant** when first seen at our unit, although may be seen by any member of the consultant team at various times. The named consultant will take the lead role if there are difficult clinical decisions to be made. They will also co-sign clinic letters and write the annual review reports.

**Health Care Assistant.** To measure height and weight, oxygen saturation by pulse oximetry.

**Respiratory physiologists.** To measure lung function.

**CF nurse specialist.** To see all patients and provide general information and support. Portacaths may be flushed if required.

**Physiotherapist.** All the children should be seen by a physiotherapist to review airway clearance techniques, exercise, inhalation therapy, posture and continence; and obtain sputum or cough swab specimens.

**Dietitian.** All pancreatic insufficient patients and all babies are seen by the dietitian, for review. It may not be necessary to be seen every clinic visit. Whilst pancreatic sufficient patients are routinely seen at annual review, they may be seen at other clinic appointments if necessary.

**Clinical psychologists.** Are available for annual reviews and may see families to commence or continue with their clinical work.

**Play specialist.** Is available to help children to manage invasive procedures (usually blood tests) on request.

**Paediatric Pharmacists.** The team can be contacted via bleep for medication related enquiries, and those related to the homecare delivery of medicines.

**Others.** The social worker or Welfare Rights Officer can also meet parents and often help guide them on how to obtain appropriate benefits to which they are entitled.

### Clinic procedures

- Children aged 5 years or less are always weighed in underwear, those older than 5 in light clothing. All children have their height measured on a stadiometer without shoes. Head circumference should be measured in children less than 1 year of age.
- Children over 4-5 years have lung function measured on a standard spirometer. All children have oxygen saturation measured on a pulse oximeter.

- Urine is tested for glucose if the child has lost weight or if they are receiving oral steroids, in which case blood pressure is also measured.
- Sputum or cough swabs are always collected for microbiology. Only sputum is sent for culturing non-tuberculous mycobacteria (NTM (cough swabs are always negative for this). Occasionally families may carry out a cough swab at home BUT this is not routine practice and should only be done after proper training.

### **Research**

Consideration is always made by clinicians as to whether the child might be suitable for one of the many research projects undertaken at RBH. Participation will in the first instance be discussed with each patient and /or their parents. Expressions of interest to participate in research studies are always welcome.

### **Shared care clinics**

We conduct joint clinics with many of our shared care hospitals. We aim to take the full Brompton MDT with us to the clinics to work alongside the local consultant and their MDT. The clinic should follow the same format as our own clinics, including the emphasis on patient segregation.

## **3.2 Annual review**

All patients are seen annually for a full clinical review of progress over the last year and for surveillance investigations; we intend to move this away from birthday time as we are aware some children associate their birthday negatively with having a blood test. This usually takes place in the normal CF clinic, with the patient attending radiology (+/- nuclear medicine) and the lung function lab beforehand. In addition, some older children and adolescents attend for annual review investigations and MDT review on Tuesdays (10am-3pm). The family will then come back to clinic 4-6 weeks later (or be seen in a shared care clinic) by their named consultant, who will have all the results available, and will agree a plan and write the report.

If a patient is admitted around the time of the annual review, this will take place as part of the admission (usually bloods on day 2 with aminoglycoside levels, and other measures e.g. chest x-ray & formal lung function on day 9-10). The SpRs must fill in the AR proform (for data entry to the CF registry database) and dictate a letter summarising the review and all results. For patients having regular admissions, bloods will always be taken for AR so that they do not need repeating in clinic.

The children will be seen for the following:

- Discussion with the nurse specialist following the CF Registry proform. This will include the number of IV and oral antibiotic courses, usual symptoms and microbiology. Some of these data are filled in prior to the appointment.
- Dietary assessment - including written evaluation of nutritional intake by the dietitian. Height & weight, growth velocity and BMI charts will be filled in.
- Physiotherapy review of airway clearance techniques, exercise and inhaled medication regimens. Posture and urinary stress incontinence will be reviewed when appropriate. Home air compressors for nebulisation should be brought in for yearly service. Parents must contact the Physiotherapy Department to book an appointment for servicing on 0207

351 8088, when they have the date for their review. Exercise testing is not routinely carried out.

- All patients are now offered the opportunity to meet with a Clinical Psychologist as part of their annual assessment. This will hopefully explore how the child with CF and their family are managing. As per CF Trust and British Thoracic Society guidelines, both the child with CF (if aged 11 years and over) and their parents/carers will be invited to complete mood questionnaires. If the families are already meeting with a psychologist, then they will not need to be seen by a psychologist at annual review unless they wish to make an appointment in advance. They will still be invited to complete the questionnaires.

## Investigations

- *Full lung function* (including plethysmography) for children over 6 years. Bronchodilator responsiveness will be carried out for specific patients only by request. This is done in the Lung Function Laboratory on the 1st floor Fulham wing and takes 1 hour.
- *Lung clearance Index (LCI)*. This test requires only passive co-operation, and can potentially be performed at all ages. The child only needs to breathe normally through a mask or mouthpiece.

The advantages of the test include (a) it is non-invasive, (b) only passive co-operation is needed, (c) the normal value is essentially the same over the whole age range, (d) it is more sensitive than spirometry to early disease. It is also frequently used as a research technique. If a child has grossly abnormal obstructive spirometry, the test will take a long time and be tiring for the child. In this situation, it is also not likely to add much useful information, so discuss with a Consultant first.

Subject to the above, LCI should be a routine part of the annual assessment and is undertaken in all children aged 5 years and above. Additionally, the test is particularly useful in children who supposedly have 'poor technique' with spirometry, and we can measure it in children as young as 4-5 years old. Whilst this may be true, equally it may mask the fact that their lung function is genuinely low. LCI should be booked through Sam Irving (ext. 8233, email [s.irving@rbht.nhs.uk](mailto:s.irving@rbht.nhs.uk)) and is carried out in Chelsea Wing level 4.

The higher the LCI, the worse is the distal gas mixing. Normal ranges for LCI are device-specific and still being established, but in general a value > 8.0 is above the normal range and >10.0 is significantly abnormal (we have rarely had values >12). Importantly, the results from different LCI devices are not interchangeable. It is therefore important that the device used is recorded alongside the result, and the same device (where possible) is used when a patient has a subsequent LCI.

In an older child with known poor lung function, there is less point in carrying out LCI as well.

- *Ventilation scan* is carried out in children too young to perform formal lung function. This is done in Nuclear Medicine Department, Level 3 Chelsea Wing and takes 1 hour. Ext 8666.

- *Chest x-ray* is not scored but we record changes and differences from the last year.
- *Ultrasound liver and spleen.* Liver ultrasound is performed as screening at the Brompton Hospital (or at the local hospital) on all children aged 5 years and above every other year (e.g. age 5, 7, 9, 11, 13, 15 yrs). It should be performed in anyone else with a palpable liver/spleen or significantly abnormal liver function test (2x upper limit of normal). If the ultrasound is abnormal or there are other liver abnormalities (hepatosplenomegaly, blood results) it will be repeated annually. It will be done without the child fasting for convenience. The only downside of that is that the gall-bladder will not be visualised well. This will not matter unless the child is having abdominal pain in which case it is important to look for biliary stones.
- *Bone densitometry (DEXA scan)* is measured every other year as screening in all children aged 8 years and over (e.g. aged 8, 10, 12, 14, 16 years). It is particularly important they are measured in patients considered to be at increased risk of developing reduced bone density (see section 8.4). These would include those who have frequent oral steroids (particularly those with chronic ABPA), those on high dose inhaled corticosteroids, anyone receiving insulin and those with FEV<sub>1</sub><50% predicted. Ext 8965. If abnormal, it will be repeated annually.
- *Continuous glucose monitoring System (CGMS)* is carried out in all 12 and 15 year old patients as a screening procedure for CF-related diabetes, in addition to those considered to be at increased risk or where there is clinical concern of CFRD (see section 8.1).
- *Sputum or cough swab* for microbiology, and sputum only for NTM.
- *Blood* is taken by the phlebotomist (or doctor). 15 ml is taken for the following:
  - Full blood count (with WBC differential)
  - Clotting studies
  - Electrolytes and creatinine
  - C-reactive protein
  - Calcium, magnesium and phosphate
  - Liver function tests (AST, ALT, ALP,  $\gamma$ GT)
  - Random glucose and glycosylated Hb
  - Vitamins A, D & E
  - Serum ferritin
  - IgG, IgA, IgM
  - IgE
  - Aspergillus RAST (specific IgE)
  - Aspergillus IgG (ICAP)

Blood bottles: 2 (red) EDTA bottles, 4 (brown) SERUM bottles (6 in older children), 1 (green) COAGULATION bottle. Bottles must be full. Use larger bottles in older children.

- *Urine* – dipstix for glucose for all with CFRD and anyone on oral corticosteroids.

## Annual Review Letter

A normal clinic letter should be dictated by the doctor who sees the patient, with available investigation results included. Results of lung function should always be reported in litres in addition to %predicted values. A report of the AR including all investigation results will be compiled by the patient's lead consultant when the results are available. Blood results will be checked within 1 week.

## UK CF registry

All data is entered on to our own hospital database and the UK CF national registry, for which the parents will have given written informed consent. This is mandatory and determines patient banding and payment to the hospital via the PbR system (see section 3.8, and appendix 17). Website – <https://cfregistry.org.uk/pages/home>. User name for staff to access our data can be obtained from our Database Team, Hannah Wright or Eva Bush.

## 3.3 Transition from paediatric to adult care

Transition from paediatric to adult care is discussed with all patients and their families from diagnosis and at every annual review. A more detailed discussion takes place from 14 years and a letter is sent to both parents and the young adult. The transition process has been divided into two parts: pre-transition and transition. Invitations to attend a pre-transition clinic are sent to all 15 to 16 year olds, this is an opportunity to meet the adult CF team and ask any questions before attending the transition clinic. There is always the opportunity to have a second pre-transition visit if this is required. Invitations are sent for the transition clinic at around 16 years of age, we aim for this to be after GCSE exams. Details included with this invitation outline the choices of Adult CF Centres and provide information about growing up with CF. The Adult CF Clinic at the Brompton Hospital may not be the Centre of choice for some patients – advice is given on how to access other services with contact details for each centre ([www.rbht.nhs.uk/cf-transition/](http://www.rbht.nhs.uk/cf-transition/)). Either way we will make the necessary referrals.

Most patients will transfer at some stage after their 16th birthday, depending on the individual and family circumstances. However we plan to transition all young adults by their 17th birthday. The Transition Integrated Care Pathway (TICP) is commenced at this time (Appendix 1). The document detailing family, social and clinical history is completed by each patient, their family, clinical nurse specialist and the rest of the MDT. The adult team are able to access this document prior to the transition clinic (Appendix 1). There is a section entitled 'all about me' which we like the young adult to fill in as a way of introducing themselves to the adult team.

Transition clinics are held on Monday and Friday afternoons in the usual paediatric clinic area. There are about 4-5 clinics per year. The adult CF Team (consultant, nurse specialist, physiotherapist, dietitian, and clinical psychologist) attend each transition clinic to give patients and families an opportunity to meet and ask questions about the move to adult care. The patients remain under the care of the paediatric team until they are seen for the first time in the adult clinic, we aim for this to be 8 -12 weeks post this clinic.



Following each transition clinic an adult CF clinical nurse specialist will arrange each patient's first adult clinic appointment on days that the same doctor, nurse specialist, physiotherapist and dietitian are in clinic to ensure continuity. The TICP is continued until after the first adult clinic appointment. A monthly paediatric/adult transition meeting is held where CF team members from both services meet to discuss all patients attending the following transition clinic and to discuss issues arising from patients who have recently made the transition to the RBH adult CF service. After making the transition to the adult CF service, adolescents are initially followed up closely to try to ensure that the change of CF team is made successfully.

If or when patients need admission to Foulis ward (the adult ward), our hospital school teachers visit regularly (and liaise with schools and colleges) to continue education for A levels (exams are taken on the ward if necessary), and university / college. The school also provide a careers advisor. A leaflet outlining educational support is available on the ward on the adult CF team website ([www.rbht.nhs.uk/patients/condition/cystic-fibrosis/cystic-fibrosis-transition/the-role-of-the-hospital-school/](http://www.rbht.nhs.uk/patients/condition/cystic-fibrosis/cystic-fibrosis-transition/the-role-of-the-hospital-school/)).

A blog has been developed on Foulis ward to improve communication between in-patients, and patients can sign on during their first admission. At admission every patient (regardless of age) is asked to sign a 'contract of care', which sets out activities expected from patients during admission (including adhering to cross infection policies). Part of the contract also includes a list of what patients can expect from the CF team.

### 3.4 Homecare & Outreach Service

The role of the Homecare Service is to provide a specialist nursing/physiotherapy input at home, and to facilitate the continuity of care between the Royal Brompton Hospital, local services and the family. The team currently comprises 4 children's CF nurse specialists; and 2 physiotherapists specialising in providing homecare for children with CF and their families. In addition, one of our dietitians and clinical psychologists will occasionally do home visits. Criteria for referral are that RBH is the child's specialist centre assuming distance is not prohibitive.

The Nursing service core hours are Monday to Friday 9am to 5 pm.

The Physiotherapy service operates Tuesday to Friday 9am to 5pm.

Contact for families and professionals is via mobile telephone (with answerphone); messages left within the hours of 9am to 4pm will be answered the same day (weekdays).

**07973173969**

**07971224068**

**07773964573**

**07483338160**

**07970 269 452**

**07791 584 749**

**Laura Hayers** (Nurse Specialist)

**Karen Henney** (Nurse Specialist)

**Katie Dick** (Nurse specialist)

**Jo Gregory** (Nurse Specialist)

**Emma Dixon** (CF Physiotherapist)

**Nicky Murray** (CF physiotherapist)

## Purpose of visits

- Monitoring and assessment including measurement of SpO<sub>2</sub>, lung function and collection of specimen e.g. sputum, cough swabs
  - between routine appointments
  - following a course of oral antibiotics
  - during course of IV antibiotics
- Flush portacaths / change portacath needles (nurses only)
- Physiotherapy service offers:
  - assessment and review of airway clearance techniques
  - advice on exercise, posture correction and stress urinary incontinence
  - education on inhaled medication use and regimens
  - infant massage.
- Education, reinforcement and encouragement following:
  - diagnosis
  - diagnosis of new complication
  - commencement of new treatments
  - preparation for transition
- Support – school/nursery education.
- Newborn Screening
  - The screening labs inform the CF nurses of babies who have been screened “highly likely” to have CF.
  - The homecare nurses with support from local health visitors, visit the families at home to inform them of the suspected result.
  - The homecare nurses are able to answer parent’s questions with specialist, up to date knowledge.
  - Parents are given an appointment for their baby to attend the Royal Brompton Hospital the next day for a sweat test where they will meet with the Consultant and a formal diagnosis made.
- Training of local teams

Home visits offer families the undivided attention of a health professional away from a busy ward or clinic in the security and privacy of their own home. This provides the opportunity for less hurried discussions about anything the family wish to talk about. In particular, practical issues can be dealt with and it gives us an opportunity to explore how the family is coping with the situation of living with a child with CF. Home visits can be an ideal opportunity to involve both parents, the child, siblings and extended family members. In order to maximise the effectiveness of visits, appointments are made with the family responding to their individual needs regarding frequency and content. The team will endeavour to make appointments at a time convenient to the family and school aged children can be seen before or after school. Additional contact, support, and follow up are also maintained by telephone on a two-way basis. Home visits should not be allowed to be a substitute for regular clinic attendance. The Clinical Psychology Team are also able to offer occasional community visits depending on the needs of each individual family.

## **Liaison**

The team aims to establish links with local services as appropriate to each individual child in order to promote continuity of care. The Homecare service is not a replacement for local services but aims to complement them in providing a specialist resource.

Liaison occurs regularly with Community Children's Nurses; Health visitors; School nurses & teachers; GPs; Practice Nurses; Social workers; Community physiotherapists; Community dietitians; local psychological well-being /mental health services (e.g. school counsellors, local child and adolescent mental health services - CAMHS).

- The team regularly sets up "shared care" with local Community Children's Nurses and Physiotherapists, visiting alternately (or as required) and on occasions jointly, ensuring telephone communication following visits and outpatients appointments.
- The nursing team are available to visit GP surgeries a visit if required when children are newly diagnosed or new to their Practice.
- They liaise regularly regarding medication requirements, linking also with local pharmacists.
- The team visits schools at parents'/carers' request to educate school staff regarding CF and the particular needs relating to the child during their school day. The homecare team will train teachers for school residential trips to ensure the child can attend without missing vital treatments. If requested by the child, class talks can be given allowing greater understanding of CF by their peers.
- The team have extended their attendance at shared care clinics and continue to act as a resource for shared care teams

Liaison with the multi-disciplinary team at the RBH –

- The team works closely with the hospital-based CF clinical nurse specialists.
- The team has direct access to medical advice at RBH at all times, and will consult with medical staff from the home as appropriate.
- Nursing team members attend a weekly multidisciplinary team feedback meeting at RBH where every patient seen the previous week is discussed.
- The community nurses may cover the CF outpatients' clinic alongside the in house Clinical Nurse Specialist. The respiratory ward round is also attended by one of the team. The team works closely with the Hospital CF nurse specialist.

## **3.5 Clinical Psychology**

The clinical psychologists are part of the CF multidisciplinary team, and can accept referrals from anybody. They can meet with children with CF their parents and/or carers, their siblings, and other family members. The psychologists provide a service to both inpatients and outpatients (and offer occasional community (e.g. home) visits depending on the requirements of the family. They are available during CF clinics if required (it is always advisable to ring prior to the clinic appointment to ensure that there is enough allocated time available). They also offer a consultation service to other members of the CF team both at RBH and at shared care centres and are available to discuss case management or referrals to the psychology service. They have also started to come to some shared care clinics in the

largest centres with the rest of our MDT. The clinical psychologists attend ward rounds and weekly multidisciplinary CF clinic meetings.

The clinical psychologists recognise that CF can affect a child and/or their family in a variety of ways. They offer the opportunity to discuss things which can arise when a child and family are living with CF (or anything else - it need not be related to CF). As well as talking and listening, clinical psychologists can offer suggestions for change and practical ways for coping with difficult situations such as managing invasive procedures (*e.g.* blood tests). Any assessments and interventions carried out would be made sensitive to the needs of the child and/or family. Confidentiality is respected and discussed with each person seen. It can often be helpful to share some information with other members of the CF team (*e.g.* what works well to help a child co-operate with their blood test) and permission may therefore be sought to do this from the child/family. Permission from the person identified as having parental responsibility for the referred child would be sought prior to a clinical psychologist formally introducing her/himself to a child unless there were very exceptional circumstances. Sometimes the psychologists will liaise with local counselling/mental health services because long term follow up is often better carried out nearer to the family's home or the degree of concerns about the child with CF and /or their family member (*e.g.* severe clinical depression) is such that more specialist assessment and/or intervention is warranted. This would not be done without the permission of the patient and/or their family.

Some reasons for referral or consultation include:

- A clinical psychologist will meet the family of newborn screened babies during their education programme. They will also meet the child and their family who has recently been diagnosed medically as having CF and/or older patients with CF new to the RBH CF service. This to introduce the psychology service and in the recognition that a new diagnosis of CF can present as a challenge to any family.
- Talking with, family, friends and people who work with a child with CF (*e.g.* teachers) about CF and managing their reactions to this.
- Helping a child to manage medical treatments *e.g.* to swallow tablets whole.
- Checking and informing (often with a medical or nursing colleague) the understanding of the child has of their CF.
- Consideration of future treatments that may be offered along with the implications *e.g.* nebulised antibiotics. Managing invasive procedures - including fear of needles.
- Challenges which may occur with the CF patient's feeding behaviour/nutrition.
- Life changes related to CF care *e.g.* transfer to adult CF services, change in treatments, consideration of possible transplantation.
- Life circumstances related to the young person or family such as new sibling, new house, stressors affecting family relationships.
- Thinking about school *e.g.* returning to school after long periods of absence; changes of school placement such as transfer to secondary school; and other school related challenges such as difficulties with peer relationships or helping to identify learning difficulties.
- Problems which may or may not have something to do with CF *e.g.* toileting problems.
- Mood/behaviour problems which may or may not have something to do with CF. As previously documented at all CF annual assessments we aim to monitor the young person's (4 years and above) and their main carers' mood and behaviour in order to identify and offer support for any challenges identified.
- Any other challenges which may or may not be attributable to CF.

- Support for parents.

Please note that this is not an exhaustive list. If you think psychology support might be helpful please do not hesitate to contact directly one of the psychology team at Royal Brompton Hospital to discuss this further.

### 3.6 Safeguarding Children Team

The Safeguarding Children Team based at RBH, deliver advice and training to all staff, as well as support to families across the Trust to ensure the safety and welfare of children and young people. They are members of the multidisciplinary team and will support staff to make appropriate referrals to Children's Social Care (CSC) within the child's local authority, if concerns are identified or further support is required such as:

- a) that a child is seen as being a child in need as a result of his/her disability, or because his/her health and development is likely to be significantly impaired, or further impaired, without the provision of services (Section 17, Children Act 1989).
- b) that a child is suffering or is likely to suffer significant harm (Section 47, Children Act 1989).
- c) where emerging problems and potential unmet needs have been identified for individual children and their families, 'Early Help' interventions are offered through multi-agency referrals. (Working Together to Safeguard Children, HM 2015).

All NHS providers are expected to comply with legislation and statutory guidance, this includes:

- Children's Act 1989, 2004.
- Compliant with statutory guidance i.e. Working Together to Safeguard Children (2015) and Section 11 of the Children Act 2004.
- Meeting Care Quality Commission (CQC) Essential Standard for Quality and Safety – Outcome 7.
- Safeguarding Children & Young People: Roles and Competencies for Health Care Staff (RCPCH Intercollegiate Document 2014).

The Paediatric Social Worker (PSW) works with CF multidisciplinary team, including the Safeguarding Children team and their role primarily is to undertake assessment and analyse family strengths and difficulties in managing the child's diagnosis and long term treatment and needs, particularly regarding family history, functioning and environment. They signpost or make referrals to appropriate services if required, whilst the child is an inpatient in the hospital and/or prior to discharge from the hospital, in conjunction with the MDT and partner agencies.

Specific PSW's role includes:

- Joint working with child, family and multi-agency professionals to ensure clear information sharing and continuity of care and services. This will include attendance at pre-admission planning and discharge planning meetings, for children with known social or safeguarding concerns.
- Following assessment, the PSW refers the child and his family to the local CSC department with the recommendation that further assessment of needs or provision of services, if required.

- Eligibility criteria and the availability of services vary in different local authorities. The responsibility to provide services lies with the child's local authority and they undertake their own assessment of needs once the child is discharged from hospital.
- Working jointly with the Family Liaison Team and Welfare Rights Officer to identify appropriate additional social security benefits or charitable support within their local area for families, prior to discharge.

#### Overall remit of the Safeguarding Children Team:

- To be the point of contact for all safeguarding children concerns throughout the Trust.
- Assess and analyse family strengths and difficulties in complex cases in conjunction with staff, children and their families, particularly regarding family history and family functioning, using risk assessment tools.
- Supporting staff in the collation of evidence of concerns and in developing safeguarding chronologies.
- Supporting staff to make referrals to CSC for safeguarding concerns.
- Offer training and guidance, as well as regular team or one to one safeguarding supervision to all paediatric staff.
- Identifying children and young people subject to Child Protection Plans or Child In Need Plans or who are Looked After Children (LAC), with early liaison with relevant multi-agency team. Ensuring attendance of a representative of RBH at appropriate strategic, core group, conference or professional meetings, as well Team Around the Child meetings.
- Supporting families with no recourse to public funds or are homeless, by liaison with appropriate CSC or local services to ensure the safety and welfare of the child.
- Attend regular child related meetings within RBH, where necessary to offer support and advice.

### 3.7 Family Liaison Team & Welfare Rights Adviser

The family liaison team support parents and carers during their child's hospital stay, particularly in relation to non-medical issues. They are able to help families if problems arise either in hospital or at home. They can also liaise with other members of the multi-disciplinary team on behalf of the families. Being far from home can be stressful, particularly if other children and partners are still at home, and also may cause extra financial burdens. Their aim is to try to alleviate that stress. If they cannot help, they usually know someone who can!

The Welfare Rights Adviser provides welfare advice to paediatric patients and their families on the following issues

- financial concerns.
- benefit advice and assistance with applications.
- housing issues.

### 3.8 Payment by Results – the mandatory tariff.

Since April 2013 there has been a mandatory tariff paid via the Specialist Commissioners to the CF centres, based on a year of care tariff that is dependent on the severity of the child's

CF disease. This is determined by the complexity adjusted yearly banding system (see below) produced from data entered on to the CF national registry. It is critical data is entered for every patient without exception, assuming consent obtained, usually by January 31<sup>st</sup> each year with the previous year's data.

This is to cover CF related care only (e.g. not A&E visits or admissions for trauma or non-CF illness). It also specifically excludes charges for high cost CF drugs – DNase, nebulised antibiotics (colistin, tobramycin, aztreonam), mannitol and ivacaftor. High cost antifungals *i.e.* voriconazole, posaconazole, liposomal amphotericin and caspofungin are also excluded from the tariff.

Part of the tariff is paid to our shared care Network Centres. Each centre must comply with the NHSE National Service Specification (appendix 16), the CF Trust Standards of Care (2011), and the Service Level Agreement signed with the Brompton. The paediatric tariff does not take into account the extra costs incurred by shared care arrangements nor costs of local community services.

The following explanation is taken from the 2016/17 National Tariff Payment System.  
[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/509697/2016-17\\_National\\_Tariff\\_Payment\\_System.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/509697/2016-17_National_Tariff_Payment_System.pdf)

### **Cystic fibrosis pathway payment**

- The CF pathway currency is a complexity-adjusted yearly banding system with seven bands of increasing complexity of patient need. The tariff relates to a year of care. The pathway does not distinguish between adults and children.
- The CF pathway currency was designed to support specialist CF multidisciplinary teams to provide care in a seamless, patient-centred manner, removing any incentives to hospitalise patients whose care can be well managed in the community and in their homes. Furthermore, it allows early intervention (following international guidelines) to prevent disease progression, for example, through the use of antipseudomonal inhaled/nebulised antibiotics and mucolytic therapy.
- Bandings are derived from clinical information including CF complications and drug requirements. The bands range from band 1, for the patients with the mildest care requirements (involving outpatient treatment two to three times a year and oral medication) to band 5, for patients at the end stage of their illness (requiring intravenous antibiotics in excess of 113 days a year with optimum home or hospital support).
- Patients are allocated to a band by the CF Registry data manager using data from the national database, the UK CF Registry.
- The pathway payments cover all treatment directly related to cystic fibrosis for a patient during the financial year. This includes:
  - Admitted patient care and outpatient attendances (whether delivered in a specialist centre or under shared network care arrangements);
  - Home care support, including home intravenous antibiotics supervised by the CF service, home visits by the multidisciplinary team to monitor a patient's condition,

- e.g. management of totally implantable venous access devices (TIVADs), collection of mid-course aminoglycoside blood levels and general support for patient and carers;
- Intravenous antibiotics provided during in-patient spells. Annual review investigations.
- For any patient admission or outpatient contact in relation to CF, the HRG is included in the year of care payment regardless of whether it is one of the CF specific diagnosis driven HRGs or not. All outpatient CF activity must be recorded against TFC (Treatment Function Code) 264 and TFC 343.
- Some elements of services, included in the CF pathway payments, may be provided by community services and not the specialist CF centre, such as home care support, including home intravenous antibiotics supervised by the cystic fibrosis service, home visits by the multidisciplinary team to monitor a patient's condition (e.g. management of totally implantable venous access devices (TIVADs)) and collection of mid-course aminoglycoside blood levels. In such cases there will need to be agreement between the relevant parties (local services and CF specialist Centre) on reimbursement from the prices paid to the specialist CF centre.
- There are a number of specified services which require local negotiation on price:
  - High cost CF specific inhaled/nebulised drugs: colistimethate sodium, tobramycin, dornase alfa, aztreonam lysine, ivacaftor and mannitol.
  - Insertion of gastrostomy devices (percutaneous endoscopic gastrostomy [PEG]) and insertion of totally implantable venous access devices (TIVADs) are not included in the annual banded prices. These surgical procedures will be reimbursed via the relevant HRG price.
  - Neonates admitted with meconium ileus who are subsequently found to have CF will not be subject to the CF pathway payment until they have been discharged after their initial surgical procedure. This surgical procedure will be reimbursed via the relevant HRG price. Once discharged after their initial surgical procedure subsequent CF treatment will be covered by the CF pathway payment. Annual banding will not include the period they spent as an admitted patient receiving their initial surgical management.
- Network care is a recognised model for paediatric care. This model must provide care that is of equal quality and access to full specialist centre care.

### **Banding definitions –**

In appendix 17, we have enclosed the section on CF from the Payment by Results Guidance for 2013-14, published in Feb 2013 by the Dept. Health. The full guidance is available on - [www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/214902/PbR-Guidance-2013-14.pdf](http://www.gov.uk/government/uploads/system/uploads/attachment_data/file/214902/PbR-Guidance-2013-14.pdf).



Banding definitions		Band						
		1	1A	2	2A	3	4	5
Therapies	Maximum number of total days of IV antibiotics	0	14	28	56	84	112	≥113
	Nebulised antibiotics ( <i>Pseudomonas</i> infection)		Yes					
	Long-term (>3 months) nebulised antibiotics <u>or</u> DNase			Yes				
	Long-term (>3 months) nebulised antibiotics <u>and</u> DNase				Yes			
Hospitalisations	Maximum numbers of days in hospital	0	7	14	14	57	112	≥113
Supplemental feeding	Nasogastric feeds				Yes			
	Gastrostomy					Yes		
Complications	CF Related Diabetes <u>or</u> ABPA w/o other complications				Yes			
	CF Related Diabetes <u>and</u> ABPA					Yes & (FEV <sub>1</sub> ≥60%)	Yes & (FEV <sub>1</sub> <60%)	
	Massive Haemoptysis <u>or</u> Pneumothorax					Yes & (FEV <sub>1</sub> ≥60%)	Yes & (FEV <sub>1</sub> <60%)	
	CF Related Diabetes <u>and</u> Gastrostomy					Yes & (FEV <sub>1</sub> ≥60%)	Yes & (FEV <sub>1</sub> <60%)	
	Non Tuberculous mycobacterium treated or difficult to treat infections (e.g. MRSA or Cepacia) requiring other nebulised antibiotics e.g. Meropenem, Cayston, Vancomycin.					Yes		

Band	Tariff (£)
1	5,033
1A	7,447
2	7,447
2A	12,036
3	18,422
4	33,224
5	40,054

2016/2017 NHSE Tariff

## 4. Admission to hospital

There are several reasons why a child with cystic fibrosis is admitted to hospital, which include the following:

- Education of family at time of new diagnosis.
- Bronchoscopy  $\pm$  pH study.
- Any deterioration in clinical condition that fails to respond to out-patient measures e.g. chest exacerbation, DIOS, CFRD.
- Elective 3 monthly admissions for IV antibiotics (usually 2 weeks).
- Elective 1 monthly admission for IV methylprednisolone (usually 3 nights).
- Elective operations e.g. portacath or gastrostomy insertion, ENT or dental operation.
- A complex presentation of a child with CF, *i.e.* symptoms and the effect that this has on their daily functioning which would warrant very close observation for a period of time by the CF MDT.

### 4.1 Admitting the child

#### Pre-admission

If an admission date is certain (unlikely to be until day before) then it may be possible to pre-order the IV antibiotics using the CIVAS (Centralised Intravenous Additives Service); this is especially useful if the admission is on a weekend.

Occasionally a child and / or their family have very particular needs (*e.g.* the child has autistic spectrum disorder) or have had a very challenging previous experience with an inpatient admission at RBH or another hospital. In these circumstances a plan ('Pre-admission Plan') is constructed which serves to document the needs and/or expectations of the child and their family and of the inpatient CF services at RBH to promote a successful admission.

#### Clerking

On admission, the reason for hospital attendance must be identified, and documented clearly in the integrated care pathway (ICP), which is available on the intranet and on Rose ward. All subsequent documentation for that admission is entered on continuation sheets as part of the ICP. Medical admission paperwork covers the following information.

- **Allergies** – Any allergies, particularly to drugs should be recorded both in the notes and on the drug chart, the type of reaction experienced should also be included (*e.g.* rash, anaphylaxis). Check it is also written on the front cover of the notes.
- **Reason for admission** (tick box).
- **Current CF complications** (tick box).
- **Past history of ABPA** - (if applicable) should be recorded with most recent IgE & Aspergillus RASTs, together with maximum values in the past year for comparison.
- **Current medication** -
  - A full drug history including the types of inhaler used (*e.g.* turbohaler, MDI with spacer etc) is mandatory. Inhaler technique must always be checked.

- Write inhaled steroids doses in mcg **not** number of puffs.
- If a patient is on oral steroids, record the starting date and dose/kg/day.
- Drug doses are often recorded in the last clinic letter **but** should be checked directly with the patient or their parents before recording and prescribing them.
- Check whether there have been problems with aminoglycoside levels in the past.
- **Inhaled antibiotics**
  - **No-one can receive a nebulised drug if it is being given intravenously.**
  - If they are on IV tobramycin they receive nebulised Colistin (even if that is the month they would have been due nebulised Tobramycin)
  - If on IV colistin they receive nebulised tobramycin rather than nebulised colistin. If they have not had nebulised tobramycin before, then they have no nebuliser whilst in.
  - The same applies to dry powder inhalers.
- Drug histories are confirmed by a pharmacist or pharmacy technician at the earliest opportunity within pharmacy opening hours.
- **Date of last admission.**
- **Last Sputum/cough swab obtained.**
- **Is annual assessment due soon?** – if so, investigations should be arranged during admission.
- **Best FEV<sub>1</sub>% and FVC% in last year.** Absolute (litres) as well as % predicted values must be recorded. These can be found from clinic letters/EPR and the respiratory physiologists are able to provide a trend graph.
- **Documented concerns about weight and height.** Growth chart are kept in the notes (paper and electronic).
- **Recent microbiology** – growths and sensitivity/resistance. The most recent positive sputum culture result should be documented with full sensitivities. Certain bacteria like *B cepacia* complex, MRSA and *M. abscessus* complex require specific action with regards to therapy and isolation from other CF patients.
- **Respiratory system:** - cough, wheeze, sputum production (quantity, frequency, colour, consistency), haemoptysis, chest pain/tightness, dyspnoea, exercise tolerance.
- **Gastrointestinal system:** - appetite, heartburn, water brash, funny taste in mouth, nausea, vomiting, frequency bowels are opened, quality of stool, abdominal pain, rectal bleeding, weight loss, calorie supplements, gastrostomy/NG tube feeds (amount, type, nights per week).
- **Genito-urinary system:** - thirst, urinary frequency, polyuria, nocturia.
- **ENT:** - nasal obstruction, epistaxis, rhinitis, sense of smell & taste.
- **Neuromuscular** - headache, paraesthesia, muscle weakness, joint pains, backache.
- **Pain.**
- A full **social history** should be taken paying particular attention to school attendance, housing, pets and active/passive smoking. Also whether social care has been involved in supporting the family either currently or in the past, and/or whether the family have worked with psychology services in the past and/or currently.

## Examination

Examination findings should be recorded in the standard way according to systems. Do not forget the ENT system, particularly nasal polyps. Blood pressure is mandatory on all patients, with particular attention paid to those on oral steroids. Check presence of glycosuria on all patients.

All children should have the following observations recorded:

- Weight (kg & centiles) in underwear when aged 5 or under, and light clothing aged over 5. If the child has been weighed fully clothed they must be weighed again. Growth chart should be in notes (or on electronic notes).
- Height (cms & centiles).
- Head circumference in <1 year olds.
- Temperature.
- Oxygen saturation in air or oxygen (include O<sub>2</sub> requirement).

## 4.2 Investigations

All children old enough will have **pulmonary function tests** (spirometry) performed following admission. If the child has been admitted from clinic, these will already have been performed and do not need repeating. **This must be performed within 24 hours of admission, INCLUDING weekends** (use the ward spirometer).

**Admission bloods.** These are generally performed at the same time as the first aminoglycoside level (pre-2<sup>nd</sup> dose) unless they are needed immediately – this is to minimise exposure to needles. For blood sampling, try to use veins on the back of the hand so that their antecubital fossae veins can be reserved for long lines. For all infants and children we use anaesthetic cream (EMLA) applied under an occlusive dressing for 60 minutes (will last up to 5 hours). Avoid Ametop due to the high frequency of allergic reactions, especially in atopic children (it may be tried if there has been a previous reaction to EMLA). You can also use Cryogesis<sup>®</sup> spray (ethyl chloride) which is used immediately before the procedure, but is only suitable for very short procedures. If coping with needles has been difficult in the past, please discuss this with a play therapist or a clinical psychologist in advance for help and support, and if necessary, defer testing unless it is absolutely urgent.

Please always check with the child and family if coping with bloods and/or needles has been challenging in the past, if so there is likely to be an existing support plan for coping with blood tests on the patient's Electronic Record. If there is no existing plan or additional support to the plan is required, please discuss this with a play specialist or a clinical psychologist in advance for help and support, and if necessary, defer testing unless it is absolutely urgent.

If the child is due annual review (usually around the time of their birthday) within next 3 months, make sure all annual review bloods are taken (usually just add immunoglobulins, serum vitamins, clotting) on day 2 when aminoglycoside levels are taken - see list on section 3.2. Remember to also complete the annual assessment paperwork, chest x-ray, liver ultrasound or DEXA scan, and arrange formal lung function for the end of the admission, usually on day 9-10.

The list of blood tests (with the appropriate bottles) required on admission is given below:

• Full blood count (FBC)	EDTA (pink) 1ml	Haematology
• Urea & electrolytes	serum (brown)	Biochemistry 3 ml minimum (alternatively lab will accept clotted blood)
• Liver function tests	serum (brown)	
• Calcium, magnesium, phosphate	serum (brown)	
• Glucose	serum (brown)	
• HbA <sub>1c</sub>	serum (brown)	
• Total IgE	serum (brown)	
• Aspergillus IgE RAST	serum (brown)	
• CRP	serum (brown)	Virology/Immunology
• Aspergillus IgG	serum (brown) 1ml	

A **chest x-ray** is only performed if clinically indicated e.g. to exclude pneumothorax or for annual assessment. They are **not** performed to check long line position.

**Sputum/cough swab** must be sent to microbiology within 24 hours of admission.

**Nasopharyngeal aspirate** for viral detection is sometimes indicated (usually under 1 year old).

**Urinalysis** must be performed on admission especially if the child is on oral steroids or there is a recent history of weight loss

#### Further investigations during admission:

- Weekly sputum / cough swab, and at point of discharge.
- Daily SpO<sub>2</sub> unless initial one >95%.
- Twice weekly spirometry (Tues, Fri).
- Twice weekly weight (Tues, Fri), those aged 5 or less in their underwear, those older than 5 in light clothing.
- Daily BP and urinalysis if on oral steroids.
- Overnight SpO<sub>2</sub> (Masimo) early in admission, especially if FEV<sub>1</sub><50% or resting SpO<sub>2</sub><92% (see section 6.16).

#### Drug monitoring

##### *Aminoglycosides* (Tobramycin, Amikacin)

- Pre-dose levels 23 hours after 1<sup>st</sup> dose (i.e. before 2<sup>nd</sup> IV dose). These are sent in a serum (brown) bottle to biochemistry. If in desired range, repeat 1 week later; and 1 week after that if having 3 weeks antibiotics. **Record results on drug chart.** See section 6.2a, part 6.IIIg.

##### *IV Polymyxins* (Colistin)

- Once weekly U + Es

##### *Chloramphenicol*

- 3-weekly WBC, so not routinely required unless having >2 week course

##### *Linezolid*

- Weekly FBC (mandatory – see BNFC)

##### *Itraconazole*

- Monthly LFTs + drug level if indicated (e.g. an interacting drug is commenced, efficacy is not observed or toxicity is suspected). See section 6.9.

##### *Posaconazole*

- Monthly LFTs + drug level to be taken after at least 1 week of commencing therapy or dose changed, if an interacting drug is commenced efficacy is not

observed, or toxicity is suspected. Take sample just before the next oral dose (if not possible then a random sample). See section 6.9.

#### *Voriconazole*

- Weekly LFTs for the first month then monthly thereafter + monthly U&Es + drug levels should be measured at least 3 days after commencing therapy or dose changes, if an interacting drug is commenced, efficacy is not observed or toxicity is suspected. Take sample just before the next oral dose. See section 6.9.

### 4.3 Venous access & long line insertion

All children will require venous access for administration of IV antibiotics. If they have a portacath in-situ, the nursing staff will access the portacath with a gripper needle on the child's admission. Otherwise long lines are our preferred method of access; however there are occasions when a short cannula or central venous access will be necessary. Long lines are usually inserted by the SpR but may be inserted by the SHO once they have been seen to have achieved competency under the supervision of an SpR.

Whatever grade of doctor, **no more than three attempts of line insertion** should be tried before asking for additional support from colleagues. We understand from research and talking with our patients that the line insertion can often be the most challenging part of their admission. We also appreciate that if this feels challenging for the child/family this can often set the tone for a difficult admission, and future problems. As such, if children have reported that venous access may be difficult for them then please identify whether there is a support plan already in place on the child's electronic patient record or ask a play specialist and/or clinical psychologist for support (see below). Similarly, should 'therapeutic safe holding' (restraint) be deemed necessary for the insertion of a long line of any child older than a toddler please ensure that a play specialist is informed and that strategies are employed to prevent and / or mitigate the necessity for this.

Some children will require sedation prior to long line insertion. In suitable children, **Entonox®** (50% nitrous oxide / 50% oxygen) should be the first choice. Relevant contraindications are pneumothorax and intestinal obstruction. Please note that the patient should have an empty stomach prior to the procedure to reduce the likelihood of nausea and vomiting, they must be *nil by mouth for 1 hour* (we no longer require 6 hour fasting) - see separate guideline for its use available on our intranet. Entonox is not used by adult service due to risk and therefore any child or young person who uses it will need to learn to manage without by transition to adult CF service.

If **oral sedation** is required, it can be achieved after 30 minutes following administration of oral midazolam (0.5mg/kg, max 20mg) or after 15 minutes following **sublingual** midazolam (<10 yrs - 0.2 to 0.3 mg/kg, max 5 mg; 10 yrs or over is 6-7 mg dose). In accordance with the trust's sedation policy, all children having oral sedation must be kept *nil by mouth (bottle milk, solids) for 6 hours (breast milk 4 hours, clear fluids 2 hours)* and written consent for sedation is required. Vein selection is made taking the needs/request of the patient (e.g. to try to access right arm if they are left handed) into account. Local topical anaesthesia should be offered (EMLA).

We currently use Vygon Nutriline PICC lines which are 30 cms in length and available in 2 French (24 gauge inner lumen, 0.6mm external diameter) or 3 French (20 gauge inner lumen,

1mm external diameter) sizes. As a general guide 2 French lines are suitable for infants and 3 French lines for those > 1 year old. Veins in the antecubital fossa are the preferred sites of insertion (preferably the side the child does not use for writing). Prior to insertion, measure the distance externally from the vein to where you wish the tip to lie (the medial end of the clavicle is the usual position for lines inserted in the antecubital fossa). We do not routinely x-ray these lines but should the child have an x-ray for another reason (e.g. chest x-ray done to check position of pH probe), don't forget to check the position of the line.

The equipment required is:

- Long line (Vygon). Each pack contains: catheter x 1, splitting needle introducer x 1, 10 ml syringe x1, filter needle x1, fenestrated drape x 1
- Surgical gown
- Sterile gloves
- Disposable tourniquet
- Chlorhexidine (Chloraprep) swab stick x 2
- Non-toothed forceps
- Sterile scissors
- 1 x pack
- Steristrips
- Clear sterile dressing ( IV 10000 or Tegaderm depending on the child's allergy status)
- 10ml 0.9% saline
- 10mls heparin saline (10 units heparin/ml)
- 10ml syringe x 1
- Green needle
- Bionector
- Bandage

Position the patient in a comfortable position with the arm extended. Remove the anaesthetic cream and use a tourniquet. Wash hands and put on sterile gloves and gown. Flush the catheter with 0.9% saline to ensure that line is intact. This is a sterile technique so clean the skin with a chlorhexidine swab stick and then place a sterile drape around the arm/leg to create a sterile field. Veins in the antecubital fossa are the preferred sites of insertion (preferably the side the child does not use for writing). An assistant should tighten the tourniquet.

Cannulate the vein and observe for a backflow of blood. Hold the needle stationary and advance the sheath. Release the tourniquet and remove the needle. Thread the line using sterile toothless plastic forceps. If obstruction is encountered try: a) pull back a few millimetres then readvance b) stroking the arm along the line of the vein, c) moving the arm from the shoulder, d) flushing whilst advancing the line. If any sign of swelling or pain occurs then stop. Once inserted to the desired length, flush with sterile heparin saline to confirm patency. Pull back the introducer sheath and split to remove from line. Apply gentle pressure to the exit site to stop bleeding. Secure the line in place initially with steristrips over the insertion site. Cut a small piece of gauze on which to place the bevel of the long line prior to securing with a sterile clear dressing. Flush the bionector and connect to the line before covering the whole dressing with a bandage.

If insertion of a longline is unsuccessful, consider a short cannula while alternate means of access are considered so as not to delay the start of treatment. Anaesthetic teams can be very

helpful particularly if central access is required. If IV access is becoming an issue for a patient, the discussion around portacath insertion should start.

**Thrombophlebitis** - there is some anecdotal evidence for the use of hydrocortisone in long lines complicated by thrombophlebitis. It is **NOT** suitable for blocked lines. It appears to be safe and can be repeated as necessary. The steroid dose is minimal so there should not be any steroid adverse effects. If it is going to work it will usually do so after 24 hours

1. Give IV antibiotics in the usual way.
2. Use 3 mg hydrocortisone made up to 3 mls (with 0.9% normal saline) into PICC line.
3. Leave in line until next dose of IV antibiotic.
4. Aspirate and flush line in the usual way prior to IV antibiotic.
5. Concurrently use 0.5% or 1 % hydrocortisone cream topically on arm (over erythematous area).

Taking bloods from portacaths has been associated with an increased risk of thrombosis, so generally we would try to avoid doing so. However this must be carefully weighed against the potential benefits, particularly for needle phobic/aversive children. Regardless of this, blood aminoglycoside levels must NEVER be taken from portacaths or longlines.

Consider use of urokinase if long line or portacath are blocked (see section 6.2d).

#### 4.4 Procedural distress

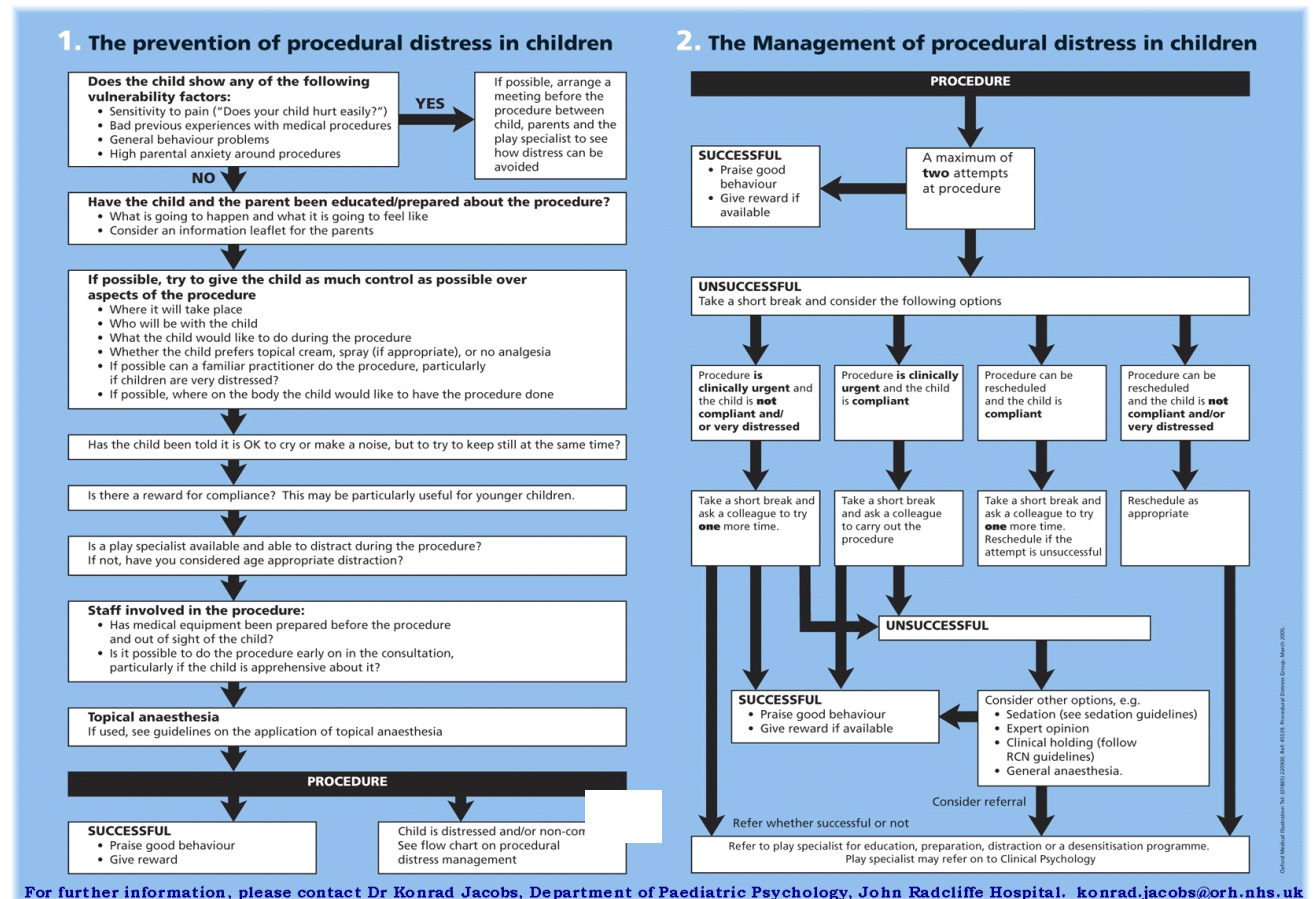
As alluded to above, preparation and planning with the child and family is essential to understand how the CF team can best help them to cope with any invasive procedure. A play specialist is routinely offered to support all children. The following are some suggestions for managing an invasive procedure in all cases, and especially when you know that the child or adolescent is feeling very anxious:

- Ask what has helped previously if/when the child had a good experience.
- Talk to the parent/carer accompanying them about their role; *i.e.*, do they themselves have any fears or anxieties about the procedure; who they want to come in to the room (often as few people as possible is most useful), who will hold the child, positioning the child, soothing the child and above all modelling calm themselves.
- In all preparatory conversations with the family, normalise any anxiety they express, and be empathic (*i.e.* “It’s understandable you feel worried/scared/etc.”, etc.).
- Encourage child to occupy themselves beforehand (gentle exercise, attend hospital school *i.e.* not to sit feeling anxious for an hour before), and keep warm and not become dehydrated.
- Give the child some choice *e.g.* which arm, who they want in the room, what they want to talk about, what distraction has worked in the past etc.
- Make an agreement with the child about how many attempts you will have and do not exceed it. This may mean that you have to take a break and try again later. Do not be afraid to ask someone else if you have missed twice.
- Consider the timing of procedures, as far as possible keep to the agreed time and do not leave the child waiting beyond this.
- If at all possible do invasive procedures in a dedicated treatment room (not the child’s cubicle/play room etc.).



- Make sure all equipment is ready before you get the child into the treatment room.
- Make sure that the child has been to the toilet and removed Tagaderm and EMLA prior to entering the treatment room to avoid prevarication.
- At annual assessment try to do bloods at the time that the child/family have indicated would be best for them - many children prefer to get the blood test done first.
- Consider who should carry out the procedure. If a child is already known to be highly distressed they would benefit from an experienced and confident clinician undertaking the procedure.
- Discuss what reward the child will receive once the procedure is completed.
- Focus on (even small) signs of coping by the child, and praise accordingly.
- Set a time limit, a distressed child is unlikely to change their mind and agree to a procedure that they have been refusing for half an hour. Take a break, re-plan and try again if necessary; again, at the end of the attempt, praise the small signs of coping/trying that have been observed, despite the procedure not being completed.
- Use of supportive holding (previously been known as restraint) warrants planning and agreement with the MDT and family unless the procedure is deemed urgent.

**Managing invasive procedures** - In order to minimise the likelihood of inducing procedural distress, please follow the flow chart below when undertaking any invasive procedure with a child or adolescent. Guidelines from Oxford Radcliffe Hospitals Multidisciplinary Procedural Distress Group, 2005.



## 4.5 Self Administration of Medicines

The Self Administration of Medicines (SAM) scheme is a means of preparing patients and their parents/carers for continuing care and discharge by ensuring that they have sufficient knowledge about their medicines and the practical skills to comply with their therapy. The SAM scheme encourages patients/parents/carers to take more responsibility for their own medicines whilst they are still inpatients. Another useful aspect of the SAM scheme is that it may alert healthcare staff to any problems the patient/parent/carer may have in adhering to the medicine regimen. It also helps to identify patients/parents/carers, that may require additional support or other strategies to ensure adequate pharmaceutical care in the home. The SAM scheme is only intended to operate in the in-patient ward setting.

**Full details are available on the intranet in the 'Medicines Management Policy for the Self-Administration of Medicines in Children'. Below is a selection of details.**

### Criteria for patient selection

- All patients/parents/carers that will be responsible for administering their own medicines at home should be considered for inclusion in the SAM scheme.
- The decision to enrol a patient onto the SAM scheme must be discussed with the multi-disciplinary team.
- Signed consent must be obtained.

The following groups of patients will not be included in the scheme:

- Patients under 12 years of age or those not deemed able to following assessment. However these patients may be included in the scheme if their parents/carers are assessed as competent and are resident with their child patient at all times.
- Patients/parents/carers who are clinically confused must not be given custody of their medicine.
- Parents who would benefit from some further observation and/or education about their medications
- Patients/parents/carers expressing suicidal/self-harm tendencies should not take part in the scheme.
- Patients/parents/carers with unstable medication requirements.
- Patients/parents/carers who will not be responsible for administering their own medicines at their homes after discharge from hospital.
- Patients/parents/carers who are unable/ unwilling to agree to participate in a self-administration scheme.
- Patients/parents/carers with a past history of drug or alcohol abuse do not have to be excluded from the SAM scheme but the need for extra supervision and education should be highlighted and documented.

### Assessment

The assessment of the patient/parent/carer to be consented onto the SAM scheme should be carried out on admission and documented by the nurse responsible for the care of that patient using the self-administration tool. In certain circumstances, the decision to consent the patient onto the scheme can be made later on in their stay. The initial assessment/consent from patients/parents/carers may be obtained at an MDT pre-admission meeting.

Throughout the period of self-administration the patient/parent/carer must be assessed by the nurse **at the start of each shift** as part of the ward routine. The patient's condition and level of supervision required to self-administer medicines may change throughout their stay. If a parent/carer is administering medicines, and will be away from the hospital for a period of time, then the level of SAM will need to be revised for that period of time

After assessment, patients fall into one of the following categories –

Level	Responsibility for administration	Responsibility for storage	Responsibility for documenting administration on Medchart®
0	Nurse	Nurse	Nurse
1	Patient/parent/carer And Supervising Nurse	Nurse	Nurse
2	Patient/parent/carer And Supervising Nurse	Nurse	Nurse
3	Patient/parent/carer	Patient/parent/carer	Nurse

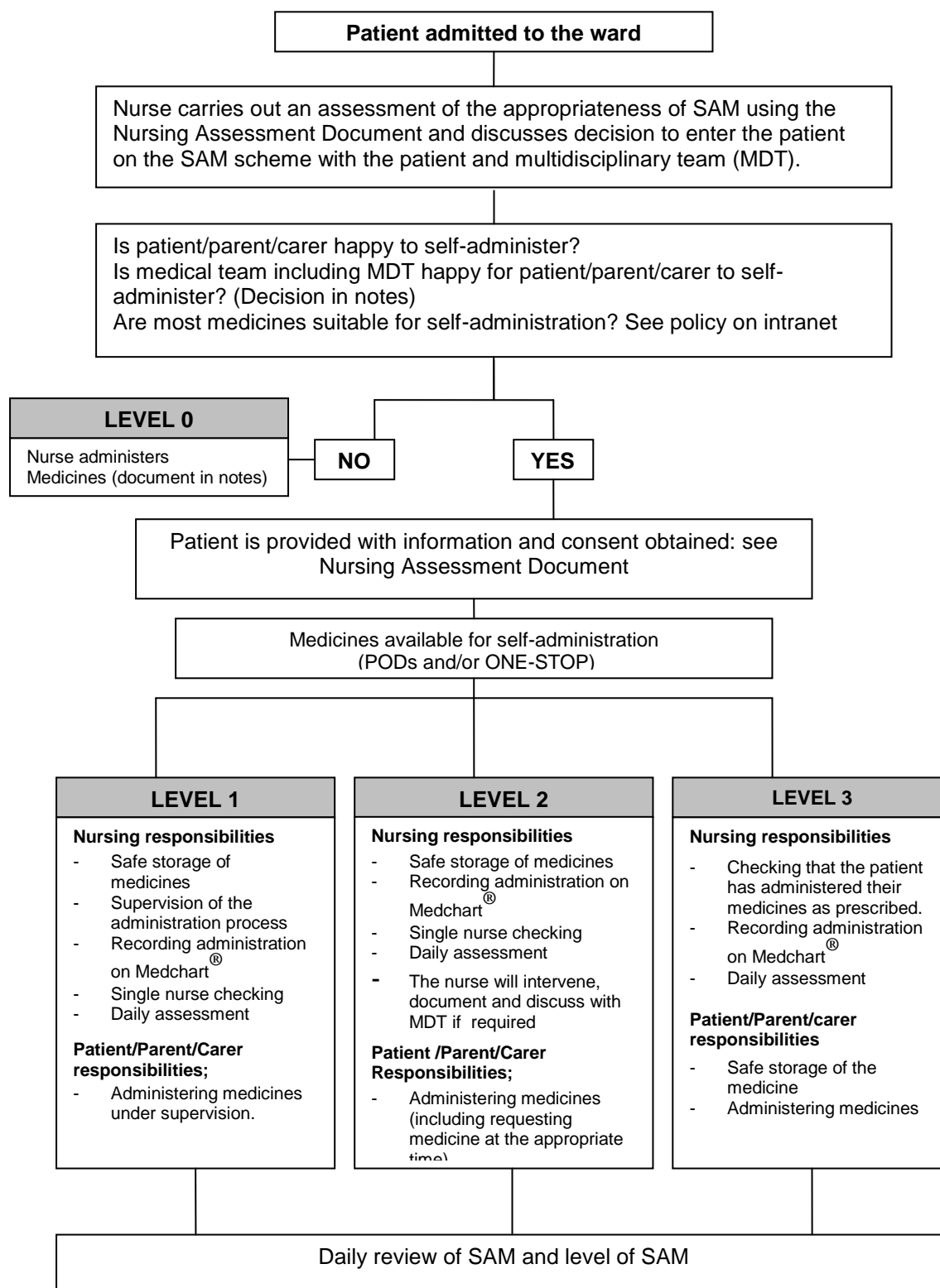
## Other information

- Education / information will be provided by the ward pharmacy team as part of the routine pharmacy service as required. If these staff are unavailable e.g. outside of normal working hours, then the nurse should provide this information.
- All medicines to be self-administered must be prescribed on the in-patient medication chart.
- As a rule, medicines suitable for the SAM scheme are those that are likely to be used on discharge, medicines that the patient/parent/carer has experience of administering prior to admission or medicines that the patient wishes to use in order to empower them to manage their condition e.g. analgesics.
- Patients/Parents/Carers will be encouraged to bring current medication supplies from home.
- Medicines to be used under the SAM scheme should be stored in the Patient's Own Drug locker. Fridges are currently not available in individual bed spaces and therefore certain drugs should be stored in the designated ward fridges until required for administration.
- Controlled Drugs **may not** be self-administered as part of the SAM scheme.
- Intravenously administered medicines **may not** be self-administered as part of the SAM scheme. However an exception to this is where patients/parents/carers are being trained to administer IV medicines so that they may be administered at home
- Administration should be checked for patients/parents/carers self-administering at level 3 at the following set times: **10:00; 15:00; 19:00 and pre bedtime** (this will vary from child to child) so that this will encompass a majority of administration times.
- Administrations must be updated on the inpatient medication chart by the bedside nurse at regular intervals, endorsing who has administered each medication at that time.

## The doctor's role within SAM scheme

- The Consultant with the responsibility for the individual patient's hospital admission must be consulted before the decision is made to enter their patient/parent/carer on to the SAM scheme.
- The Consultant has the right to stop any patient/parent/carer under their care to enter the SAM scheme. Any such decision should be clearly documented and communicated to the admitting team and explained to the patient/parent/carer.
- The Doctor should always discuss changes to the patient's medication therapy with the patient and inform the nursing staff of prescription alterations.

## SAM pathway



## 4.6 Discharge

All children should have a discharge letter done on Inflex before discharge. There is a specific CF summary, which includes:

- The indication(s) and general conclusions about the admission.
- Weight on admission & discharge.
- Spirometry results (absolute and % predicted FEV<sub>1</sub>, FVC) on admission & discharge.
- All drugs on discharge – medications prescribed during the admission can be converted into discharge medications on Medchart®. The discharge prescription will then be sent through to Inflex automatically.
- Ensure you fill in the section on Inflex ‘changes to medications and reasons for those changes’.
- Plan for review - when / where (this should usually be by 4-6 weeks in CF clinic).
- Relevant results including positive microbiology.
- Pending results.
- Plan for tests necessary at home (e.g. WBC after 3 weeks if still on chloramphenicol)
- Date of next admission if elective (3 monthly IVABs, monthly IV immunoglobulin).
- Whether any extra plan needs to be made for further admissions to promote success (*e.g.* how successful invasive procedures were managed).

A copy of the discharge should be given to the parents before discharge. A copy should then be filed in the patient’s notes by the ward clerical staff and published onto EPR.

## 4.7 Infection control

There are concerns about cross-infection between children with CF and these dictate that certain precautions need to be adhered to for all CF children. Segregation is in place in clinic and for in-patients, including in the school rooms etc to minimise contact between CF patients. There is a downside in that social interaction with peers is severely curtailed, and we believe that the children can benefit from talking to each other so do not wish them to be in ‘solitary confinement’. There are international guidelines and many families are anxious about cross-infection and we adhere to these views. Although our ward staff will support and reinforce these measures, we also strongly request that parents/carers help us to ensure that the children stick to the rules.

Generally, personal hygiene is emphasised and children are encouraged to cover their mouths when coughing, then to wash their hands (front and back, and all spaces between). Hands should be washed regularly and they must be taught not to share (with other CF children) cups, cutlery and so forth.

The formal rules are summarised below:

### 1. Ward

- Each patient will either be in a cubicle or in a bay with no other CF patient. No other CF patient or parent is permitted to be in that area at any time. **Children with CF should not enter any other CF child’s room.**
- We also separate children with CF from those with non-CF bronchiectasis/PCD.

- We want to discourage waiting around in corridors on the ward.
- No sitting or waiting around the nurses station, including during the evenings.
- Disinfectant hand rub dispensers are inside each cubicle and each bay for use by staff, all children, families and visitors. USE THEM!
- Doctors **must** clean stethoscopes between patients.
- We have 7 cubicles with their own ensuite shower/toilet and a further one with its own toilet. Children may sometimes be in a bay in which case they use the shared ward bathroom/toilets. However there will be medicated wipes available for parents to use if they wish, before their child uses the bathroom.
- Physiotherapy is carried out in the children's own rooms only. When coughing up sputum, sputum pots with covers should be used, but if tissues are preferred, these should be disposed of immediately in a yellow bin bag.
- Children infected with MRSA *Burkholderia cepacia* and *M abscessus* complex will stay inside their cubicles for the whole admission, although may spend time off the ward.
- When can patients be considered free of their organisms?
  - *B cepacia*: when they have been free of the organism for 1 year, with at least 3 negative sputum or cough swabs or BAL samples in that year. Caution though if the original isolation was on sputum or BAL, and subsequent samples are cough swabs only.
  - MRSA: when they have had 3 negative swabs. If MRSA on skin swabs only – follow Brompton hospital policy - see hospital policy on intranet (<http://www.rbht.nhs.uk/about/policy-and-performance/mrsa-screening/> updated April 2016). If MRSA on sputum/cough swab/BAL – 3 negative respiratory samples, each one taken at least 1 week apart. Caution again as for *B.cepacia* re type of respiratory sample obtained.
  - *M abscessus* complex: considered free when they have had 4 negative samples over 1 year since their 1<sup>st</sup> negative sample. See also sections 3.1 and 6.2a part 6.VII.
- All patients will have a pre op wash with specified detergent on the morning of any surgical intervention as per paediatric department practice to reduce post operative infections.

## 2. Daily Plan

- The daily plan is an integrated plan to be used by the patient, their family and the multidisciplinary team to timetable in appointments, investigations, treatments and school 'time slots'. This will help the children know what is planned for each day. The plan is kept by the beds.

## 3. School Room

- We actively encourage attendance at our hospital school during inpatient stays for **all** patients. This not only serves to help the children to keep up with their studies but also helps them to feel as ordinary as possible during their time on Rose Ward. The hospital teaching staff are also able to look at each child's academic progress and, with the permission of the child and/or their parents to share with the wider CF team any concerns about their learning. Teaching staff attend weekly ward rounds. If permission is given from child/parent, a record of engagement with hospital school is forwarded to the child's community school on discharge.

- The school room has 5 separated areas, 2 primary classrooms and 3 secondary classrooms.
- There will be one CF child in each area only at any time. CF pupils will have access to the schoolroom according to their daily plan.
- They will also be provided with school work from the teachers that they can continue with by their bed space.
- The relevant area is cleaned between patients.

#### 4. Playroom

- The Play Team can support children from 0-16 years.
- Rules for the playroom are similar to school rules.
- Two children with CF can now use the area at one time (one in main room, one in smaller playroom protected by glass walls/door. time. CF children will have access to the playroom according to their daily plan.
- Play sessions will be arranged by the play leaders at the bedside at times when other CF children are having their turn in the playroom.
- Most children with CF are asked (and prefer) to eat in their cubicles/off the ward. Occasionally when a younger child is alone in their cubicle they will be encouraged to eat with some of the other patients (who do not have suppurative lung conditions) in the playroom.
- The relevant area is cleaned between patients.
- Playroom staff finish at 5pm and the playroom closes after supper.

#### 5. Youth Club and School Holiday Program

- When these take place in the school room, the same rules apply as with standard school time.

#### 6. School trips & other outings

- The school is committed to equal opportunities and all children will have access to school trips and outings during their admission, assuming they are well enough. We will have to manage transportation to ensure our guidelines are adhered to (ie, we do not want several children with CF in one minibus). However more than one child with CF may be at the venue e.g. park, museum etc. at the same time. If parents do not want them to go, this will be respected but parents must enforce this.

#### Specific organisms

Particular care is necessary for children who are infected with -

- *Burkholderia cepacia* complex
- MRSA
- *Mycobacteria abscessus* complex
- Multi-resistant *Pseudomonas aeruginosa*
- Respiratory viruses e.g. RSV or Influenza

The following organisms are not of particular concern –

- *Stenotrophomonas maltophilia*. Patients with *S maltophilia* are no longer put in the same category as regards isolation as those with MRSA or *B cepacia*, as our experience and a number of publications have shown the organism is not a major problem in CF.
- Non-tuberculous mycobacteria (NTM) – that is NOT abscessus.



The risk of transmission is related to the level of intimacy of contact. The child is put into a room with private washing and toilet facilities. Items including toys and TVs should be kept in the room and washed when taken out, before use by another child (this includes a stethoscope). Hands are washed and rubbed with Hydrex before entering and leaving the room. Socialising with other children is discouraged and visiting other children in their rooms or being visited by other patients is not allowed. It is important not to stigmatise patients and the reasons for their relative isolation must be carefully explained. It is also important that children with *B cepacia* realise that they do not pose an infection risk for healthy school friends. Relatives of patients colonised with MRSA may also carry the organism. Nasal swabs will confirm this, but are not routinely requested.

Bactroban (mupirocin) nasal ointment may eliminate the organism but recolonisation frequently occurs. In the event of an outbreak, staff with direct patient contact will be screened on the recommendation of the Infection Prevention and Control Team. Such screens will include nose and any skin lesions, particularly those on the hands. Screens will be coordinated by the Occupational Health Department. MRSA positive staff will be given appropriate treatment.

We would suggest though that GPs are asked to 'surface treat' (chlorhexidine and mupirocin) the child's family (parents & siblings). It is also helpful if the child's clothes and bedding are cleaned in a 60°C. wash during the eradication period.

Children with Burkholderia species and MRSA do not attend the CF clinics and like all our CF patients, do not mix with other CF children in the hospital school and play room. These patients will attend clinic on the 2<sup>nd</sup> Friday of each even month (Feb, April, June, Aug, Oct, Dec). Patients with MRSA will be booked into earlier time slots and those with *B cepacia* having later time slots. Due to the adult *B cepacia* clinic being held downstairs, patients will be advised to come in via Fulham Road entrance and go straight up the stairs and through physiotherapy into clinic. The HCA/Nurse will take prescriptions down to pharmacy so they do not mix with patients waiting downstairs.

### Segregation clinics

- Clinic appointment letters give a specific appointment time and this is now crucial. It is very important that these times are kept to, so that the clinics run smoothly. If patients arrive early, we will have to ask them to leave the clinic area until the allotted time unless a clinic room happens to be available. We will then contact them on a mobile phone if the room becomes free early. If they are late for the appointment, they may have to wait until the end of clinic to be seen. These clinics are very complicated to run hence the need for such a rigid policy.
- Each child is allocated to one room, and all the members of the CF team (physiotherapist, dietitian, doctor, CF nurse) come to see him/her in that room.
- All procedures are undertaken there (height & weight measurement, lung function, cough swab/sputum collection, blood testing).
- There will be no sitting in the waiting area as children will only be in their own clinic room; we will encourage children to bring their own toys and books etc with them. At the end the family leaves out-patients immediately.

- Between patients, the room is thoroughly cleaned (desktops, chairs, other surfaces, sinks) and the next patient enters.
- We will continue to have free slots at the end of clinics to see children at short notice who have become unwell and phoned us urgently. Patients must not arrive without telephoning to book a slot however. Of course, all children needing to be seen will be seen, as is now the case.
- It is important appointments are cancelled if the child is not coming, in order not to waste a slot.
- Some of our annual assessments are done on Tuesdays during a general respiratory clinic, improving efficiency and reducing risk.
- All children with MRSA or *B cepacia* come to clinics reserved for them only on the SECOND FRIDAY of the month with MRSA in the first wave and *Burkholderia* in the second wave.
- All children with any form of NTM come to second wave appointments only, because of the greater time (45 mins) required between patients with NTM for aerosols to disappear.

## 5. Making the diagnosis

Since October 2007, newborn screening for CF has been in place throughout the whole of the UK (1<sup>st</sup> July 2007 for those born in our region). At our centre, the majority of new diagnoses are now through this route. Conventional methods of diagnosis are still used to confirm the screening results and will be needed for the small proportion of CF children (estimated at 3 per year for London and South East England) in whom the diagnosis was missed by screening. About 5% of babies & infants diagnosed with CF were missed on screening in the 4-year audit. These will often have a mild phenotype. We no longer use the term 'atypical' CF.

### 5.1 Newborn Screening

Immunoreactive trypsinogen (IRT) is measured on a dried blood spot obtained on the Guthrie card at day 6 of life. Samples with abnormally raised IRT levels will undergo CFTR mutation screening as per the flow chart (see below). Some children require a second heel prick.

Positive screen results are conveyed directly by the screening laboratory to the specialist centre and the screening pathway initiated.

The CF Nurse Specialist liaises with the baby's Health Visitor to discuss the result and arrange a joint visit to the family. This takes place within 5 working days on a Monday or Wednesday afternoon, enabling the sweat test to be performed the following day on a Tuesday or Thursday morning. The Health Visitor is requested by RBH not to contact the family until 9 am on the day of the visit, to arrange the appointment with them, so we do not prolong the waiting time and anxiety. The HV will be briefed by the nurse specialist to explain to the family that a nurse from the hospital will accompany them regarding part of the new born screening results and that they suggest both parents may wish to be present at the visit. We are auditing the parents currently to see if this is still the best way to organise our first contact.

In the home it is explained that CF is likely, but that a sweat test is required and an appointment has been arranged at the Royal Brompton the following day. The family will be seen by one of the CF nurse specialists, and if possible, briefly by the consultant, to introduce themselves. The sweat test is performed, which is mandatory (even if two genes have been identified), to rule out any possibility that the screening sample has been misidentified. Results are available within an hour, allowing, in the majority of cases, the diagnosis to be confirmed to the family by the Consultant; in rarer cases where the diagnosis is unclear, we follow a different pathway - see below. The Consultant will then take a full history, carry out an examination and answer the parents' questions. The basics of CF may be discussed but at this time of great stress, we attempt to limit the amount of information conveyed to parents, most of which will be discussed at the Education Admission. Similarly, screened babies are usually well.

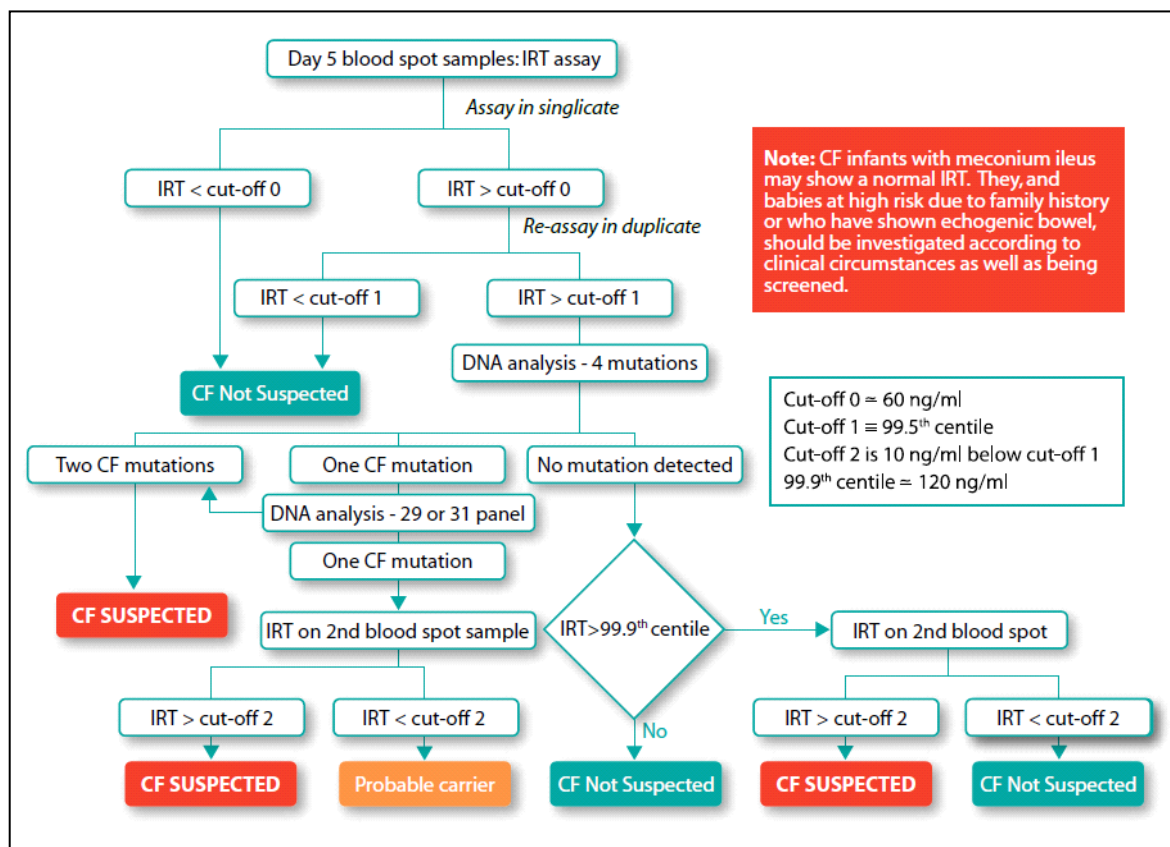
Treatment will usually not be initiated at this time with the exception of pancreatic enzyme supplements if symptoms are indicative of pancreatic insufficiency (abnormal stools, very hungry baby, concerns over weight); if there is doubt the dietitian will see the baby that day. A sample will be collected for stool elastase or parents are given a pot to send back. Just occasionally oral antibiotics are needed as the baby has chest symptoms.

The child's GP will be informed by the consultant or nurse specialist once the diagnosis of CF is confirmed and in some cases a shared care consultant is also contacted.

A two day educational admission will be arranged for the week after diagnosis. Families are usually admitted to a cubicle in the Sleep Unit, and may go home overnight if they wish. A timetable is pre-arranged to ensure that each member of the MDT has an allocated slot in which to teach the family about their role within CF. They will meet with the consultant, nurse specialist, home care nurse, dietician, physiotherapist, clinical psychologist, pharmacist and family liaison officer. The consultant, dietician, nurse specialist and physiotherapist meet with the family on both days to answer any questions that may have arisen.

Medication and physiotherapy are started during the admission.

After the two day admission the home care nurse visits the family the next week to offer support and go over what was taught during the admission. They review medications, physiotherapy and any problems that have arisen. The child is then seen in clinic the following week. These appointments are made during the two day admission.



Older siblings of babies diagnosed by screening will have a sweat test; usually the parents are keen for this to be done soon to allay their worries. However it is not advisable to do this during the education visit as we have had a case of an asymptomatic older sibling being diagnosed at that difficult time; offer to do this before the visit, or arrange for the local hospital to do it.

## 5.2 Clinical presentation

This is rare now that newborn screening is well established. However it is **essential** that the possibility of a CF diagnosis is not ignored or 'ruled out' if a baby has been born since screening began as screen failures do occur. Additionally, children born before screening may present late with clinical features, as may babies born abroad. Lack of experience of clinical staff may actually lead to further delays in diagnosis in such groups of children. The history and/or examination will usually raise suspicions of the CF diagnosis. Common features are recurrent respiratory infections and failure to thrive with steatorrhoea (but do not be fooled by the thriving child). Other features in a baby that mean CF must be excluded include meconium ileus, rectal prolapse, salty tasting skin, prolonged obstructive jaundice, electrolyte disturbance suggestive of Pseudo-Bartter's syndrome and unexplained haemolytic anaemia, hypoalbuminaemia and oedema. Finger clubbing and nasal polyps in an older child are also important, as is isolation of *S. aureus* or *P. aeruginosa* from the respiratory tract. Confirmatory investigations are outlined below. If in any doubt, we do a sweat test, and if anyone at all (including parents) is worried about CF, we do a sweat test.

## 5.3 Sweat testing

Sweat testing will reliably make the diagnosis in 98% of patients. Despite the availability of genotyping (and because of its limitations) the majority of children in whom CF needs to be excluded will undergo sweat testing. This group will include the following:

- Baby with a positive newborn screen.
- Child with suggestive history / symptoms/ examination.
- Sibling of a known case (even if asymptomatic).
- More distant relative of known case if clinical suspicion.

We perform the sweat test using the macroduct system, and analysis can be reliably performed on small quantities. Minimum of 20 minutes and maximum of 30 minutes is the recommended testing time. Sweat testing can be performed once a baby is > 48 hours old although often inadequate samples are obtained in the first few weeks.

As with any of these techniques, it is extremely important that they are performed by personnel who are experienced. Only the CF nurse specialist, Day-case nurse or trained out-patients nurses carry out our sweat tests. The sweat is analysed by the Biochemistry lab and results include sweat volume and  $\text{Cl}^-$  levels. National guidelines for sweat testing have been updated in 2014 -

[http://www.rcpch.ac.uk/system/files/protected/page/Sweat%20Guideline%20v3%20reformat\\_2.pdf](http://www.rcpch.ac.uk/system/files/protected/page/Sweat%20Guideline%20v3%20reformat_2.pdf).

### Results must be interpreted in the clinical context

Normal range  $\text{Cl}^-$  <30 mmol/l;

Borderline  $\text{Cl}^-$  30 to 60 mmol/l (although in infants, this is still highly likely to be CF).

CF confirmed  $\text{Cl}^-$  >60 mmol/l.

Chloride is the primary ion measured; sodium should not be measured alone. We do not measure conductivity and do not advocate its use. The diagnosis of CF should be made on the

basis of 2 sweat test results not one, we take 2 samples at the same time from different limbs. If there is any doubt over a result, repeat the test or discuss it with a consultant. Flucloxacillin, commonly listed in old texts as a cause of false positive sweat tests, has no effect on a sweat test result.

**False negative results.** Cases are increasingly recognised where the clinical picture of CF is supported by genotyping, but in the presence of a normal sweat test (<1% CF patients). Beware therefore of excluding the diagnosis (in highly suggestive cases) on the basis of a normal sweat test alone. Genetic testing would be the appropriate next step (see below). Discuss the case and the possibility of nasal potential difference testing with Prof Jane Davies (see later).

**False positive results.** Many theoretical causes as listed in textbooks, most of which do not appear to cause problems in routine clinical practice. Those which may be encountered include malnutrition or skin disorders such as severe dermatitis/eczema. Transient increases in sweat electrolytes have also been reported in young patients with immunodeficiency states.

## 5.4 Genetic analysis

There are currently at least 2000 identified mutations in the *CFTR* gene, although not all of them are definitely associated with the clinical picture of CF. Mutations fall into different classes (I-VI), with commonest in the Caucasian population being a class II mutation, F508del (formerly)  $\Delta$ F508. Nomenclature has changed recently (see appendix 11).

The CFTR2 website is a growing resource which provides excellent data on gene mutations and their expected effects. See [www.cftr2.org](http://www.cftr2.org).

**In all children with a diagnosis of CF, we will now seek to fully identify two gene mutations including full gene sequencing if required because:**

- In a child diagnosed with CF:
  - it facilitates screening for other family members.
  - and allows prenatal diagnosis of future pregnancies.
- Is an eligibility criterion for mutation-specific therapy (ivacaftor) and may allow enrolment into clinical trials of other agents
- For pregnant mothers of affected children, cord blood testing should be planned for the newborn sibling at the time of birth (arrange with mother in clinic, give form and blood bottle).
- Generally older siblings will have a sweat test for diagnosis rather than genetic analysis. The latter would detect carriers, which is something that should be postponed until the sibling is old enough to decide whether they wish to know their carrier status (usually mid teens and older).
- We will also use extensive genotyping in cases of borderline diagnosis.

Based on current knowledge, genotype analysis should *not* be used to guide prognosis in an individual child, except rarely (and very cautiously) in the case of mutations usually associated with pancreatic sufficiency (e.g. R117H). Pancreatic status should be confirmed with a faecal elastase in all cases; PS may evolve into PI over time, so repeat measurements should be considered and attention paid to symptoms and nutritional progress. Although

studies have shown a milder lung phenotype in certain groups such as these, patients with typical, severe lung disease have also been described, hence it is best not to prognosticate in individual cases. There can also be problems occasionally with a genetic diagnosis of CF in a patient who is asymptomatic with no apparent CF phenotype. These must be discussed with the consultant.

### **Limitations of mutation analysis**

Due to the large number of identified mutations, and the extreme rarity of many of these, it is only practical to screen for a few on a routine basis. This will usually include the commonest 50 mutations (which is standard at our genetic referral lab, Kennedy-Galton and costs £156). Clearly therefore failure to detect mutations does not exclude the diagnosis. The above is of particular importance in a child of non-Caucasian origin. There is now a specific panel of mutations, which are common in the Asian community. It is therefore **CRITICALLY IMPORTANT** that in every case the child's ethnic origin is included on the request form so that the most likely mutations can be looked for. Full gene sequencing can be performed if specifically requested but is expensive (in the order of £500) and time-consuming; whilst previously we would not have performed this routinely in patients with a clear-cut biochemical diagnosis, this should now be done, for the reasons above. Samples should be sent to the Biochemistry Laboratory who will forward them to Kennedy Galton Centre (KGC, see below); they now perform extended analysis so we no longer send samples to Manchester.

### **Practicalities of genetic testing**

Take blood (2-5ml) into EDTA bottle.

Complete genetics form.

Samples need to be either given to Jackie Francis or sent to our Clinical Biochemistry Laboratory who will forward them.

Samples from outside the Royal Brompton Hospital should be sent to:

DNA Laboratory (Cystic Fibrosis)  
Kennedy Galton Centre  
Level 8V  
Northwick Park & St Mark's NHS Trust  
Watford Road, Harrow  
Middlesex HA1 3UJ

Tel: 0208 869 3180

## **5.5 CF Screen-Positive, Inconclusive Diagnosis (CFSPID)**

There are two scenarios in which making a diagnosis after a positive NBS is less easy:

- Borderline sweat test (30-60 mmol/L) in the presence of zero or one gene mutation.
- Normal sweat test in the presence of 2 mutations, at least one of which is of uncertain significance. The significance of mutation can be looked up on CFTR2 website on [www.cftr2.org](http://www.cftr2.org) which currently covers the commonest mutations, although the database will grow.

There has been a recent Delphi consensus process (*J Cyst Fibros* 2015;14:706-13) upon which our management is based and the terminology agreed of 'CF Screen-positive, Inconclusive Diagnosis (CFSPID)' – see Appendix 10. It is essential that the diagnostic uncertainty is shared with the parents and we avoid any temptation to 'label' a baby prematurely; undoing a CF diagnosis poses its own problems for families. Babies with <2 mutations should have full *CFTR* sequencing *without delay*.

### Mutations of varying clinical consequence

There are a number of mutations in this category. Most common one leading to this scenario is R117H/7T (if R117H is reported, always make sure the 7T/5T variant is included, otherwise *check with lab*).

- R117H/5T leads to low levels of CFTR function and is considered a diagnostic mutation;
- R117H/7T leads to variable amounts of CFTR function and is so commonly found in non-CF populations in combination with F508del, that this is not completely diagnostic. Some patients with these mutations will have CF, usually pancreatic sufficient and often presenting with symptoms much later in life, and others will not.
- 9T is very rarely seen associated with R117H, so if lab report says F508del/ R117H and 9T/5T, the R117H and the 5T are together, (sometimes termed *in cis*), and the 9T can be ignored. The child therefore has the diagnostic 5T mutation.
- Other mutations in this category (this not comprehensive, so if in doubt, check CFTR2): D1152H, L997F, 5T.

### Follow up

- All CFSPID babies should be referred to Prof Jane Davies' general respiratory clinic, where they will receive further information, clinical surveillance and further CFTR functional testing (repeated sweat testing +/- nasal PD, stool elastase) until the clinical picture becomes clearer.
- The main aim is to avoid over-medicalisation, whilst maintaining sufficient observation of the baby to detect any concerns. CFSPID is not a diagnosis, nor was it intended for long-term use. We seek clarification over time of the clinical status:

#### (1) Evolve into CF:

- increasing sweat Cl-
- evolution of clinical symptoms - development of pancreatic insufficiency would be enough in itself; respiratory symptoms can be more difficult, as all young children get coughs. Severe or persistent symptoms would be of concern, as would those accompanied by positive cultures such as *P. aeruginosa*.
- CFTR dysfunction confirmed on nasal PD (although this is very difficult in young children)
- these children will be transitioned into the CF clinic and will then be entered onto the database; they may continue to have a milder clinical course than their conventionally diagnosed counterpart.



**(2) Remain well with normal or borderline tests:**

- at the time of writing, we are considering how best to undertake long term care of these children. It is likely that we may see them with decreasing frequency and/ or transition to telephone follow up during childhood.
- in this case, we would bring the family back when the child reaches adolescence to discuss the risk that some of these patients may acquire chest disease (sometimes significant bronchiectasis) in adulthood. Smoking avoidance etc. will be discussed.
- Jackie Francis is the CFSPID nursing link, through whom any enquires can be passed.
- Michele Puckey, Consultant Paediatric Psychologist, has an interest in this field and can be consulted for help; these parents often find the uncertainty extremely difficult to deal with.
- At the current time, these babies should not be entered onto the national registry, although work is in place to adapt the registry to include a specific CFSPID section. Should they acquire a diagnosis of CF later, they will be added then.

**5.6 Antenatal screening**

Carrier parents contemplating another pregnancy should be referred for genetic counselling in order to decide whether they would like antenatal screening (CVS, which can be performed around 10-12 weeks gestation or amniocentesis which is usually slightly later).

On the basis of the limited number of mutations screened for, some CF children will be, for example, F508del/-, meaning one detected and one undetected allele. Failure to detect both mutations in the proband does not rule out the possibility of antenatal or sibling diagnosis, as linkage analysis may be possible. Parental blood samples would be required.

When the mother of a child with CF has a subsequent pregnancy, it is important that when they are in clinic with their CF child, we discuss the possible outcomes of the pregnancy. Specifically, the baby is at risk of meconium ileus (particularly if we know the first child is F508del homozygous should it turn out to have CF. Our advice is that the child is not taken home until it has established feeding and had a normal bowel motion. In addition, we recommend that a cord blood sample is taken for DNA analysis, and we give the mothers a form for CF genetics with the relevant blood bottle (EDTA red bottle) to hand to their midwife. The cord blood result is usually ready before the Guthrie card CF screening result is available. We expect that the mother will have informed their obstetrician that they already have a child with CF.

**5.7 Pre-implantation diagnosis**

For parents wishing to consider pre-implantation diagnosis, to ensure an unaffected fetus, we usually ask their GP to refer them to Mr Yacoub Khalaf at Guy's and St Thomas' Hospital Centre for Preimplantation Genetic Diagnosis.

Their website states the criteria for starting PGD treatment -

- You are under the age of 39 for women;
- You complete and return our questionnaires;
- You are living together in a stable relationship;

- (For women) your hormone levels are within a range that suggests that your ovaries will respond to treatment;
- an accurate test is available and there is a license from the HFEA;
- the PGD team agrees that you are suitable for treatment;
- there are no concerns about the welfare of any child conceived using our treatment; and
- Funding is available– either from the NHS or yourselves if you choose to pay for your own treatment. Private costs are £8000 per cycle plus drug costs (£1000-2000).

There may be an issue with CCGs agreeing to pay for the procedure. Referral forms are downloaded from [www.pgd.org.uk](http://www.pgd.org.uk) and sent to -

Centre for Preimplantation Genetic Diagnosis  
11th Floor, Tower Wing  
Guy's Hospital  
Great Maze Pond  
London SE1 9RT

Tel: 0207 188 1364

Email: [pgd@kcl.ac.uk](mailto:pgd@kcl.ac.uk)

## 5.8 Other tests

These may be supportive of the diagnosis:

- **Stool elastase:** low in CF with pancreatic insufficiency (usually <15 mcg/g). Normal levels (are expected by day 3 in term infants and by 2 weeks of age in those born less than 28 weeks gestation, so tests should not be performed before this time.
 

Normal	> 200	mcg/g stool
Mild/moderate pancreatic insufficiency	100-200	mcg/g stool
Severe pancreatic insufficiency	< 100	mcg/g stool

These are sent by our biochemistry lab to Biochemistry Department of Sandwell and West Birmingham City Hospital. For newborn screened babies, the lab will prioritise samples to try to get the result back in 4 days, so that it will be ready for when the parents come in for their Education Visit.

- **Nasal potential difference (PD):** difficult in small children as requires co-operation, but may be useful in older indeterminate cases (over 8-10 years). Can be done easily on young children whilst under general anaesthetic, e.g. for bronchoscopy. We rarely obtain useful readings in the presence of nasal polyps or if there has been previous nasal surgery, and it should definitely be postponed if the child has had a cold within the last 2 weeks. It is a difficult and time-consuming investigation and will therefore usually only be done once all other CF investigations are complete. Please refer to Prof Jane Davies (via PA, Gina Rivellini, [g.rivellini@imperial.ac.uk](mailto:g.rivellini@imperial.ac.uk), 0207 594 7980), who runs a specialised nasal PD clinic monthly.

## 5.9 Routine investigations for newly diagnosed patients

For many years we have carried out routine surveillance bronchoscopy and pH study on all newborn screened infants at 3 months of age. Our latest audit of data no longer supports use of routine bronchoscopy over surveillance swabs, which has been aided by the introduction of induced sputum cultures. We are also aware that it is quite difficult for the families to have their baby undergo this general anaesthetic procedure. We will certainly have a low threshold though for diagnostic bronchoscopy and BAL in young children if there is any clinical concern, and induced sputum has not been helpful.

Our data has revealed 50% infants have gastro-oesophageal reflux. We will continue to have a low threshold for starting reflux therapy when babies have symptoms. Furthermore, if infants have recurrent growths of coliforms (*e.g. Enterobacter, Escherichia, Klebsiella, Citrobacter*), we will assume the child has reflux, treat accordingly and consider a pH study.

Blood is taken if the CF genotype is not known from the heelprick screening sample, although the laboratory may have stored DNA if extended genotyping is required so check first. Otherwise blood is not taken until 1<sup>st</sup> annual review.

## Respiratory care

### 6.1 Chest exacerbations

A chest exacerbation is a serious adverse event. Around 30% never recover their previous spirometry, and multiple exacerbations are associated with an accelerated decline in lung function, and greater likelihood of progression to transplantation or death. A rapid and focussed response is essential. If the family is worried they will usually phone the CF nurse specialist or the ward. Sometimes telephone advice can be given (by nurse specialist, SpR or more senior doctor only) but often the patient will need to be seen. Preferred option is in the next clinic, but they may be seen on the ward in special circumstances. Remember with the segregated clinic system the family cannot be told they can turn up any time in the afternoon of the clinic day. They **MUST** telephone out patients for a time slot, but tell them to ring back if Appointments will not give them an appointment. If the family comes from a long way away, then consider using the local hospital, but brief whoever will see them there and ask for a report back. Some indications of chest exacerbation are:

- Increased cough, and in particular a new or increased ‘wet’ cough should always be taken seriously.
- Adverse changes in sputum production (volume, colour, consistency).
- Haemoptysis.
- Increased dyspnoea.
- Chest pain or tightness.
- Malaise, fatigue and lethargy.
- Fever > 38° C. Note that most CF chest exacerbations are **not** accompanied by fever.
- Loss of appetite or weight loss.
- Drop in FEV<sub>1</sub> or FVC >10% from previous recording.
- Adverse changes in chest sounds on auscultation (crackles, wheeze). However a clear chest on auscultation does **not** exclude an infective exacerbation. Much more sensitive is palpating the chest while the patient coughs or huffs. New or increased palpable secretions should always be taken seriously.

If the situation is dealt with over the telephone, it is essential that the CF nurse specialist is informed, so appropriate follow up (home care team, telephone) can be arranged. It is important to send (or arrange for GP or local hospital to send) sputum or a cough swab to microbiology; an NPA may be performed in infants. A chest x-ray is only occasionally useful. **A clear-sounding chest does not mean there is no infection present.** Antibiotics should be prescribed, initially orally (unless the child is obviously very unwell); with IV antibiotics given if the child fails to respond. Do not keep on and on with oral antibiotics if the child has not responded. Whereas it is completely fine to give repeated oral courses to cover viral colds if the child is well between colds, multiple oral courses to the chronically symptomatic, non-responding child are not useful. At most, one general course (e.g. co-amoxiclav) and one anti-pseudomonal course (ciprofloxacin) or chloramphenicol should be given before resorting to IV antibiotics. Some children need IV antibiotics from the start.

The published literature shows that virtually all improvement in spirometry occurs by day 13, and if there is no improvement by day 7, this is an adverse prognostic sign. We therefore need to formally reassess progress on **day 6-9**, and if there is no improvement in spirometry consider (a) induced sputum or bronchoscopy to determine if there is an untreated infection;

(b) additional mucolytics; (c) change in IV antibiotics; (d) consideration of another diagnosis, e.g. ABPA, reflux and aspiration; (e) non-CF associated coincident diagnosis; (f) ensure child is well hydrated.

IV antibiotic courses may be extended to a third week because of symptoms or to increase time to next relapse, but spirometry is unlikely to improve. Multiple pulmonary exacerbations should lead to consideration of activating the 'challenging CF' protocol. At the very least, a crude adherence check (prescription uptake and downloading data from their nebuliser) should be performed.

## 6.2 Antibiotics

### 6.2a Policies & specific organisms

#### 6.2a 1. Introduction – some principles

Note that if a patient is still symptomatic or has a positive culture after an appropriate course of antibiotics, admission should be discussed with a consultant. We should not give endless oral courses; the use of more than two successive courses of oral antibiotics for the same exacerbation must be discussed with the consultant; but this is a different situation from the child who gets completely better, and a few weeks later has a 2<sup>nd</sup> oral course, from which they get better again.

**Drug doses.** In general, high doses are required because of high renal clearance and also to ensure high levels of tissue and sputum penetration (see drug formulary section 11). Use the serious infection doses, and round up not down. Do not prescribe silly volumes e.g. 3.44 ml - the nurses cannot measure them accurately, and neither can you. CF is a serious condition and the aim of therapy is to push antibiotic doses to the upper therapeutic range. When results of sputum culture are available, confirm that all organisms are covered by the chosen regimen. However, if the child is improving clinically on antibiotics to which the organisms exhibit *in vitro* resistance, do not automatically change them (but discuss with consultant). There is no evidence that *in vitro* sensitivity testing correlates with clinical outcomes.

#### 6.2a 2. Viral colds

**Viral colds at home or in clinic, with no or minor chest symptoms (i.e. not major exacerbation).**

Always inform the CF nurse specialist or the home care team to arrange at least telephone follow up, and local hospital/GP as appropriate. It is particularly important that this happens for 'out of hours' calls taken by the SpR.

- i. Use treatment dose of co-amoxiclav for minimum of 2 weeks (see para iv).
- ii. If on flucloxacillin prophylaxis - **stop it**. Give treatment dose co-amoxiclav for minimum of 2 weeks (see para iv).

- iii. If on no prophylaxis, you must prescribe an antibiotic, which will cover *S aureus* and *H influenzae*. 1<sup>st</sup> choice is treatment dose co-amoxiclav; acceptable alternatives would be a macrolide (clarithromycin or azithromycin), although microbial resistance is a concern. We do not tend to use oral cephalosporins although the concern with *P aeruginosa* relates more to their prophylactic use. Note that cefixime has no anti-staphylococcal activity, and should not be used in this context.
- iv. They must be given for **a minimum of 2 weeks, but carried on for at least 1 week once the child is symptom-free**. So if for example, the child is completely well after the 1<sup>st</sup> week, then they can stop the antibiotics at 2 weeks. If it takes 2 weeks to become symptom free, the antibiotics can be stopped at 3 weeks. If however the child is not symptom free at 2 weeks, the parents must contact the CF nurse specialist for assessment.
- v. It is important to differentiate [1] the child with a cold who gets better, and then has another cold soon after; for them repeated courses of oral antibiotics are appropriate (especially in the younger children during winter); from [2] the child given repeated courses of antibiotics, who does not get better, and who needs IV antibiotics instead. Remember a normal child with a normal cold may have symptoms for 3 weeks, and 10 colds a year is normal in a pre-school child.
- vi. Oral ciprofloxacin for **2-3 weeks** if no course within previous 3 months, and previous isolation of *P aeruginosa*. It is a *consultant decision* to extend course beyond 3 weeks. In general, we try to reserve ciprofloxacin for exacerbations rather than simply to cover a minor cold.
- vii. The same is true for chloramphenicol which is very expensive in the UK. Co-trimoxazole is also used, but concerns about the rare complication of bone marrow suppression remain.

### 6.2a 3. Surveillance respiratory cultures

Cough swabs/sputum must be sent every time a child is seen in clinic, the ward or at home. Also culture sputum if produced for non-tuberculous *mycobacteria* on annual assessment visit, in a child who is unwell but culture-negative, on bronchoalveolar lavage, and on admission for an exacerbation, and also when previously cultured. Culture of cough swabs for NTM is **not** useful. Remember to write 'CF' as the diagnosis so the laboratory put up the cultures to the panel of antipseudomonal antibiotics.

**Positive surveillance cultures.** If a child is known to be chronically infected with a particular organism (3 positive samples in the last year), and the child is well and asymptomatic, a positive routine clinic swab is not necessarily treated, although often will be. The decision not to treat **MUST** be discussed with the Consultant.

### 6.2a 4. Treatment of unknown organisms

- Check previous cultures i.e. is the child chronically infected with an organism.
- Consider whether it is a viral exacerbation.
- Ensure cough swab/sputum collected for culture.

**Oral treatment for mild exacerbation –**

- Oral co-amoxiclav for minimum of 2 weeks, but for at least 1 week after the child is symptom-free (see above, 2.iv for details)
- Consider oral azithromycin 10 days.
- Consider oral ciprofloxacin 14 days especially if PsA grown in past.
- If severe, admit for IV antibiotics (see below).
- If the child is not symptom-free at 2 weeks, the CF Unit must be contacted by the parents. Our CF nursing team though will take the initiative and speak to the parents anyway.
- If spirometry was reduced at diagnosis, it must be repeated.

**For any gram-negative organism we must have full identification & extended sensitivities.** Sometimes it turns out to be a *Pseudomonas* (not *aeruginosa*) and it is not enough to accept a report that says ‘coliforms’ or ‘gram-negative bacilli’ for example, from a local hospital. Ask the laboratory to send the strain for typing to the Public Health England Laboratory at Colindale (see appendix 20 for contact details).

**6.2a 5. Intravenous antibiotics – principles for unknown organism**

i. **Choice of intravenous antibiotics.** This may depend on previous sputum results.

- *No previous P aeruginosa* - must cover common pathogens including *S aureus*, *H influenzae*, *Moraxella catarrhalis* as well as possible first isolate of *P aeruginosa* (especially young infants). Start with meropenem (more gram positive and anaerobic cover than ceftazidime), and tobramycin.
- *Chronic infection with P aeruginosa* – ceftazidime & tobramycin is 1<sup>st</sup> line unless previous sensitivities or patient experience that another combination works better, suggest otherwise. If *S aureus* is isolated within the last year, add in IV teicoplanin rather than high dose oral flucloxacillin. Flucloxacillin is not used IV as it causes problems with IV lines and may cause backache.

**ii. When to change antibiotics**

There is no evidence that *in vitro* sensitivities correlate with *in vivo* outcome. Therefore, if the child is improving on ‘best guess’ antibiotics, but the *Pseudomonas* comes back ‘resistant’, do NOT change drugs without first discussing with the consultant. If the child is not responding, a change may be indicated whatever the sensitivities – again, discuss with the consultant. If a change is made, do it at such a time that the CIVAS (Centralised Intravenous Additives Service) can be used to fill the new prescription (section 11.1d).

**6.2a 6. Treatment of specific organisms**

- A positive culture result will guide choice of antibiotic treatment, although the evidence that culture results predict treatment is weak. Do not change antibiotic therapy which is working just because of a culture result.
- **First** isolation of an organism is always treated.

## **6.2a 6 L. *Staphylococcus aureus***

### **Ia. Prophylaxis**

- The question of staphylococcal prophylaxis is based on a few studies only and evidence for benefit is weak. However it is our policy to start it in all newborn screened children, unless there is a compelling reason not to, *i.e.* not tolerated, or allergy. If the child really will not take flucloxacillin, try another brand if available. It may be necessary to switch to co-amoxiclav, but we are reducing our use of co-amoxiclav as a prophylactic agent. In penicillin allergic children, if the history is dubious or uncertain we will test to ensure they have a true penicillin allergy before considering using a macrolide (with a strong history, testing is unnecessary). However, *S aureus* in particular, rapidly becomes macrolide resistant. See formulary section 11.1a for doses.
- Once aged 3 years, flucloxacillin (or co-amoxiclav) prophylaxis should be reviewed, and only continued if *S aureus* is repeatedly cultured, in which case the possible reasons for this (e.g. non-adherence) need to be considered. **The default therefore will be to stop staphylococcal prophylaxis at 3 years of age** (in line with CF Trust national guideline). Oral cephalosporins should not be used for prophylaxis (or if at all possible for treatment) because of evidence implicating this class of antibiotics as causing a greater prevalence of infection with mucoid *P aeruginosa*.

### **Ib. Exacerbations**

- If already on flucloxacillin prophylaxis, give treatment dose for **4 weeks** if *S aureus* is isolated and thought to be cause of the exacerbation.

### **Ic. First isolation**

- *In a well child* (clinical judgment) receiving flucloxacillin prophylaxis, we use oral co-amoxiclav for **4 weeks**.
- *In a well child* (clinical judgment) **not** receiving flucloxacillin prophylaxis, we use oral flucloxacillin for **4 weeks**.
- *In an unwell child* admit for IVABs. Use Meropenem + Tobramycin + teicoplanin for 14 days as 1<sup>st</sup> line.

### **Id. Re-growths**

- *Re-growth less than 6 months* from 1<sup>st</sup> growth - oral flucloxacillin for **4 weeks**.
- *Re-growth after more than 6 months* from 1<sup>st</sup> growth - treat as for 1<sup>st</sup> growth (see above).
- *Further re-growth within 6 months* - Two oral anti-staphylococcal antibiotics (*e.g.* rifampicin and fusidic acid) for **4 weeks**.

### **Ie. Chronic infection**

- If there are more than 2 isolates of *S aureus* in a year, give prophylaxis with flucloxacillin as above (remember under 3s will be on flucloxacillin anyway).
- For those repeatedly culturing *S aureus* despite regular high dose flucloxacillin, consider other treatments, especially in older children. For example co-amoxiclav; fusidic acid and rifampicin (in combination), co-trimoxazole or nebulised vancomycin if this persists.



- **Use of linezolid** – see below (section 6.2a 6 IV).

### **6.2a 6 II. *Haemophilus influenzae***

#### **IIa. First isolation**

- *In a relatively well child* (clinical judgment) we use oral co-amoxiclav for **4 weeks**. This may be combined with azithromycin or clarithromycin; one further course of a cephalosporin can be given if no eradication/persistent symptoms. The sole indication for cefixime is proven *H influenzae* isolation in pure culture, with no response to first line antibiotics.
- *In an unwell child* admit for IVABs. Use Ceftazidime + Tobramycin for 14 days.

#### **IIb. Re-growths**

- *Regrowth less than 6 months* from 1<sup>st</sup> growth - oral co-amoxiclav for **4 weeks**
- *Re-growth after more than 6 months* from 1<sup>st</sup> growth - treat as for 1<sup>st</sup> growth
- *Further re-growth within 6 months* - clarithromycin for 14-28 days (assuming not resistant).

#### **IIc. Chronic infection**

- This is most uncommon. If  $\geq 2$  isolates of *H influenzae* in a year, consider co-amoxiclav prophylaxis, although evidence is even less secure and we are reducing our use of this drug as a prophylactic agent. Long term azithromycin may be continued for anti-inflammatory / immunomodulatory effects, but it is not good for *S aureus* (due to resistance) and so is not used for prophylaxis, unless no other option is available. Watch out for *H influenzae* macrolide resistance as well. **Cephalosporins are not to be used** for long term prophylaxis because of worries about increased *Pseudomonas* isolation.

### **6.2a 6 III. *Pseudomonas aeruginosa***

If the report indicates the organism is **resistant** to colistin, this may well be a *Burkholderia* species not *Pseudomonas*, and the sample must be sent to the Public Health England Laboratory at Colindale (see appendix 20 for contact details).

#### **IIIa. First isolation**

- If grown on cough swab we carry out eradication but have changed our regimen -
  - **3 weeks** oral ciprofloxacin (or dual therapy intravenous antibiotics if unwell)
  - **PLUS 1 month** nebulised **tobramycin** twice daily.
- After eradication therapy for new *P aeruginosa*, patients will all have an induced or spontaneous sputum culture checked at 5-6 weeks (*i.e.* 1-2 weeks after finish tobramycin) to see if eradication has been successful.
- If they remain symptomatic and sputum culture was negative, they will have a BAL. We will not rely on a cough swab to prove successful eradication.

**IIIb. Failed eradication**

- If eradication has failed, it is likely IV ceftazidime + tobramycin will be used, especially in infants, and certainly if the child is unwell.
- If the child is well, give another 3 weeks oral ciprofloxacin + 3 months nebulised therapy. This will usually be 1 month colistin – 1 month tobramycin – 1 month colistin.

**IIIc. Subsequent regrowths**

- Isolations of *P aeruginosa* after six months or more of clear cultures are **always** treated. We assume this is a new isolate so attempt re-eradication with 3 weeks oral ciprofloxacin plus 1 month nebulised tobramycin.
- If unwell, a 2-week course of dual therapy intravenous antibiotics are given.
- If the child is known to be chronically infected (& on nebulised antibiotics), but is well, it may well be correct to offer no additional treatment. However, do not take the statement ‘Chronic Pseudomonas Infection’ in the letter on trust; all letters must state date of last isolation and whether mucoid/non-mucoid. Check on EPR whether the child is a regular isolator (in which case treatment may well not change), or if the child has had several negative cultures over many months, in which case an attempt at ‘re-eradication’ is made (see below). If in doubt, get out the previous culture results and discuss with the Consultant.
- It is important to arrange a follow up culture at the end of the course (local hospital or home care team can do this), and monthly thereafter for at least three months.
- **Long term nebulised antibiotics –**
  - If the regrowth occurred within the year of eradication therapy, after re-eradication, we use long term nebulised antibiotics. This is usually colistin.
  - If regrowth happened after a longer gap, over 1 year, after re-eradication we do not necessarily start long term nebulised antibiotics.
  - If they were on colistin when they had the regrowth, consider switching to nebulised tobramycin alternating monthly with colistin.
  - If they had regrowths despite alternating colistin/tobramycin, consider nebulised Aztreonam lysine (Cayston®) as 3<sup>rd</sup> line for 1 month (Consultant decision). This may need to continue alternating monthly with colistin.
  - If there have been no *P aeruginosa* growths for 2 years consider whether long term antibiotics can be stopped.

**IIId. Choice of IV antibiotics for *Pseudomonas aeruginosa***

- Check for drug allergies.
- 1<sup>st</sup> line is ceftazidime + tobramycin.
- 2<sup>nd</sup> line is meropenem + tobramycin (this may be 1<sup>st</sup> line if Staph aureus also grown).
- The parents/patient often knows which combination has worked best in the past and it is often worth going with their choice (unless there is a good reason not to).
- Known antibiotic sensitivities on last sputum/cough swab PsA culture not always relevant.

- Subsequent choices (not in particular order) – aztreonam, colistin, amikacin, (see formulary). We rarely use piptazobactam because of allergy including cross reactions.
- If a child is receiving 3 monthly IV antibiotics, we will consider not using an aminoglycoside for each course.
- **Intravenous fosfomycin** is relatively new. *Consultant decision* only, for very resistant *PsA* in children 12 years and above and adults. It is now licensed in UK.
- We never use IV gentamicin (it is not in our formulary).
- Check whether patient allowed aminoglycosides (known renal, hearing problems).

### IIIe. Aminoglycosides.

Due to safety and nephrotoxicity considerations, **tobramycin** is our 1<sup>st</sup> line aminoglycoside (we DO NOT use gentamicin), assuming the organisms are not resistant to it. This is based on its superior MIC, less nephrotoxicity, and data suggesting that *P aeruginosa* is more often resistant to gentamicin than tobramycin.

Note that ototoxicity is a proven side-effect of aminoglycosides, in particular amikacin, and families should be warned about this and offered the information sheet each time. The warning must be documented in the medical notes. For children embarking on 3 monthly IV antibiotic courses, or IV amikacin for NTM treatment (that may be repeated) a consent form must be signed.

Audiometry should be performed:

- as a baseline at the start of commencing treatment for NTM (IV amikacin) and repeated after 1 year.
- in all children starting on regular 3 monthly IV antibiotics and will be repeated yearly.
- if a child ever has a high aminoglycoside trough level.

Audiology should be arranged by referral to the child's local audiology clinic.

If any hearing deficit is detected or tinnitus is reported then consideration of stopping aminoglycoside therapy and switching to alternative treatments should be made.

**N-acetylcysteine.** A systematic review has shown that the antioxidant N-acetylcysteine (NAC) has a protective effect against aminoglycoside-induced hearing loss, reducing the risk of ototoxicity by 80% (Kranzer et al, Thorax 2015).

- We will use oral N-acetylcysteine at the time of IV aminoglycoside therapy for (a) those receiving IV amikacin (for NTM) and (b) 3-monthly antibiotics.
- We are starting this new policy for the most at risk group, and will see how the children tolerate the NAC. In time we may decide to use this for all courses of IV aminoglycosides.
- There are no data on its use with nebulised amikacin and we are not using this currently.
- See formulary for doses of tablets. Children  $\geq 12$  years will have 600mg BD, and can use 600mg tablets; those  $< 12$  yrs will take 300mg BD years old (the 600mg tablets are scored and halve easily); and for children unable to take a tablet they disperse in a small amount of water.

There is evidence that once-daily dosing of aminoglycosides is less toxic and results in more effective bacterial killing than conventional three-times daily dosing. There is also evidence that the incidence of *P aeruginosa* resistance to aminoglycosides may decrease with once-daily rather than three-times daily administration. In addition, less money is spent on

equipment such as needles and syringes and importantly for the child with CF, there is a need for fewer blood tests because trough serum levels only need to be monitored. It also saves on nursing time for drug administration. The aminoglycoside regimen is now:

Tobramycin	10 mg/kg once daily over 30 minutes
Amikacin	30 mg/kg once daily over 30 minutes

**The aminoglycoside should ideally be administered in the morning or early afternoon because there is a circadian variation in renal toxicity. We are doing levels 23 hours after the 1<sup>st</sup> dose, and it is given around 2pm, so levels are taken at 1pm.**

Note that these are doses for CF patients ONLY; doses may need to be reduced in other situations.

You must know before you prescribe whether there has been a high trough level during any previous course – ask the family specifically, and search Electronic Patient Record for the information. If there has, the dose should be reduced by **20%** from the outset, and ensure the renal function is measured alongside any trough doses.

### Measurement of trough levels

- a) Serum aminoglycosides levels should be measured **23 hours** after administration of the **first** dose (i.e. 1 hours before 2<sup>nd</sup> dose), and also 23 hours after any adjustment. We repeat them weekly thereafter.
- b) Serum urea and creatinine should be measured at the time of first cannula insertion and **with each trough level**. Occasionally it may be necessary to just use a finger prick for trough levels, in which case urea and creatinine can be omitted. They would have to be done though if the drug level came back high. Note that false positive high levels have been reported from blood samples taken from a finger contaminated with the antibiotic.
- c) Levels should NEVER be taken through the same line that the antibiotic was given and that includes portacaths/longlines. Label blood form – ‘TROUGH’.
- d) Aim for trough < 1mg/l for tobramycin, and trough < 3mg/l for amikacin. The result must be written on the drug chart and the next dose will not be given unless this is done.
- e) If the trough is >1mg/l (or >3mg/l for amikacin) omit the next dose and check the trough level 24 hours after the omitted dose. Only once the trough level has fallen to below 1mg/l (3mg/l amikacin) can the patient be re-dosed, reducing the dose by 20%, and the trough level re-checked after 24 hours. Wait for this level to come back and only continue if level is <1mg/l (<3mg/l amikacin).
- f) If the patient’s renal function remains unchanged throughout the remaining course continue on the reduced dose and recheck the level weekly thereafter.
- g) Peak levels are not done routinely but may be taken if there is concern about clinical progress on a reduced dose. This should be taken 30 minutes after the end of the infusion. Aim 20-30mg/l for tobramycin.
- h) Each time levels are done, document in the notes or Electronic prescribing chart:
  - Date/time blood taken
  - Dosage regimen
  - Results (also on the drug chart)
  - Any change to dosage
  - Any other action taken

Consider measuring aminoglycoside trough levels more frequently if –

- Dehydration
- Intercurrent diarrhoea and/or vomiting
- DIOS
- Other nephrotoxic drugs e.g., ibuprofen.

### III.f. Chronic *P aeruginosa* infection

See NHSE Clinical Commissioning Policy for inhaled therapy first published Dec 2014.

<https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/01/a01-policy-inhld-thrpy-cf.pdf>

- **Chronic *P aeruginosa* infection is defined** for analysis purposes by the Leeds criteria:
  - Never: never cultured
  - Free: cultured previously but not in last year
  - Intermittent: cultured in < 50% of samples in past year (must be 4 samples per year)
  - Chronic: cultured in > 50% of samples
- 1<sup>st</sup> line treatment for chronic infection is long term inhaled colistin.

For children chronically isolating *P aeruginosa* and doing badly, consider rotating tobramycin and colistin nebulisers. Tobramycin should be considered if, despite continued therapy and good adherence to treatment, lung function continues to decline or there is a requirement for more than one course of IV antibiotics in the preceding year. *Consultant decision* to start inhaled tobramycin.

- **Aztreonam lysine** for inhalation (Cayston) is licensed for children >6 years old, and is routinely funded for the treatment of appropriate adults and children with CF in accordance with national clinical criteria. It is not commissioned by NHSE for continuous use (i.e., every month) but only for alternate month use.
- A stepwise approach is recommended, colistin remains 1<sup>st</sup> line, alternating Tobramycin/colistin remains 2<sup>nd</sup> line treatment. Aztreonam is our 3<sup>rd</sup> line alternating with colistin. **Consultant decision.** Nebulised levofloxacin is not licensed for <18 years.
- Aztreonam lysine may be considered if there is still progressive loss of lung function (defined as greater than 2% per year decline in FEV<sub>1</sub> as % of predicted) or there is continued need for IV therapy for exacerbations i.e., more than 2 per year despite therapy with an alternating regimen of tobramycin and colistin. This may be prescribed either alternating with colistin or tobramycin depending on the clinical response to those medications previously.
- Patients should be recommended not to expose themselves to loud noises *e.g.* loud music played through headphones / earbuds, when receiving intravenous aminoglycosides.
- Children must have a bronchoconstrictor challenge organised with the physiotherapists when starting for the first time; the first dose of every nebulised antibiotic is given in hospital, with pre- and post-nebulisation spirometry. If bronchoconstriction occurs, use pre-dosing with a bronchodilator, and repeat the supervised challenge. Nebulised

salbutamol can be added to colistin (but **not** tobramycin or aztreonam). Otherwise it should be given beforehand via a spacer. See section 6.15b.

- **Long term intravenous colistin.** Occasionally (although not for many years) we have used long term twice daily IV colistin for children unable to last even 3 months without 2 week courses of IV antibiotics. This is a *consultant decision*. See formulary for the dose - the usual total daily dose divided into 2 doses

### IIIg. Dry powder antibiotic inhalers (see also section 6.15d).

- It is important to note that even if the child has been safely using a nebulised antibiotic, if it is planned to switch to a dry powder, the first dose must be given under supervision to check for bronchoconstriction (book challenge with Physiotherapy Dept. using their request form). It is essential to check the child knows how to use the device, as with all inhaled medication. See section 6.15b.
- **TOBI Podhaler**  
Tobramycin given by the TOBI podhaler has been shown to be non-inferior to TOBI™. It should be offered to children who are either using nebulised tobramycin or are being started on it. It is not the first-line treatment for *Pseudomonas aeruginosa* infection; the existence of this device does not alter our choice of inhaled medication. Like nebulised antibiotics, the inhaled is excluded from the PbR tariff, so we are reimbursed if we prescribe it. The first month will be prescribed in clinic and supplied by our pharmacy; subsequently it will be supplied by the hospital's homecare provider.
- **Colobreathe turbospin**  
Colobreathe to deliver colistin is now available, and has been shown to be equivalent in efficacy to nebulised TOBI™. The current clinical commissioning policy for Inhaled Therapy for CF states that as per NICE guidance, this can be used for patients who have previously been prescribed colistin nebulised treatment and would continue to benefit from treatment, but have otherwise become intolerant or have struggled to adhere with nebulised treatment and therefore would be switched to a more expensive product such as Tobramycin nebules. The first month will be prescribed in clinic and supplied by our pharmacy; subsequently it will be supplied by the hospital's home care delivery service.

## **6.2a 6 IV. MRSA**

- For 1<sup>st</sup> isolation in sputum/cough swab, we attempt eradication as there are data showing MRSA adversely effects lung function. We treat for **1 month** with 2 oral agents, usually rifampicin plus fusidic acid or trimethoprim or co-trimoxazole. Beware of hepatic toxicity. We used to give 3 months therapy but the US study showed 2 weeks was successful.
- Prophylactic flucloxacillin or co-amoxiclav should be stopped in patients with MRSA until the MRSA is successfully eradicated.
- Nebulised vancomycin can also be considered (see formulary).
- Vancomycin and teicoplanin are IV drugs active against MRSA. Teicoplanin does not require blood levels and is the preferred choice.
- The decision to treat chronic MRSA infection is a clinical one based on signs, symptoms and investigations, and should be in accord with hospital infection policy.

- Consider using linezolid (see below), available orally and IV, when traditional agents fail (*consultant decision*).
- Check current Hospital Policy on the intranet; also remember surface decontamination protocols. Ensure whole family undergoes decontamination (their GP will need to prescribe this).

**Linezolid.** Is an oxazolidinone, and is available orally and IV. Oral bioavailability is 100% so IV preparations rarely required. It may be useful for *MRSA* or *Staph aureus* refractory to 1<sup>st</sup> line treatments. It can cause blood dyscrasias so full blood counts must be monitored weekly throughout treatment and there are now reports of optic neuropathy with courses >28 days. Therefore, linezolid should only be started on consultant approval and initially we will aim for 2-week courses. For those on prolonged (4 weeks or more) or repeated courses, ophthalmological assessment is mandatory and should be repeated every TWO months. Also consider use of high dose pyridoxine (vitamin B<sub>6</sub> 100mg od) to reduce risk of cytopenias for prolonged courses. Where possible patients should be warned to immediately report any visual changes, regardless of treatment duration.

### **6.2a 6 V. *Burkholderia cepacia* complex**

The *Burkholderia cepacia* complex consists of many well-established genomic species called genomovars: some examples are *B. cepacia*, *B. multivorans*, *B. cenocepacia*, *B. vietnamiensis*, *B. stabilis*, *B. ambifaria*, *B. dolosa*, *B. anthina*, *B. pyrrocinia* and *B. pseudomultivorans*. Although previously commonly referred to by genomovar number, these names should now be used in preference (e.g. old genomovar 3 is *B. cenocepacia*) and only the first of these species should be referred to as *B. cepacia*. Culture requires specific, selective media and every attempt should be made to fully identify strains at the molecular level; misidentification is common. Several species have been reported in epidemics and incidence has decreased since the widespread adoption of strict segregation and cross-infection control measures. Reports have confirmed some strains as conferring an adverse prognosis (e.g. *B. multivorans*, *B. cenocepacia* and *B. dolosa*) and *B. cenocepacia* is an exclusion criterion for many transplant programmes because of a clear survival disadvantage post-surgery.

- If detected at shared care hospital, please notify Brompton for advice. Ask the laboratory to send the strain for typing to the Public Health England Laboratory at Colindale (see appendix 20 for contact details). The local diagnosis may be wrong, because really experienced, CF specialist laboratories are needed to type unusual organisms. This is true also for any other unusual and rare organisms. Whilst waiting for the confirmation, it may be appropriate to start some therapy as even if not *Burkholderia*, it will be some type of gram negative bacteria e.g. *Pseudomonas* spp.
- Patients who become infected with BCC do not come to usual CF clinic, but are now being seen in clinics held on the 2<sup>nd</sup> Friday of the month in even numbered months (Feb/Apr/June/Aug/Oct/Dec). If they are on the ward, they are kept isolated in a cubicle for the whole admission.
- **Eradication** -: this must be discussed with the consultant. We attempt to eradicate 1<sup>st</sup> isolation with IV antibiotics, and choice will depend on sensitivities, and may include meropenem, temocillin.

- **Chronic suppressive therapy** - As the *B. cepacia* complex bacteria are uniformly resistant to colistin the choice will be between nebulised ceftazidime, meropenem, tobramycin, aztreonam lysine or temocillin. Long term oral therapy may be considered including doxycycline.
- We may also consider oral trimethoprim or co-trimoxazole for minor symptoms in a chronically infected patient.

#### **6.2a 6 VI. *Stenotrophomonas maltophilia***

- This: usually clears spontaneously and is frequently not pathogenic; however in some patients it is associated with new symptoms and changes in lung function. If symptomatic, treat with an oral antibiotic if one available. Antibiotic sensitivity testing is not always reliable for this organism, so co-trimoxazole is usually the best option. Can also use a 2-4 week course of chloramphenicol (currently a very expensive option - £450-1700 for 2 weeks), or trimethoprim, or minocycline if >12 years old (doxycycline may be used as an alternative as it is once daily – sensitivity to minocycline should imply sensitivity to doxycycline). If the child meets criteria for a pulmonary exacerbation, and *S. maltophilia* is the only organism isolated, consider high dose intravenous co-trimoxazole (*Pneumocystis jiroveci* treatment dose, Consultant decision). It may be necessary to start at a lower dose and work up.

#### **6.2a 6 VII. Non-tuberculous mycobacteria (NTM)**

This includes a large number of species and the commonest to affect the lungs are -

- ***M. avium* complex** (MAC) which includes the species *M. avium*, *M. intracellulare* and *M. chimaera*. MAC is classed as a slow-grower.
- ***M. abscessus* complex** (MABSC) are rapid growers and this group are now the commonest found in the UK, and include the subspecies *M. abscessus abscessus*, *M. abscessus massiliense* and *M. abscessus bollettii*.
- **Other species** found include *M. kansasii*, *M. xenopi*, *M. malmoense*, *M. fortuitum* and *M. simiae*.

When grown in the sputum of children with CF, a decision on whether to treat will need to be made. Some NTM can be present as commensals and have no significant effect on respiratory function or nutritional status. The exception is *M. abscessus* complex, which has increasingly been found to cause significant lung disease.

If NTM is isolated from sputum – 2 further samples should be requested, preferably over a 2 month period to allow for natural clearance of the NTM. A single isolate of NTM should NOT be treated, unless from a BAL (or induced sputum). The decision to treat is a consultant one. It is important to ensure symptoms are not wrongly attributed to NTM, and other causes have been treated before NTM treatment is started.

Azithromycin monotherapy should be stopped whilst awaiting confirmation of a diagnosis of NTM pulmonary disease.

Cough swabs must not be sent for NTM culture. Sputum or BAL is sent for AFB smear and NTM culture -



- At annual assessment visit (if productive of sputum)
- In a child who is unwell but culture-negative
- Any child having a bronchoalveolar lavage
- On admission for a chest exacerbation
- When previously cultured

Antibiotic sensitivity testing is performed on initial samples. All first isolates of NTM are sent to the reference laboratory for molecular typing.

**Patients with *M abscessus* complex will be kept in isolation on the ward, and seen only in 2<sup>nd</sup> wave (3.15) slots in clinic so that the room is not used again that day**

**Treatment: See appendix 2 for detailed antibiotic policy** on treatment of NTM. In general:

- *M avium* complex is treated with oral rifampicin, ethambutol and azithromycin irrespective of sensitivities for 18 months. Remember ophthalmic checks for ethambutol.
- *M abscessus* complex - typically there is a 3 week intravenous induction phase, which may need to be repeated if the child deteriorates during the consolidation phase. Consolidation is for 18-24 months with four medications, usually a combination of oral and nebulised.

Patients are treated for at least 12 months after the first negative NTM culture whilst on treatment (culture conversion). Patients are considered free of NTM when they have had 4 negative samples over a year after stopping treatment. This means they cannot be considered truly negative until at least 1 year off treatment.

If NTM was only isolated on a BAL in a non-sputum producing child, and if an induced sputum cannot be obtained, the child will need a BAL in a year to be considered negative.

Patients who fail to clear MABSC may be considered for long term suppressive therapy, this may take the form of nebulised therapy or long term dual oral therapy.

### **6.2a 6 VIII. *Achromobacter xylosoxidans***

- There is a dearth of evidence, so always discuss with Consultant.
- For first isolation we attempt eradication and may use intravenous antibiotics if the child is unwell. This usually includes IV colistin. High dose IV co-trimoxazole (*P jiroveci* treatment dose) may also be considered (consultant decision), and it may be necessary to start at a lower dose and work up.
- If intravenous therapy is given, it is probably wise to give nebulised colistin as well for 3 months at least, possibly also with an oral antibiotic, if the *Achromobacter* is sensitive to one suitable for medium term use.
- Otherwise we may use oral co-amoxiclav for 1 month and nebulised colistin for 3 months. Oral alternatives are co-trimoxazole or minocycline (if age > 12 years), depending on the sensitivities.
- For established chronic infection nebulised colistin is used long term, with nebulised meropenem as 2<sup>nd</sup> line.

**6.2a 6 IX. *Serratia marcescens***

There is very little in literature in CF patients and unclear what to do with it (adult unit unsure also but they tend to attempt eradication with oral followed by IV antibiotics). We do see a few cases and decide on an individual basis i.e. if child unwell and this is only isolate, we would tend to treat. Check sensitivities of isolated organism. Otherwise we may just repeat cultures and watch progress.

**6.2a 6 X. Influenza**

NICE guidelines state that oseltamivir and zanamivir are recommended to prevent flu if **all** of the following apply:

- The amount of flu virus going around is enough that if someone has a flu-like illness it is likely that it has been caused by the flu virus
- The person is in at 'at risk' group (i.e. all our CF patients)
- The person had been in contact with someone with a flu-like illness and can start treatment within 36 hours (for zanamivir) or within 48 hours (oseltamivir).

Hence if our patients are immunised against influenza as they should have been, then they do not need Oseltamivir or zanamivir. If the child has not been immunised, they must be encouraged to see their GPs early for a prescription when there is a high flu incidence. Oseltamivir (Tamiflu) (must be given for H1N1 influenza) is taken twice daily for 5 days, it comes as suspension or capsules and dosage by age/weight is in BNFc. Appropriate swabs (nasopharyngeal aspirate or sputum or viral throat swabs) should be taken for virus detection to confirm the diagnosis.

**6.2b Drug allergy & desensitisation****Allergy**

In acute reactions, stop the infusion & give:

- IM adrenaline (<6 years 150 micrograms, 6-12 years 300 micrograms, >12 years 500 micrograms) – doses repeated if necessary at 5 minute intervals according to blood pressure, pulse and respiratory function).
- IV chlorphenamine (< 6months 250microgram/kg (max 2.5mg); <6 years 2.5mg; 6-12 years 5mg; >12 years 10mg), continued orally at usual doses for 24-48 hours to prevent relapse).
- IV hydrocortisone (< 6 months 25mg ; <6 years 50mg; 6-12 years 100mg; >12 years 200mg), continued three times a day for 24-48 hours to prevent relapse.
- Monitor BP/HR/SpO<sub>2</sub>/RR.
- Listen to the chest.
- Consider giving oxygen and a plasma expander.
- Document event clearly in the notes, and on allergy section of dug chart.
- Inform consultant.
- Make sure child and family know which is the offending antibiotic, and this information is written all over the notes and becomes part of that child's diagnostic list on letters and summaries.

The majority of allergic reactions are ‘late onset’ occurring many days after the antibiotic course starts; rather than a more immediate allergic reaction, which can take place within minutes of taking a drug. The late reactions may present in a variety of ways, often with non-specific features, including rashes, unexplained fevers, nausea, vomiting, diarrhoea, joint pain, muscle pain, lethargy, abnormal liver function results and abnormal haematological results. Management of these reactions is essentially to recognize them early and to stop the relevant drug, if it can be worked out which drug is causing the reaction. Improvement in symptoms should be seen within a few days. If there is diagnostic doubt, consider referral to the St Mary’s Allergy service.

Do not attempt to restart a similar class antibiotic for at least 48 hours.

Antibiotic desensitisation (see below) may be considered if the child has multiple antibiotic allergies. This can be undertaken with incremental introduction of the antibiotic at low dose, usually with prior treatment with systemic corticosteroids and antihistamines. If this is considered contact the pharmacy team at the earliest opportunity to discuss further.

Piperacillin/tazobactam (Tazocin, piptazobactam) is rarely used because there is a high incidence of allergy (usually at day 10), and because of cross reactivity, patients may become hypersensitive to other antipseudomonal penicillins. It has also been recorded to cause reversible bone marrow suppression – thrombocytopenia, neutropenia.

## Epipens

It has been advised by the CF Trust that all patients who receive the full course of IV antibiotics at home should have an Epipen. At Royal Brompton, we strongly advise the 1<sup>st</sup> dose is given in hospital. There are no references documenting anaphylaxis on second dosing of antibiotics when no reaction was observed after the first dose. Symptoms may still occur as a delayed reaction, sometimes 48-72 hours later, usually in the form of a maculopapular exanthema or urticaria.

There are however 2 case reports which record separate incidences in which adult patients previously not allergic to cefazolin have had anaphylactic reactions upon receiving their first dose on the second occasion.

The need for an Epipen cannot be completely excluded if the patient has not reacted to the first dose of the antibiotic, as delayed symptoms may occur later when the patient has been discharged. However these are generally mild in nature and may not require the use of an Epipen. In the UK, the practice of prescribing an Epipen to all patients having home IV antibiotics is not common. We must stress though that it is our practice and recommendation that **the 1<sup>st</sup> dose is always given in hospital** (see section 6.2c). Additionally any child, who has had a previous allergic reaction to an IV antibiotic, must have an epipen at home if receiving further home IV antibiotics.

## Desensitisation

*(Adapted from the material printed in the UK CF Trust Antibiotic Treatment for Cystic Fibrosis Guidelines, 3<sup>rd</sup> edition, May 2009 and <http://www.cysticfibrosismedicine.com>).*

Frequent high-dose intravenous antibiotic treatment in CF patients increases the incidence of drug-associated hypersensitivity reactions. These reactions have been reported with most of the antibiotics in regular use for patients with CF, including aminoglycosides,  $\beta$ -lactams, and quinolones. The choice of antibiotics may therefore be limited by a history of previous allergic reactions, denying patients optimal treatment.

Antibiotic tolerance may be induced by following desensitisation protocols, although it should be noted that the patient will need desensitising to the drug at the start of **EVERY** treatment course and repeated during a course of therapy if more than one day's doses are omitted. The outcome of the desensitisation procedure must be documented in the medical notes, and if a reaction occurred, the exact nature of the reaction must also be documented.

An example of such a regimen is shown below. The principals behind this regimen can be adapted for other drugs, and if a desensitisation regimen is being considered, then please discuss with a member of the paediatric pharmacy team in advance of the patients admission:

### Example Regimen

- Administration of a  $10^6$  times dilution of the drug followed by 6 x ten-fold increases in the concentration (starting with the least concentrated) until the therapeutic dose is given (final dose calculated using patient's weight)
- Each dilution is infused consecutively over 20 minutes.
- During the desensitisation process, which takes about 2–3 hours, the patient is observed for signs of allergy.
- If all infusions are tolerated, the therapeutic dose is continued until the course is completed.
- Example of a desensitisation regimen for final dose Ceftazidime 2g (2000 mg)
  - Ceftazidime 0.002 mg in 20 ml sodium chloride 0.9% (NaCl)
  - Ceftazidime 0.02 mg in 20 ml NaCl
  - Ceftazidime 0.2 mg in 20 ml NaCl
  - Ceftazidime 2 mg in 20 ml NaCl
  - Ceftazidime 20 mg in 20 ml NaCl
  - Ceftazidime 200 mg in 20 ml NaCl
  - Ceftazidime 2,000 mg in 20 ml NaCl.
- Adrenaline, hydrocortisone and an antihistamine should be readily available and the appropriate doses for the patient known before starting the procedure (Some patients benefit from treatment with antihistamines pre and during desensitisation)
- Facilities for full resuscitation should be close at hand.

If a reaction (anaphylaxis, wheezing, swelling, itching, urticaria) occurs during desensitisation, the procedure should be stopped and no further attempts should be made to administer that antibiotic to the patient.

### Procedure at RBH

1. If a patient requires desensitisation, the paediatric pharmacy team should be alerted prior to admission, with as much notice as possible.

2. Medications that require desensitising will each have an individualised regimen (produced by the paediatric pharmacy team) with instructions for preparation and administration.
3. All doses for the desensitisation regimen should be prescribed on the 'once-only' STAT side of the chart.
4. Each of the drug solutions will be administered to the patient as 20 minute infusions. Once an infusion has finished, the next one should be started immediately. The entire process will take approximately 2-3 hours.
5. Adrenaline, Chlorphenamine and Hydrocortisone should ALWAYS be prescribed on the 'when required' (prn) side of the drug chart. They should also be drawn up and ready to administer to the patient if required. (Please refer to the latest copy of BNF-C for appropriate doses or above in allergy section).
6. If a reaction (anaphylaxis, wheezing, swelling, itching, hives) occurs during desensitisation, the procedure should be stopped and no further attempts should be made to administer that antibiotic to the patient. Please note, that some patients may feel nauseous which can usually be relieved with the use of a regular anti-emetic.
7. If a reaction occurs, the reaction and its exact nature must be documented in the patient's medical notes.
8. If the patient tolerates the desensitisation regimen, the final dose should be prescribed on the drug chart (regular IV section) and should be continued for the remainder of the course.
9. If doses are omitted for more than one day, the full desensitisation process will need to be repeated.

### 6.2c 3-monthly IV antibiotics

In <5% of our patients, regular 3-monthly IV antibiotics are needed. This tends to be in those with a more rapid decline in CF lung disease, which may or may not reflect the amount of treatment received at home. When we find children are having 3-4 courses IV antibiotics anyway, it is easier for families to plan the admissions in advance. We will try to arrange a date for the next course at the time of discharge.

Generally we try to stick to these guides –

- Consider whether a portacath would be helpful.
- Courses must be at RBH at least every other time (with the alternate being at home or local hospital).
- We will try to use aminoglycosides only on alternate courses.
- We will use oral N-acetylcysteine every time aminoglycosides are used.
- Parents are to sign consent form for use of aminoglycosides.
- Audiometry testing at start and then annually.
- After 1 year consider whether it is still necessary and document this. Usually we move to 4 monthly courses before stopping regular IV antibiotics. If 3-monthly regimen is continued beyond a year, then reconsider at least annually and document at annual review.

## 6.2d Home IV antibiotics

- Lack of bed space is not an indication for home IVABs. However if a long delay is anticipated, other solutions such as using the local hospital or home IVABs should be discussed with the on-call or named Consultant.
- The first dose of both antibiotics should always be given in hospital.
- Any Parents/Carer wishing to undertake home IV therapy must be carefully selected and be discussed with the CF Nurse Specialist and Consultant before any decision is made.
- Families must be able to follow instructions provided, be fully aware of the treatment burden and be happy to carry this out. There is a training pack and the CF nurse specialists or the nurse in charge of the ward must be satisfied the parents are competent.
- Home IV therapy is optional and never compulsory Parents must **not** be pressurised (even if the child is anxious to go home) and must be happy to undertake the task. They must be confident of being able to continue with other aspects of the treatment i.e. extra physiotherapy and attention to diet.
- Families who have carried out home IVs in the past should be asked each time whether or not they are happy to do so again. In particular if there has been a long gap, consideration needs to be given to training needs (see below). Likewise, each time, an assessment will be made by the Consultant and CNS as to whether Home IV therapy is the most appropriate method for that specific occasion.
- Patients requiring >1 course IV antibiotics per year should have at least one (or part of) course of treatment in hospital per year.
- Antibiotics must be ordered 48 hours before IVs are due to start therefore prescriptions need to be in pharmacy by 12 pm at the latest. Prescription pads can be found on Rose Ward, Outpatients and in pharmacy.
- Shared care doctors can fax over requests to 020 7351 8763 for the attention of the CF CNS (Mon-Fri 9.00-17.00) or contact the Respiratory Registrar on call directly via the hospital switchboard.
- Families should be warned about the risk of acute renal failure with intercurrent diarrhoea and vomiting, or use of nephrotoxic drugs like NSAIDs, if an aminoglycoside is prescribed. In that event, doses of aminoglycoside should be withheld pending our assessment.

Parents/carers must complete the home IVAB training booklet and be signed off in the following:

- IV line - to look for leaks and signs of infection/thrombosis.
- Infection control.
- Allergic reactions - what to look for and to stop drug immediately and seek medical advice.

- Drug administration and importance of correct timing (especially for aminoglycosides).
- Use of the Baxter Intermate device.



Please refer to training book for full details. This is available from the CF Nurse Specialists or Rose Ward.

Patients must have their 1<sup>st</sup> dose of antibiotics on Rose ward or their local shared care centre. Before discharge the following **MUST** be arranged:

- Consent and competency form should be signed and placed in the notes.
- Inform home care nurse/ physiotherapist or local community service, local hospital team if applicable and GP.
- Aminoglycoside levels or Us & Es (if on Colistin) must be arranged and booked.
- Children are usually seen after the 1<sup>st</sup> week of IVABs in clinic or by the CF home care nurse or physiotherapist and at the end of the 2<sup>nd</sup> week in the clinic or on the ward, *before* the line has been removed.
- CF paediatric physiotherapy homecare team alerted and verbal contact or home visit arranged.

## 6.2e Portacaths (Totally Implantable Venous Access Devices)

**Indications** - recurrent problems with venous access in the setting of need for recurrent courses of IV antibiotics. It is not a solution for significant procedural anxiety (needle phobia) because needle insertion is still required monthly for flushing. However, for many children with CF who have tolerated increasingly numbered, time consuming and challenging long line insertions and as such are becoming more fearful of each new occasion, a portacath can be helpful. As such, each individual child's situation will be considered involving input from the child's family and MDT.

**Site of insertion** - usually via a subclavian vein into the SVC. The port is usually buried on the upper lateral chest, away from the shoulder joint and breast tissue. Ideally it should be on the non-dominant side. However the final decision has to be left to the surgeon. If the child has had previous central neck lines, imaging of the neck (Doppler ultrasound or MR venogram) may be required to identify a suitable site for insertion.

**Protocol for insertion** – Consent will be taken by surgeons. Investigations: CXR, full blood count, coagulation including thrombophilia screen, U&E, group & save. If the thrombophilia screen is abnormal, discuss with Paediatric Consultant and Haematologist.

When possible, children will commence intravenous antibiotics for 48 hours prior to surgery (this can be at home or local hospital). However if IV access is a big issue, then we would wait until the portacath is sited before starting IVABs, and use oral e.g. ciprofloxacin instead.

**Surgeon** - Mr Simon Jordan (or Mr Michael Dusmet) will do older children (> age 5) at RBH, and we also ask Mr Simon Clarke, Paediatric Surgeon at Chelsea and Westminster Hospital, especially for the smaller children. A formal referral by letter to out-patients is usually made. Surgeons take consent for the procedure. Consider also whether a blind lavage or bronchoscopy should be performed at the time of anaesthesia to obtain material for culture; **also discuss with the paediatric consultant (Jane Davies) as bronchoscopy, lavage and endobronchial biopsy may be performed for research purposes once consent obtained.** Physiotherapy is intensified for at least 24 hours before surgery. Patients will usually be admitted to RBH prior to surgery. Protocols currently variable, so check with CF Nurse Specialist.

#### Post insertion -

- Chest x-ray done and looked at for line position and pneumothorax.
- Analgesia - **Regular** paracetamol 15mg/kg (max 1 gram) 6 hourly +/- Ibuprofen 5mg/kg (max 400mg) 8 hourly **or** Diclofenac 1mg/kg (max 50mg) 8 hourly. Be wary of using ibuprofen/diclofenac when patients are taking aminoglycosides. Opiate analgesics may be required (Oramorph 0.1mg/kg every 4 hours) during the first day or so but a laxative should be given at the same time
- Physiotherapy and early mobilisation are important.
- Antibiotics continued for a minimum of 48 hours post-procedure, and until patient is pain free and back to usual respiratory status.
- Portacath may be used from the time of insertion and the needle should be left in by the surgeons.
- Usually dissolvable sutures are used - check before patient goes home. There is some evidence that using the port to take blood samples increases the risk of line infection. This may be a difficult issue, because the child may have poor veins. Consider the use of fingerpricks where possible, and discuss with an experienced nurse specialist or Consultant. **Subsequent management** – 4-6 weekly flushing with 3ml 0.9% sodium chloride followed by 4mls of heparinised saline (ready-made as 200 units per 2 mls). This is arranged through the CF nurse specialist with the home care team, local community paediatric nurses or local hospital. Families may eventually learn to do it.
- Local anaesthetic cream is used.
- Always use the proper needle (straight bevelled).
- Always use aseptic non touch technique.
- Not to be touched by the inexperienced, particularly inexperienced doctors.
- After flushing, clamp the line (using clamp nearest the needle) then remove needle.

#### Complications –

- **Failure to access port** – difficulty may be due to lack of experience. If this is an issue, discuss with nurse in charge or CF CNS.
- **Blockage** - consider Urokinase 5,000 units in 3ml 0.9% saline instilled into port. Leave for 2-4 hours then aspirate and flush gently with 3ml 0.9% sodium chloride followed by 3ml heparinised saline (10units/ml). Use with caution if there is a history of bleeding or significant haemoptysis.



- **Port leak** – a hole or break in the catheter may occur. Diagnosis is with a contrast portogram.
- **Local infection** around the port - clean area, if device is visible then it needs removing but if the inflammation is superficial then treat with systemic antibiotics after swabs and blood cultures have been taken. Antibiotics should be administered via another line.
- **Line infection** usually demands surgical removal. After cultures have been taken, systemic antibiotics via another route and possibly injecting vancomycin or teicoplanin into the system may work. Thrombus may form which may lead to septic pulmonary emboli. Blood cultures and an echocardiogram may help the diagnosis and sometimes radio-opaque contrast can collect in a thrombus if injected down the line. Beware of injecting into a line that may have thrombus around it - you may cause pulmonary embolism, so think first and be careful. Consider anti-coagulation.
- **Catheter fracture ± embolisation** - fragments should be retrieved at cardiac catheterisation. Refer immediately to on-call consultant in paediatric cardiology. Remember that one of the commonest causes of pulmonary emboli in children is an endovascular foreign body. In a CF child with pleuritic pain and/or breathlessness and/or haemoptysis at least consider this diagnosis. VQ scanning is a waste of time. Consider spiral CT with contrast or even angiography if this is a real possibility. Catheter fracture has been reported after a road traffic accident in a child wearing a seat belt.
- **Tinnitus** – at the time of antibiotic administration may indicate line migration into the neck veins passing cranially.

### 6.3 Corticosteroids

#### Indications for oral steroids:

- Allergic bronchopulmonary aspergillosis.
- Severe intractable bronchospasm / severe small airways disease.
- Long term use as an anti-inflammatory agent is contraindicated in most cases due to the adverse risk-benefit ratio.
- Terminal care – may act as general ‘tonic’.

We tend to use prednisolone which must **not** be enteric-coated otherwise absorption is poor in CF. Dexamethasone may also be used and anecdotally may be better for those whose behaviour/mood is adversely affected by prednisolone (NB *prednisolone 5 mg = dexamethasone 0.75 mg*). Dose regimen for ABPA is in section 6.9. For severe bronchospasm, dose is 2 mg/kg prednisolone administered in the morning after food, which will be reduced as soon as possible, depending on the response. We sometimes use intravenous methylprednisolone 10-15 mg/kg/day (max dose 1gm) for 3 days, repeated monthly – for severe cases and when compliance with oral prednisolone is an issue.

Attention must be paid to potential adverse effects, particularly glucose intolerance as sometimes overt CF-related diabetes is precipitated. Patients must be told to report polyuria & polydipsia. Regular urinalysis for glycosuria is important, particularly in older children. Other problems are growth failure and hypertension (measure BP in clinic), less commonly oral candidiasis, cataracts, osteoporosis, and Cushing’s syndrome. Exposure to chicken-pox in a child who has not yet had it, may require varicella-zoster immunoglobulin (see section 10.2 on immunisations). If a child is on long term oral steroids itraconazole will usually be given in case there is exposure to aspergillus.

## Indications for inhaled steroids

- Symptomatic wheezing that requires regular bronchodilators, in a similar regimen to BTS guidelines for asthma. Especially in atopic children and those with predominance of eosinophils in sputum or BAL. Ideally acute bronchodilator reversibility should be documented.
- Long term use as an anti-inflammatory agent in an asymptomatic child is probably not indicated. Although in theory it would seem useful due to the nature of the persistent lung inflammation, benefit has not been proven.

We use budesonide or fluticasone, and occasionally ciclesonide (with its small particle size), but not usually beclometasone. Devices used depend on the age of the child, but nebulised steroids are rarely used. In older children, at low or moderate doses (<400 mcg/day budesonide, <200 mcg/day fluticasone) dry-powder inhalers (DPI) are most suitable. High doses of inhaled steroids are preferably given via a spacer device to reduce mouth deposition and potential systemic side effects. However there will be some older children for whom a spacer is unacceptable and then a DPI should be used. Use of a standard metered dose inhaler alone must be actively discouraged.

Side effects may include a reduction in final height (long term asthma studies suggest 1-2cm loss), oral candidiasis (so mouth must be rinsed after the dose, especially if using DPI) and rarely a hoarse voice. Always consider whether the dose can be reduced whenever the child is seen in clinic, or indeed stopped. Remember the issue of adrenal suppression in those also on itraconazole. Finally, there may be an association of ICS use with acquisition of NTM.

Children with wheezing that does not respond to inhaled steroid prophylaxis, should be started on a twice daily **long-acting  $\beta_2$ -agonist** (LABA) in a combination inhaler (Seretide or Symbicort). The patient must never take the LABA alone (without an inhaled steroid) so we do not prescribe salmeterol or formoterol inhalers.

## 6.4 DNase (Dornase alfa, Pulmozyme)

DNase is a synthetic enzyme that cleaves neutrophil derived DNA in sputum to reduce viscosity and thus in theory to aid sputum removal. Studies demonstrate 5-8% overall improvement in FEV<sub>1</sub> but this masks a wide response range from deterioration to marked improvement (over 20%).

### Indications:

It should be a *consultant decision* to start DNase in all cases

- Our policy is to consider starting DNase for **ALL PATIENTS WHEN THEY ARE 6 YEARS OLD, whatever their lung function** (as per European CF Society recommendations). Our intention is that it would be unusual for a child aged 6 and above not to be commenced on it.
- For our current older patients, its use needs to be discussed. We would strongly suggest we start any child
  - whose FEV<sub>1</sub> is <85%.
  - who hardly expectorates at all but has symptoms.
  - who has persistent wheezing.

- We would consider it in preschool children if there is concern over their respiratory status (especially those with persistent cough relating to mucus plugging) and have a low threshold, especially for those over 2 years of age, however we do not advocate routine use in under 6s.

Other indications include.

- Persistent or recurrent focal x-ray changes e.g. consolidation in a lobe or segment, when we would consider bronchoscopy with instillation under direct vision – see section 6.14. It would be expected a child like this would already be on DNase regularly.
- During an admission for a chest exacerbation it may be useful, and we would follow the recommendation of the physiotherapists.

There is some evidence for prophylactic benefit as a trial of use in 6-10 year olds with near normal lung function showing a reduction in exacerbation rate and a halt in deterioration of lung function. There seems to be no clinical difference between daily and alternate days treatment but we mostly use daily dosing. A further study showed a reduction in overall DNA with DNase use as a proxy for reduced inflammation.

The Cochrane review 2016 showed **no** DNase lung function superiority compared to hypertonic saline in 3 trials and superiority in one – this is relevant in a cost-restrained setting although DNase toleration is superior.

**Dose** - Trade name: Pulmozyme 2.5mg by appropriate compressor and nebuliser ie, standard or faster E-flow or I-Neb (if using the I-Neb 1ml DNase is nebulised and the rest is discarded). The default will be to use DNase daily, but consideration can be given to alternate day therapy after 6 months in those who are well or who find the daily treatment a particular burden (6.4). In practice this is unusual. This is an expensive drug (about £7500/year if used daily). RBH is now responsible for the prescription. A new prescription will be given by our pharmacy, with future prescriptions via the home delivery service (and we are still reimbursed).

There is **no need** in children to do a bronchoconstriction trial when first starting DNase – confirmed by manufacturer (adults do this however).

There is no evidence that increasing the dose to 5 mg once daily, or 2.5 mg twice daily gives extra benefit. Occasionally our physiotherapists will suggest it for in-patients having an exacerbation, and we would consider it, but first try hypertonic saline once daily (with DNase once daily).

**Timing** - DNase – Timing is decided on an individual basis. In most cases it is given at least 30 mins pre-physiotherapy. Cochrane review states “RhDNase can be administered before or after ACT to suit the individual, although in children with well-preserved lung function FEF<sub>25</sub> was improved if RhDNase was given prior to ACT. If RhDNase is given before ACT it should be a longer time interval than immediately before ACT”

**Judgement of response:** A trial should be 3 months long especially for the most severely affected (FEV<sub>1</sub> <40%). There is a good correlation between response at 3 months and that seen after 12 months treatment.

**Side effects:** an exceedingly safe drug - rare and mild; hoarse voice occasionally and rash sometimes seen. There is **no** need to stop its use in patients with haemoptysis or pneumothorax

## 6.5 Hypertonic Saline

Hypertonic saline (HS) is sodium chloride in solution at a higher concentration than normal saline (which is 0.9% 150 mmol/L sodium). Many concentrations are available in different countries (3%, 6%, 7% etc.). We almost always use 7% (but not higher concentration) as it is superior to 3% if tolerated. Its mode of action is to osmotically draw water into the airways to hydrate the mucous and aid clearance.

### Indications:

- a) Long term mucus hydrator. Should be considered in the same way as DNase (section 6.4) and as a cheaper alternative. However studies show that some patients respond better to DNase and others to HS so a trial of therapy is important. Little positive evidence in those <6 years (a signal seen with improvement in LCI in the ISIS study). We commonly use HS once a day in the morning just pre-physiotherapy and DNase before the evening physiotherapy because of the time lag between DNase and physiotherapy.
- b) Short term use in an exacerbation to aid removal of sticky secretions.

**Risk of bronchoconstriction.** Always give salbutamol 2-4 puffs of 200 mcg before **every** dose and spirometry **must** be performed before **and** after the first dose in hospital prior to home therapy. Occasional patients have to stop because of pronounced bronchoconstriction (FEV<sub>1</sub> reduced >15%, or by 10-15% with symptoms) despite salbutamol.

**Dose:** 4mls 7% HS once or twice a day via nebuliser just before physiotherapy. We use 7% sodium chloride in 4ml plastic ampoules. Prescribable by GPs.

**How to give:** By nebuliser. In the eFlow (or Pari) given in one go but always 1ml left. By I-Neb always use LILAC chamber and you have to nebulise twice i.e. 2ml each time. The new AeroEclipse breath actuated nebuliser nebulises to dry but there is no comparative efficacy data currently. You can combine the HS nebuliser (NOT DNase) with a physiotherapy device e.g. Acapella, PEP or Aerobika if there are patient adherence issues. Our physiotherapists must teach the children how to do this.

**Side Effects:** Bronchoconstriction (see above), and it really does taste salty! May have to titrate up from 3% in younger children and those who don't initially tolerate 7%.

**Warnings:** **Not** recommended to make up nebulised antibiotics with HS

## 6.6 Mannitol

Inhaled dry powder mannitol is an osmotic agent (like hypertonic saline) that may increase mucociliary clearance in CF by improving cough clearance and rehydrating the airway surface liquid layer. To date, two published trials and two phase 3 studies suggest that it may

improve lung function in some older patients with CF. The most recent paediatric study (CF-204) in children aged 6-17 yrs was positive but is not yet published, although company data has been made public (Dec 2015). A NICE 2012 review of the role of inhaled mannitol recommended its use in adults with CF; once the paediatric study is published, it is hoped that NICE will extend their recommended use to children.

It should be considered third line (after DNase and HS) in those who do not respond to DNase and fail to respond to, or tolerate, hypertonic saline (HS).

**Indications:** Long term use in children with troublesome symptoms *e.g.* unproductive persistent cough or very sticky sputum, not responding to either DNase, HS or both.

**Dose:** 400mg twice a day. Comes in 40 mg gelatine capsules so 10 capsules via **specific** inhaler device - quite an onerous therapy.

**Side Effects: Bronchoconstriction.** Must have spirometry pre and post first test dose and ALWAYS pre-treat with salbutamol 2-4 puffs. Up to 25% have significant bronchoconstriction despite salbutamol precluding its routine use.

**Response:** Highly individual, some really respond well, others effectively zero so a therapeutic trial and outcome monitoring is important.

*Inhaled Dry Powder Mannitol is only licensed in adult 18 years and above and not currently included in the clinical commissioning policy for children. We are hoping this will change but until this does NHS England funding via IFR is required prior to initiation, and its use is a Consultant only decision.*

## 6.7 Long term azithromycin

There are several indications for azithromycin:

- a) As a conventional antibiotic (see section 6.2a) for treatment of respiratory infections especially if Mycoplasma or Chlamydia are being considered.
- b) As a long term anti-inflammatory agent, although it's mechanism of action is unknown. Studies show improvement in FEV<sub>1</sub> (median 5.5%) and reduction of oral antibiotic usage. It is believed to be effective in those with and without chronic *Pseudomonas* infection.
- c) **Part** of treatment of non-tuberculous mycobacteria (appendix 2)

**Criteria for long term use:** Very similar to those for DNase (see section 6.4) and should include those not benefiting from a 3 month trial of DNase.

**Dosage:** 250 mg once daily (<40kg) or 500 mg once daily (≥40kg) **three times a week** (Mon Wed Fri).

**Judgement of response:** Onset of action is slow (at least 2 months) and a minimum 4, preferably 6 month trial is required. *If there is no improvement it should be stopped after 6 months.*

**Side Effects:** Theoretically liver function abnormalities and reversible tinnitus although only one transient LFT abnormality was observed during our study. Liver function tests should be performed at any time blood is being taken for other reasons and at annual assessment. One study found symptom free, **small** increases in QTc from normal to borderline in 4 adolescent males but no children. Use of azithromycin **and** erythromycin (prokinetic) long term should be avoided due to potential additive side effects. There are some anxieties in the literature about Azithromycin acting as a single agent NTM treatment promoting either growth or resistance, although examining our own data and the US and French studies suggests no increased risk of isolating NTM in those on AZM. Indeed we and the French study found that long term AZM may reduce the NTM risk.

When AZM is started, consider stopping prophylactic flucloxacillin or co-amoxiclav, unless there is a good reason to continue, ie patient is known to have macrolide-resistant organisms.

## 6.8 Ivacaftor

In 2012, ivacaftor was approved by NHS England for clinical use in CF patients 6 years of age and above with at least one copy of the G551D mutation. All eligible patients in our clinic were commenced on this oral preparation, which is planned for long-term, uninterrupted use. The drug has since been approved for the other known gating mutations (G178R, S549N, S549R, G551S, G1244E, S1251N, S1255P, G1349D). Funding for the granule formulation has now been agreed (Dec 2016) for children aged 2-5 years with the same group of mutations. We should be aware of everyone's genotype at diagnosis and prepare for starting treatment on or shortly after their 2<sup>nd</sup> birthday. Children (< 18 yrs) with R117H are not eligible for treatment. See Clinical Commissioning Policy July 2015 - <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/10/a01pc-ivacft-cystic-fibrosis.pdf>

Ivacaftor (Kalydeco<sup>TM</sup>) is a small molecule drug which binds to CF at the cell surface and leads the chloride channel to open (this is termed 'potentiation'). Class 3, the 'gating' mutations lead to channels which are not open often enough, and when open are open for shorter time periods; the commonest of these is G551D. Phase 3 trials demonstrated significant improvements in FEV<sub>1</sub> (around 16-17% of baseline), reduction in exacerbations, significant weight gain, and a large drop in sweat chloride (often into the borderline, or even normal, range) in G551D and the other gating mutations. Trials have confirmed more modest efficacy in adults with the class 4 (conductance) mutation R117H, but efficacy was not evident in children for whom the drug is not licensed in Europe.

Ivacaftor is administered twice daily and it is crucial that it is taken with or very shortly after a high-fat meal or snack (with the usual pancreatic enzymes if used), as otherwise absorption is poor. Tablets must not be chewed.

### *Side effects*

- Were minimal in trials, although rashes are common.
- Rises in liver function tests were observed in some patients, and although these did not differ significantly from the placebo group, monitoring has been put in place (see below). This was seen more commonly in the 2-5 yr old age group, and was more common in children with previously raised LFTs. Dose reduction recommendations are available for patients with significant hepatic or renal impairment.

- The finding of cataracts in neonatal rats exposed to high doses of the drug in utero has led to additional vigilance in clinical trials and prescribed use; whether there is any link in humans is unclear. However cases of non-congenital lens opacities without impact on vision have been reported in paediatric patients treated with ivacaftor. Although other risk factors were present in some cases (such as corticosteroid use and exposure to radiation), a possible risk attributable to ivacaftor cannot be excluded. Baseline and follow-up ophthalmological examinations (annually in those under 12 years) are recommended in paediatric patients initiating ivacaftor treatment.

*Drug interactions:* There are some significant interactions, most importantly:

- **Azole antibiotics:** (itraconazole, voriconazole, posaconazole) lead to inhibition of the breakdown pathways of ivacaftor and accumulation of the drug. If co-administration is necessary, the dose of ivacaftor should be reduced; manufacturers suggest to twice weekly although this comes from modelled data, not human PK studies, and anecdotally, this may lead to loss of efficacy. Consultant advice should be sought in this event. Ivacaftor levels are not currently available, but sweat  $Cl^-$  could provide a useful surrogate for bioavailability.
- **Fluconazole** affects these pathways less than other azole antifungals but nevertheless manufacturers recommend reducing the dose to once daily.
- **Clarithromycin:** also leads to accumulation of the drug so manufacturer suggests reducing ivacaftor to twice weekly. There is no interaction with azithromycin, we recommend using AZM instead.
- **High dose corticosteroids:** may significantly decrease serum levels of ivacaftor and reduce efficacy.
- **Rifampicin, Rifabutin:** will significantly reduce ivacaftor levels; co-administration not recommended.
- **St John's Wort:** as for Rifampicin.
- **Grapefruit** (or juice) and **Seville oranges** (realistically, this is only marmalade; edible oranges are all fine): should be avoided as they reduce serum levels of ivacaftor. 'Lilt' fizzy drink does contain pure grapefruit juice, but in such small quantities, it is fine

**Pre and on-treatment monitoring & stopping criteria** (see proforma in appendix 6).

Due to the very high cost of the drug, the Commissioners in England have mandated monitoring and have imposed stopping criteria. See [www.england.nhs.uk/wp-content/uploads/2013/04/a01-p-b.pdf](http://www.england.nhs.uk/wp-content/uploads/2013/04/a01-p-b.pdf).

- **Sweat test** should be done within the 6 months prior to starting treatment and again at the next routine appointment (around 8 weeks).

The patients will be considered to have responded to treatment if either

- a) the patient's sweat chloride test falls below 60mmol/L **OR**
- b) the patient's sweat chloride test falls by at least 30%.

In cases where the baseline sweat chloride test is already below 60 mmol/L, the patient will be considered to have responded to treatment if either

- a) the patient's sweat chloride test falls by at least 30% **OR**
- b) the patient demonstrates a sustained absolute improvement in  $FEV_1$  of at least 5%. In this instance  $FEV_1$  will be compared with the baseline pre-treatment level one month and three months after starting treatment. Obviously this does not apply to 2-5 year olds.

If these changes do not occur, adherence problems and issues including taking it with fat, swallowing whole, concomitant medication, should be thoroughly explored. If no explanation is found, the sweat test should be repeated the following week and ivacaftor stopped if there is still an inadequate change. Experience has now shown though that clinical response does not correlate with sweat chloride changes.

- **Liver function** tests needs performing every 3 months for the first year but can then be done with annual assessment.
- **Stool elastase** in 2-5 yr olds before starting then at 6 months.
- **Ophthalmology examination** before starting, and annually in under 12 yr olds.

These drugs are an active area of research within the department, for example effects on LCI and serum/ sputum research markers. Please ensure that Prof Jane Davies is informed *before* a new patient is commenced on treatment. We are also requesting a number of additional investigations including LCI and serum/ sputum research markers. Please ensure that Prof Jane Davies is informed before a new patient is commenced on treatment.

### Orkambi

The commonest CF mutation, F508del, results in CFTR protein which does not reach the cell surface and it has clearly been shown that ivacaftor, as a single agent, is ineffective. Although efficacy was confirmed when ivacaftor was used in combination with the corrector molecule, lumacaftor (Orkambi<sup>TM</sup>), funding through NHSE has been declined on the basis of lack of cost effectiveness (<https://www.nice.org.uk/guidance/indevelopment/gid-tag530>). Small numbers of patients may be receiving Orkambi through a named patient programme.

## 6.9 Aspergillus & other fungi

### 6.9a Aspergillus fumigatus

*Aspergillus fumigatus* is a fungus that grows at 37°C. and the spores are of a size that they are deposited in the distal airways. The fungus can produce a large number of toxic and allergenic exoproducts. It can cause several lung problems in CF. In general, we advise avoidance of situations where there can be high levels of this fungus: mucking out stables (it is commonly found in damp hay), building sites (common when knocking down old buildings), and exposure to compost (heaps and bags). In general, if children insist on horse riding this must be done out in the open, and they should avoid being inside the actual stable.

There are rare reports of an ABPA-like picture being a complication of other strains of *Aspergillus*.

1. **Allergic bronchopulmonary aspergillosis (ABPA)** is a serious potential cause of lung damage in CF (prevalence varies 0.6 - 11%). Early pick-up depends on screening and high clinical suspicion. We perform baseline screening at annual review with blood tests, all sputum/cough swab/BAL samples are tested for it.

**Diagnostic criteria** - This can be a very difficult diagnosis to make, because in the context of CF, most of the major and minor criteria can be positive in the absence of ABPA. Atypical cases may lack some or all of these criteria – maintain a high index of suspicion, and discuss with the Consultant if in doubt.



**Clinical –**

- Increased wheezing/chestiness/chest tightness/chest pain particularly if failing to respond to antibiotics and inhaled medications.
- Fever and malaise.
- Thick sputum with brown or black bronchial casts.

**Investigations –***Major Criteria*

- CXR pulmonary infiltrates > 1cm diameter and segmental collapse.
- High serum IgE - especially an abrupt recent 4-fold rise to >500 iu/ml, which falls with prednisolone therapy.
- High specific aspergillus IgE RAST. The normal value <0.35 kuA/L may rise 10-100x in ABPA. Note that level >5.7 is highly indicative of ABPA (100% sensitivity, 94% specificity).
- Positive aspergillus IgG (ICAP) >90 mgA/L is positive in CF.
- Eosinophilia ( $> 0.4 \times 10^9/l$ ).
- Positive skin prick test to aspergillus antigen (3mm > control).
- Reversible bronchoconstriction.
- Central bronchiectasis.

*Minor Criteria*

- *Aspergillus fumigatus* culture from sputum (NB found in 30% of all CF patients).
- Brown/black plugs in sputum.
- Late skin test reaction.

NOTE Total IgE measured in IU/ml which = kU/L or kIU/L; 1 IU = 2.4ng

Specific IgE measured as kUA/L [A=allergen], often abbreviated to kU/L

**Treatment -**

For the first episode we use corticosteroids in conjunction with an oral antifungal agent.

**Oral corticosteroids:** Prednisolone, given in the morning after food (not enteric coated as it is not well absorbed in CF) is normally used at a starting dose of 2mg/kg/day (max 40mg) for 2 weeks, then halve the dose for 2 weeks, review at 1 month to assess for clinical response and to plan further weaning. We taper the dose by halving it [e.g. 20 mg daily goes to 10 mg daily etc.] **or** move to alternate day dosing [so if on 20 mg daily, move to 20 mg every other day, before reducing to 10 mg every other day etc.]. Reduction steps tend to occur every 2 weeks. We re-evaluate the clinical response with lung function, and total IgE, and we consider a repeat CXR. Note though that in some cases who do well, the IgE does not fall, so treat the patient not just the IgE level.

Inhaled and nebulised corticosteroids are used by some, but not by us – there is no evidence for their use.

**Pulsed IV methylprednisolone.** This is attractive for the non-adherent patient, and may have fewer side-effects, at the cost of more inconvenience. We use IV methylprednisolone 10mg/kg ONCE per day for 3 days every month, maximum dose 1gm. The 3-day pulses are

usually given on 3 occasions, a month apart, but may need to be longer depending on the response. Decision to use should be discussed with the consultant, but this is increasingly our preferred option.

**Itraconazole** [1<sup>st</sup> line antifungal] is used routinely for treatment of ABPA, in combination with oral or intravenous corticosteroids. For patients <12 years give 5mg/kg **bd** (max 200mg bd), or >12 years 200 mg **bd** orally (monitor liver function) and continue whilst they remain on steroids.

The liquid preparation should always be prescribed on an empty stomach. The capsules are poorly absorbed and are a last resort (as the liquid has a poor taste so may be refused), they must be taken with acidic drinks (e.g. Coca-Cola, orange juice, but not grapefruit juice), but **with** food.

**Itraconazole is stopped 1 month after the oral steroids are finished.**

Stop ranitidine/omeprazole if possible to improve absorption. Liver function tests should be performed if blood is being taken anyway for repeat ABPA markers, otherwise do them for prolonged courses e.g. at least after 1-2 months or if there is a history of liver dysfunction (see BNFC for recommendations). NB. It should also be given to anyone taking oral steroids (for whatever reason) if there is any suggestion of concomitant aspergillus infection while they are taking the steroids. Beware of drug interactions e.g., with rifampicin, omeprazole; and inhaled corticosteroids can cause adrenal suppression if also on itraconazole.

#### *Itraconazole levels*

We do not measure itraconazole levels routinely. However levels may still be indicated if there are concerns that a patient is not responding adequately to treatment; about toxicity; they are taking capsule form; or if interacting drugs are introduced. Please note that trough levels are taken.

- Trough sample should be taken after patient has been taking for at least 14 days (usually taken at the last bloods prior to discharge)
- Range: parent molecule: 0.5 - 2mg/l & total (including active metabolite) of 1 - 4mg/l
- 1ml of serum into clotted blood vacutainers

#### **Failure to respond to initial therapy (steroids and itraconazole)**

If clinical response is still poor:

- Consider IV methylprednisolone if oral steroids were used first line, or consider further pulse of methylprednisolone.
- Check to see if serum level of itraconazole is therapeutic. If not, consider increasing dose before changing to our 2<sup>nd</sup> line agent posaconazole (see below) taking note of any sensitivities available.

**Posaconazole** [2<sup>nd</sup> line antifungal] is a newer azole antifungal. A recent audit carried out at RBH showed that it is better tolerated than voriconazole, and therapeutic levels are readily obtained, particularly with the tablet formulation. It is an alternative when itraconazole is not tolerated or effective and it is critical to treat the patient with a second line agent. It would be prudent, before changing to posaconazole, to check to see if the serum level of itraconazole

was therapeutic. If not consider increasing the dose first. Treatment is for **6-12 weeks** depending upon therapeutic response.

Blood levels must be obtained when initiating therapy as there is still little published dosing information in children. It is not licensed for children under 18 years so it is a *consultant decision* to use in older children.

#### *Posaconazole levels*

- Pre-dose sample may be taken after patient has been taking for at least 1 week.
- Range: 1 – 5 mg/L.
- 1ml of serum into clotted blood vacutainers.

### **Relapses**

Relapse is common, be alert to this possibility even up to 2-3 years after 1<sup>st</sup> episode. A repeat course of steroids (as above) will be needed, consider using IV pulse methylprednisolone if relapse has occurred within a year of first episode of ABPA. High doses of steroids may be needed for a long time, but the aim is always to try to use as short a course as possible so close follow up is needed. Side effects are discussed in section 6.3 on use of steroids.

A repeat course of antifungals will also be required as per guidance above, in some cases posaconazole may be considered first in preference to itraconazole for relapses, but this will be dependent on time from last episode and is a consultant decision.

### **Hard to treat or frequently relapsing ABPA – other approaches**

- **Nebulised amphotericin** (non-liposomal) may be used in difficult cases twice daily after physiotherapy (check for bronchoconstriction and use bronchodilator pre-dose). If it essential to use it, and the child does not tolerate the normal amphotericin, consider using nebulised liposomal amphotericin; note the high cost.
- **IV caspofungin** may be an option in refractory cases. Its use is a *consultant decision*.
- **Omalizumab** - the anti-IgE monoclonal antibody may rarely be considered on the basis of case reports; this is a *consultant decision* and funding approval will be needed prior to starting. Subcutaneous injection every 2 to 4 weeks depending on IgE level.

### **Post script - we have now stopped using voriconazole**

Whilst it has better absorption than itraconazole and is not affected by gastric pH, its use is limited by side effects, particularly severe photosensitivity (in some cases despite use of high factor sun screen). With a recent MHRA alert highlighting the risks of squamous cell carcinoma following phototoxic reactions, as well as the risk of liver toxicity, we have effectively stopped using it. It would be exceptional and obviously is a consultant decision.

Liver function tests are mandatory (weekly for the first month and then monthly thereafter), and must not be forgotten. It is also imperative that patients are advised on sun protection. Similarly to itraconazole, adrenal suppression has been reported in patients on voriconazole also taking inhaled corticosteroids.

#### *Voriconazole levels*

- Pre-dose sample may be taken after patient has been taking for at least 3 days
- Range: 1.3 - 5.7mg/L

- 1ml of serum into clotted blood vacutainers

## 2. Other manifestations of aspergillus lung disease

- **Positive culture only** - *Aspergillus fumigatus* may be found in routine sputum or BAL samples, the significance of this in an asymptomatic child with normal ABPA blood markers is unclear. We are increasingly trying to eradicate it when seen with a one month course of oral liquid itraconazole and we will always treat if found at BAL.
- **Aspergillus bronchitis** - it is becoming increasingly clear that *Aspergillus fumigatus* causes more than ABPA, and aspergillus bronchitis is recognised in children who have grown *Aspergillus* in sputum and often have chronic respiratory symptoms or more exacerbations. They will usually show evidence of an immunological response (positive *Aspergillus* IgG (ICAP) >90 mgA/L) but no rise in total or specific IgE (i.e. no hypersensitivity). We would treat this with a three-month course of itraconazole in the first instance. If symptoms return on stopping the itraconazole a course of posaconazole would be 2<sup>nd</sup> line.
- **Invasive disease** is rare but may occur in severely debilitated, immunosuppressed (including steroids) or neutropenic patients. It is heralded by worsening of symptoms and progression of x-ray shadows, sometimes with cavitation, haemoptysis and pleuritic pains. Metastatic fungal spread is also possible. CT scan is useful to confirm the diagnosis. Such cases warrant treatment with IV caspofungin.
- **Mycetoma** is rarely seen in CF but has been described. Suspect if halo sign in a cavity and 6-8 positive IgG ICAP. Confirm with CT. Treatment individualised - too rare to offer guidelines.
- **Amyloidosis** is a late, incredibly rare and ominous complication of ABPA and sometimes CF alone. It should be considered if the following occur: proteinuria with oedema (nephrotic), goitre, hepatosplenomegaly not due to CF liver disease.

## Indications for intravenous antifungal therapy

This is a *consultant decision* only and is made after consultation with microbiology.

- Severe, chronic and persistent aspergillus lung disease (including ABPA), with multiple side effects from conventional steroid therapy.
- Invasive aspergillosis
- Patients on NTM treatment requiring ABPA treatment when drug interactions may be problematic (*e.g.* with rifampicin).

First line is Caspofungin (it is easier to administer and cheaper). 2<sup>nd</sup> line would be Liposomal amphotericin.

### 6.9b *Scedosporium apiospermum* & *Lomentospora prolificans*

*Scedosporium* is the second commonest fungus isolated in CF respiratory secretions; *Lomentospora prolificans* has been renamed recently from *Scedosporium prolificans*, and is highly drug resistant. Similarly to *Aspergillus* it can cause fungal balls in cavities and can be found in paranasal sinuses. Clinical implications are poorly understood; it is often not associated with symptoms. We are now much more likely to consider early attempts at eradication especially if symptomatic but only after treatment for other causes of cough or exacerbation have been treated and excluded.

If treatment is considered –

***Scedosporium apiospermum*** – we will use posaconazole. If fail to eradicate consider voriconazole which has a lower MIC.

***Lomentospora prolificans*** – we will use posaconazole + terbinafine.

The microbiology lab will supply azole sensitivities and treatment may be guided by these when available, although we would still try to avoid voriconazole because of the side effect profile.

Rarely, *Scedosporium* has been known to cause an allergic bronchopulmonary mycosis (similar to ABPA), and an azole should be used for this with consideration of corticosteroids, this will be a consultant decision.

### 6.9c *Candida albicans*

*Candida* is commonly grown in sputum and cough swabs, and is usually from the mouth. The use of long term antibiotics is usually blamed. Do not forget to ask about perineal *Candida*, it is common in infants with nappy rash and can be present in older children. Local treatment will be given if the child is symptomatic *i.e.* sore mouth, visible white plaques; using nystatin 100,000 units/ml 1ml swished around the mouth and swallowed QDS for a minimum of 7 days. Alternative is miconazole.

However, it is not expected to be found in BAL fluid (unless nasal approach is used where it still may be a contaminant from the pharynx). We tend to treat with up to 2 weeks of oral fluconazole if found in BAL (see BNFC for dosage).

### 6.10 Haemoptysis

Streaky haemoptysis is common with chronic infection but may indicate deterioration so sputum should be cultured and a course of antibiotics considered. Haemoptysis must be differentiated from haemetemesis. The source is usually from hypertrophied tortuous bronchial arteries supplying areas of chronic airway inflammation. *S aureus* is the one bacterium that has been identified to be associated with an increased likelihood of massive haemoptysis. Massive, profuse haemoptysis due to vessel rupture can be life threatening (>250 mls/24 hours is the conventional level, but anything more than half a cupful over 24 hours merits referral). Bad haemoptysis is usually seen in patients with bad lung function, but has been reported in patients with normal spirometry. Please contact us. This occurs in 1% patients/year. In CF haemoptysis, remember the possibility of pulmonary embolism if the child has a portacath (see above). The patient may experience a gurgling sensation which is a

reliable lateralising symptom indicating the bleeding site. The patient is likely to be very scared - reassurance is essential.

Primary management is resuscitation if needed (incredibly rare) - lay patient on side (gurgling side down), give oxygen. There is no evidence to suggest that stopping DNase is necessary, but if the child is taking NSAIDs, stop them. Consider stopping hypertonic saline if massive haemoptysis if the HS is causing more coughing. Physiotherapy may have to be adapted - seek advice from the Physiotherapist.

### **Investigations -**

- Hb & platelets.
- Coagulation.
- Group & save or cross-match blood.
- Sputum culture
- CXR can show new infiltrates but may not change and is of little use in localising the bleeding source.

### **Initial management –**

- Mild haemoptysis with an infective exacerbation will normally settle without specific intervention.

For more severe cases -

- Give blood and correct coagulation defects if necessary (IV vitamin K/ FFP / cryoprecipitate).
- Start intravenous antibiotics; *S aureus* cover must be included.
- Continue with gentle regular physiotherapy, but omit chest clapping for 24 hours. This is essential so contact our physiotherapists for advice.
- Stop any NSAIDs.

### **Physiotherapy management –**

There are no studies relating specifically to haemoptysis and chest physiotherapy. Instead, general advice is given based on clinical experience. It is important to continue with chest clearance to remove blood and infected secretions. These physiotherapy guidelines for haemoptysis are based on those used by the Adult CF Unit at Royal Brompton Hospital.

Management is aimed at clearing secretions without increasing the bleeding. This may result in temporarily stopping manual techniques, adjuncts and positive pressure and then reintroducing them gradually. It is preferable to wait 24 hours post-bleed before starting positive pressure, adjuncts or manual techniques (then only one at a time). In some cases, these will need to be restarted sooner for effective sputum / old blood clearance. This should be discussed with a senior member of staff.

- Initially ensure the source of blood is not from the mouth, nose or stomach.
- Next work out how much blood the patient has cleared in the last 24 hours.

### **Positioning**

- It is useful to note the activity and position at the time of active haemoptysis. The weakened artery may rupture due to increasing heart rate or increasing the flow of blood when the area of lung supplied by the artery is dependent (bronchial arteries lie posteriorly so supine may exacerbate bleeding).

- If the patient can establish the location of the bleed, it is advisable to avoid chest clearance with the affected lobe dependent (bleeding lung down).
- If the haemoptysis is severe the bleeding location should be dependent (bleeding lung down) while the bleed is active to avoid asphyxiation.
- When the bleeding has subsided, you can place the bleeding lung uppermost to facilitate drainage as needed. Chest clearance can be resumed a couple of hours after active bleeding as per the moderate protocol.

### NIV

- In the presence of moderate haemoptysis NIV should be discussed with a senior adult CF physiotherapist and the medical team. If the patient is known to have type II respiratory failure and is on nocturnal NIV it is likely it will need to be continued.
- In the presence of massive haemoptysis NIV should be discussed with the physician/crash team.

<b>Physiotherapy management in the presence of haemoptysis</b> (CF Trust guidelines on physiotherapy management 2011)	
<b>MILD</b>  Streaking or <5mls in 24 hrs. Sputum and blood mixed together	<ul style="list-style-type: none"> <li>• Reassurance</li> <li>• Normal airway clearance regimen</li> </ul>
<b>MODERATE</b>  5mls to <250mls blood in 24 hours Fresh blood  1 white sputum pot = 250mls	<ul style="list-style-type: none"> <li>• Airway clearance techniques should minimise increases in intrathoracic pressure.</li> <li>• Airways clearance with ACBT or AD initially.</li> <li>• Minimise unproductive coughing.</li> <li>• Positioning – see below.</li> <li>• Avoid moderate and high intensity exercise.</li> <li>• Continue nebulised DNase.</li> <li>• Consider stopping HTS or mannitol if causes coughing – discuss with senior.</li> <li>• Graded approach to reintroduce ACT if no further bleeding – in discussion with senior.</li> </ul>
<b>SEVERE</b>  > 250mls blood in 24 hours	<ul style="list-style-type: none"> <li>• Urgent medical review.</li> <li>• Position patient with bleeding lung down.</li> <li>• Discuss with senior physiotherapist.</li> <li>• Oxygen / humidification.</li> <li>• When bleeding has subsided resume treatment as for moderate.</li> </ul>
<b>Post Bronchial artery embolisation (BAE)</b>	<ul style="list-style-type: none"> <li>• Chest clearance can resume after the procedure in consultation with the physician and radiologist.</li> <li>• Analgesia pre ACT may be required.</li> <li>• Start gentle exercise and build up.</li> <li>• Transient dysphagia are common afterwards.</li> </ul>

### **Further management -**

Most bleeds will cease in response to this approach but if massive bleeding persists, or if repeated bleeding occurs over a short period (daily for 7 days with >100mls on 3/7 days) consider:

- **IV vasopressin** (Argipressin) is occasionally useful - the paediatric dose is 0.3 units/kg (maximum 20 units) over 20 minutes followed by 0.3 units/kg/hour (maximum 1 unit/kg/hour) continued for 12 hours after bleeding has stopped and gradually withdrawn over 24-48 hours (maximum duration 72 hours). It can lead to water intoxication and can cause bronchoconstriction. **IV terlipressin** (for children >12 years) has fewer side effects; dose (from BNFc) is 2mg then 1-2mg every 4-6 hours until bleeding is controlled, (maximum duration 72 hours); this is used by the adult unit.
- **Bronchoscopy** - It is rarely useful in the acutely bleeding child. If you are considering this procedure initially try flexible, then consider a rigid, under general anaesthetic. With massive haemoptysis, go straight to rigid bronchoscopy. This can be technically very difficult but may allow clot removal (beware precipitating further bleeding), tamponade of bleeding site using a Fogarty catheter, or haemostasis with thrombin glue or iced saline lavage/vasoconstrictor lavage.
- **Selective bronchial angiography and embolisation** can only be carried out by experienced specialists in a tertiary centre. Numerous dilated tortuous bronchial arteries are often identified some of which may take origin from aberrant sources. Actual source of bleeding is difficult to discern but generally a number of large vessels (>2.5mm) are embolised using variable sized gel foam pledgets. Great care to avoid spinal artery (with consequent paraplegia) and other systemic artery embolisation is necessary. Post embolisation pain requiring narcotic analgesia and transient dysphagia are common. This is not a cure and many patients develop new vessels within months or years that may bleed and so require further embolisation.
- **Oral tranexamic acid** has been used long term in recurrent bleeders with some success. Dose is 15-25 mg/kg tds (max 1.5 g/dose). It may be prescribed acutely as well (oral or IV).
- **Oral atenolol** has been used on an anecdotal basis - *Consultant decision*, and remember even selective  $\beta$ -blockers can cause bronchoconstriction. Starting dose is 0.5 mg/kg once daily (max 12.5 mg OD). Dose can be titrated up if necessary.
- **Lobectomy** may be considered as a last resort.

## 6.11 Pneumothorax

See BTS guidelines -

<https://www.brit-thoracic.org.uk/document-library/clinical-information/pleural-disease/pleural-disease-guidelines-2010/pleural-disease-guideline/>

Please contact us. A high index of suspicion is needed - consider the diagnosis if there is unexpected deterioration, unexplained chest pain, or worsening breathlessness. If in doubt, do a CXR but CT scan may be needed to detect it or determine optimal site for drain placement. The incidence of pneumothorax increases with age (overall 8%) and is a marker of severe lung disease. It carries a bad prognosis, particularly if the chest drain cannot be rapidly removed. All but the most trivial pneumothorax in a stable patient mandates admission to hospital.

A tension pneumothorax is an emergency that requires urgent treatment with a chest drain, regardless of the CF. A small asymptomatic pneumothorax can be managed by observation alone and may resolve but in an already hypoxic patient, such a leak may cause decompensation. If the patient is decompensating or has a large pneumothorax, management includes -



- Monitor SpO<sub>2</sub> and give oxygen (check for CO<sub>2</sub> retention).
- Intercostal chest drain.
- Local anaesthesia and subsequent oral analgesia.
- Antibiotics (IV antibiotics are prudent in all but the most trivial pneumothoraces).
- Gentle physiotherapy must be continued, techniques and adjuncts may need changing (no PEP masks or IPPB). Deep breathing with inspiratory holds is encouraged. Please discuss this with the senior physiotherapist at Brompton.
- If the child is using BiPAP, this is a difficult dilemma, and BiPAP may need to be withheld temporarily. Seek senior physiotherapy and medical advice.

The lung may be slow to re-expand and if after three days there are no signs of resolution with a continuing air leak, then consult with surgeons (discuss with the paediatric consultant first). There is anecdotal evidence of the use of endobronchial valve placement in people with CF. Surgery should be considered if no progress is being made. In some centres there is 50% mortality if a patient has a chest drain for more than one week. Similarly, recurrences are common (>50% ipsilateral and up to 40% contralateral) necessitating surgery. Sclerosing pleurodesis or pleurectomy make subsequent transplant very difficult although are not an absolute contraindication to future transplantation. Localised abrasion pleurodesis +/- surgical resection or thoracoscopic stapling of blebs lead to less adhesion so are preferable options, unless transplantation is never going to be an option (which is rarely the case). Pleurodesis is recommended for first ipsilateral recurrent pneumothorax.

No spirometry for 2 weeks after resolution.

Remember also BTS guidelines about flying after a pneumothorax – need to wait at least six weeks.

## 6.12 Intractable wheezing / severe small airways disease

At least 50% of CF patients are atopic on the basis of skin prick testing to common allergens, although if aspergillus is excluded the prevalence of atopy is the same as that of the non-CF population. The great majority are well controlled with conventional ‘asthma’ type treatment using standard BTS guidelines for asthma.

In contrast, the foregoing discusses a small (and we have found with time a markedly rarer) group of patients characterised by -

- Little if any sputum production (despite large amounts in the chest).
- Wheezing.
- Tight chest.
- A severe obstructive lung function pattern.
- Little if any bronchiectasis on CT scan.
- Often but not always IgE >500 iu/l.
- May be more common in girls.

These children should not be managed without consultant input as they pose an extremely difficult management problem and would also compulsorily fall into the category requiring a ‘challenging CF protocol’ (see section 6.13).

Particularly ominous is the patient who used to be a 'conventional sputum producer' who quite suddenly stops producing and begins to wheeze. There is no research on this subject so all suggestions are empirical.

- Check adherence to treatment recommendations, no physiotherapy equals no sputum.
- Is there ABPA? This is the most common and conventional explanation.
- Is there *Aspergillus fumigatus* in the sputum?
- Is there a new bacterium in the sputum- including Non-tuberculous mycobacteria?
- Is there an obvious clinical atopic history (not just skin testing) for example animals, HDM etc?

If these all negative:

- Consider CT scan to assess structural damage / bronchiectasis (including expiratory views).
- Consider bronchoscopy and pH study.
- Consider CF-related diabetes and perform a CGMS test (continuous glucose monitoring system).

### Treatments –

- Begin **long-acting  $\beta_2$ -agonist** (salmeterol or formoterol). If >6 years formoterol (Oxis) via a turbohaler is preferred because it is a pure agonist. Under consultant supervision, doses can be empirically increased. Watch for side effects (tremor, palpitations etc.) then cut back. There are risks of hypokalaemia so serum potassium should be checked if high dose is to be continued (bananas are rich in potassium). There is also a theoretical risk of lengthening the cardiac QTc interval and an ECG should be considered if using high doses after 2 weeks therapy (note - we have never seen a case). Symptomatic benefit must be proven and home peak flow or FEV<sub>1</sub> monitoring considered.
- **Symbicort** (budesonide/formoterol combination) can be used regularly with extra 'as required' doses administered through the day. Maximum we recommend is 400/12 twice daily with 4 extra doses of 200/6 allowed per 24 hours.
- Increase **inhaled steroids** to 800 mcg twice a day equivalent dose of budesonide. However there is increasing evidence that steroids (oral and inhaled) increase the risk of isolating NTM so as always a consideration of risks and benefits is required.
- Consider using short acting  $\beta_2$  agonists, 10 puffs 3-4 times a day via a spacer.
- Consider Tiotropium inhaler – an antimuscarinic agent. Although only licensed >18 years it may still be necessary for this difficult problem in younger patients. This is a *Consultant decision*. We should use the Spiriva® Handihaler (dry powder) 18 mcg once daily. We do not use the Respimat® MDI as the product license specifically states not to be used in CF; however there have been recent publications using the Respimat® in patients with CF.
- Consider slow release theophyllines e.g. Slophyllin – see BNFC for doses.
- Consider also IV aminophylline for an in-patient with severe wheezing (use standard acute asthma doses).
- Consider a trial of Montelukast.

If above fails after 2-4 weeks:

- **Prednisolone** 2mg/kg/day in the morning for 14-21 days then review. If successful then try to wean over two weeks to 1mg/kg alternate days.

- **Pulsed methylprednisolone** can also be considered 10mg/kg once a day (maximum 1 gm/day) for 3 days (3 doses in total) and this can be repeated as a single dose weekly in severe, intractable cases. This is given as an infusion over 30 mins, there is a risk of heart failure if given as a bolus.

If there are persisting problems, consider alternative diagnoses again (ABPA, new bacteria) and ensure bronchoscopy, pH study CT chest scan and CGMS have been performed. In this situation, or if the patient is better but with unacceptable steroid side effects consider:

- **IV immunoglobulin** therapy e.g. Flebogammadif. Dose 1g/kg over 16 hours on two successive days then 1g/kg on a single occasion each month. Trial should last 6 months. Benefit not usually seen till 3 months. Bloods should be taken before each dose for IgG, IgA, IgM, IgE and liver function tests; IgG subclasses should be measured before initiation of the regimen. Before initiating therapy, patients undergo bronchoscopy with biopsy, pH study & CT scan and CGMS unless recently done.

As part of the DoH Demand Management Plan, we are now required to obtain confirmation of funding from the patient's CCG **before** initiating treatment. It is also mandatory for outcome data to be collected to ensure reimbursement (Flebogammadif is excluded from the payment by results tariff). For CF this is improvement in FEV<sub>1</sub>; improved exercise tolerance and reduction in days of school. Where IV immunoglobulin therapy is being considered contact the pharmacy team as soon as possible, as this process can take weeks. See trust guideline on the intranet.

NOTE: Pre-treat patient before **EACH AND EVERY** dose with antihistamines (e.g. cetirizine or chlorpheniramine) and IV hydrocortisone as Flebogammadif, especially the first dose, can activate complement with impressive side effects (severe headache, flushing etc.).

- **Azithromycin.** No objective evidence in this situation but 250mg/day if <40kg or 500mg/day if >40kg given daily for six months may be beneficial although the effect may take at least 2 months to be seen.
- **Subcutaneous terbutaline** has also been occasionally very successful, although we have not needed to use it for 15 years. Dose is 2.5 mg/day (5ml) of the intravenous preparation rising over 7 days to 5mg/day (10ml) to avoid side effects, and occasionally up to 10mg per day. We use a Thalaset needle and a Canè Crono ambulatory infusion pump. Treatment must be started as an in-patient. Potassium depletion does not appear to happen; side effects tend to be local soreness/bruising around the needle site. It has been used with little psychological harm in children as young as 8 years but it does require careful management. Our asthma nurse specialists must be involved in setting this up.
- **Methotrexate.** Has been used in a few patients but response is often disappointing. The dose is given **ONCE A WEEK**, on the same day of the week. The standard dose is 10 mg/m<sup>2</sup>/week and this dose is reached gradually over a number of weeks. Increments are usually 2.5 mg, which is the strength of 1 tablet (it also comes as 10 mg tablets). A 3-month therapeutic trial is undertaken. Higher doses up to 20 mg/m<sup>2</sup>/week would be considered if no benefit occurs at 10 mg/m<sup>2</sup>/week. Folic acid 5mg is given 48 hours after the Methotrexate and regardless of the methotrexate dose

Bloods are taken weekly for FBC, LFTs, electrolytes & creatinine, once stable on the maximum dose they can be done monthly. All prescribers must complete the 'Methotrexate Patient Held Monitoring and Dosage Record' when initiating therapy and monitoring treatment (kept in Paediatric outpatients). The consultant who initiated the therapy must be identified in the book and take full responsibility for dose changes and the course of treatment. This booklet contains information about methotrexate treatment, doses and blood results, and must be retained by the patient. This booklet should be brought to all appointments where therapy is being reviewed. Always check for drug interactions (see BNFC).

### 6.13 'Challenging CF' protocol

#### *Introduction*

Clearly some of this protocol will have already been done as part of the child's routine clinical care. We activate this protocol if we are 'stuck' despite routine measures; this replaces the decisions e.g. to admit for a bronchoscopy, usually taken in a busy clinic or at the weekly post-clinic MDT meeting. This protocol is based on what we do successfully with our MDT approach to severe asthma.

#### *Definitions (which are guides, not prescriptive)*

- a. Any child whose spirometry is worse than -2 Z-scores.
- b. Any child who receives  $\geq 3$  courses of intravenous antibiotics annually (whether planned electively or unplanned).
- c. Any child requiring home oxygen (almost invariably will have been assessed in the protocol long before this stage).
- d. Any child in 'nutritional failure' – BMI < 2 Z scores below the mean; drop in weight or BMI centiles by 10% over a year.
- e. Any child with a severe CF pulmonary complication.
  - Massive haemoptysis.
  - Pneumothorax.
  - Therapy resistant ABPA or other cause of severe steroid dependency.
- f. Any child whose self or parent-reported symptoms are significantly different to what a clinician would expect (either over- or under-estimated) and/or any child whose everyday life functioning (school attendance, exercise tolerance) appears at odds to the objective clinical signs of disease severity).
- g. Any child in whom there is refusal or extreme reluctance to give prescribed treatment by the carers.

#### *What are the likely causes?*

1. Non-adherence to therapy - we need to obtain objective data.
  - obtain record of GP and hospital (RBH and local) prescriptions;
  - home visit to check medications (where stored, whether still in original wrappings, how given, knowledge of medications, expiry dates);
  - physiotherapy knowledge of techniques they are supposed to know;
  - down-loading data from nebulisers about usage;
  - blood levels if on prednisolone. Consider also if on itraconazole or posaconazole.
  - Exploration of the beliefs held about the treatments and the understanding of how they should be administered by the child patient and their family/carers.

2. Adverse environment
  - passive or active smoking (salivary/urinary cotinine)
  - allergen exposure (RAST and skin tests)
  - home environment, including nebuliser cleanliness (very important if ABPA the issue).
3. Significant co-morbidity – upper airway disease (ENT evaluation including imaging where appropriate), gastro-oesophageal reflux (pH study, GI referral if any doubt)
4. Social challenges - parenting/other. Needs sensitive assessment to look at family's strengths and challenges.
5. Nutritional failure (especially if relatively good pulmonary function)
  - *Impaired glucose metabolism* - check CGMS, home glucose monitoring (see section 8.1).
  - *Malabsorption* - basic GI screen including food diary, faecal fat microscopy, coeliac screen, ESR, urinary electrolytes, and GI referral if still an issue.
  - *Gastro-oesophageal reflux* (pH study, GI referral if any doubt)
6. Psychosocial circumstances. To include assessment of adherence to treatment, beliefs about treatment, and of the child and family and their relationships with the statutory and voluntary services that support them (e.g. school).

‘Bad lung disease’ of which there are two main types which need to be separated by investigations (below)

- ‘Distal and dry’ – the child who has small airway disease with air trapping on CT scan, non-sputum producer and dry airways on bronchoscopy. MUST exclude reflux. Need to explore systematically acute bronchodilator reversibility, pulsed methylprednisolone, possibly intravenous immunoglobulin. See section 6.12.
- ‘Pan-airway and productive’ – the child who has bad proximal bronchiectasis and marked purulent airway secretions. Make sure we know everything about what is growing in the airway (including anaerobes, NTM, unusual gram negative rods, consider getting 16sRNA studies for the real oddities) by BAL (consider induced sputum regularly also), then rotating nebulised antibiotics, 3 monthly intravenous antibiotics, long term macrolides, DNase, hypertonic saline, different physiotherapy techniques

### **Protocol:**

**Step 1:** Obtain prescription records and have uptake assessed by Pharmacy. Multidisciplinary assessment but at a planned separate visit, not part of the busy routine clinic. See nurse specialist, physiotherapists, dietician, psychologist, and pharmacist. Tests will include RAST and/or skin prick tests, urinary cotinine if not already done. Refer to ENT outpatients. Ideally get all this done in one admittedly tiring day. Home visit jointly by nurse specialist and physiotherapist; the team feel this may need to be done on two occasions.

**Step 2:** Detailed assessment of the information to date. Depending on the results, an admission may need to be planned. This will be similar to the severe asthma protocol, and if it is thought that admission is needed, this will be planned in detail.

**Step 3 (Nutritional):** 3 day admission (see above). Nicola Bridges or Saji Alexander to see with sugar results in OP, GI referral after the admission if we are still struggling. See section 7.1 for algorithm.

**Step 3 (Respiratory):** Admission for CT scan, LCI, bronchoscopy and pH study. Formal lung function with bronchodilator reversibility, exercise testing, overnight SpO<sub>2</sub> and TcCO<sub>2</sub>.

(If appropriate, the respiratory and gastrointestinal steps can be combined in one admission)

**Step 4:** Review of all the above with full MDT, then see consultant, again outside routine clinic, formulation of action plan with the child and family.

## 6.14 Bronchoscopy

Indications in CF:

1. Need for **microbiological diagnosis** in a non-sputum producing child:
  - Not responding to IV antibiotics.
  - Not previously infected with *P aeruginosa* in whom there is clinical concern due to persistent deterioration (do not simply start empirical antipseudomonal therapy).
  - After eradication of new *P aeruginosa*, patients will all have an induced or spontaneous sputum culture. If they remain symptomatic and sputum culture was negative, they will have a BAL. We will not rely on a cough swab to prove successful eradication.
  - **A cough swab / sputum sample must be taken on the same day prior to the bronchoscopy.**
  - We try to obtain an induced sputum (usually in children above 2-3 years) before deciding on a bronchoscopy (section 6.15e), and this practice has meant we need to do fewer bronchoscopies, certainly in older children. Arrange with the physiotherapy dept.
2. **Therapeutic suctioning:**
  - Persistent focal area of collapse / consolidation on chest x-ray, may also include instillation of DNase (2.5 mg in 10 mls 0.9% sodium chloride (normal saline)).
  - It is rarely of value when chest x-ray changes are generalised.
3. **Other indications:**
  - Intractable wheezing to exclude bronchomalacia.
  - Lavage for fat-laden macrophages to exclude aspiration.
  - Persistent defect on isotope ventilation scan.
  - Lung function lower or LCI higher than expected (previously assumed due to technique).
  - Haemoptysis may occasionally require rigid bronchoscopy.
  - At the time of a general anaesthesia for another procedure (may be a non-bronchoscopic BAL).

Bronchoscopies are performed on Monday or Friday afternoons in Theatres, booking for in-patients is done through bed managers. Bookings for out-patients who are to be admitted are through the Bed Manager (ext 2118). The bronchoscopy health care assistant (HCA) must also be informed.

They are all done under general anaesthesia, and often patients will have had no antibiotics prior to the procedure but often require minimum 48 hours IVABs after if significant secretions are seen. In practice bronchoscopy is often done at the start of a 14 day IVAB course when the patient is not doing well and no microbiology is available or nothing is ever grown.

No other preparation is required, but a procedure-specific consent form must be signed. Patients must have no food or bottled milk for 6 hours, breast milk for 4 hours, and clear fluids up to 2 hours before the procedure.

It may be useful for a physiotherapist to be present during the procedure. Sometimes DNase may be instilled down the bronchoscope suction channel to a localised collapsed area that is obstructed by thick mucus. The dose is 2.5 mg in 10 mls 0.9% sodium chloride, and then a small amount of air is instilled down the bronchoscope to ensure no drug is left in the suction channel.

Bronchoalveolar lavage fluid is sent to microbiology for culture (including NTM, fungi), virology for immunofluorescence, and cytology for fat-laden macrophages. Protocol is to use 4 aliquots of 1ml/kg lavage, usually from right middle lobe or lingula (or worst looking lobe).

To potentially increase the microbiological yield, we lavage from THREE lobes.

All CF patients undergoing bronchoscopy must be discussed with Prof Jane Davies re inclusion in research studies.

## 6.15 Chest physiotherapy

### 6.15a Airway Clearance Techniques

A paediatric physiotherapist is available in clinic to assess all patients and discuss and review their physiotherapy management. The airway clearance techniques (ACT) used vary within age groups and are always assessed on an individual basis:

- **Babies and infants**– Techniques taught may include modified gravity assisted positioning (this is NOT tipping) and intermittent chest clapping; as well as infant positive expiratory pressure (PEP), assisted autogenic drainage (AAD) and age appropriate exercise.
- **From 2 years and upwards** – When the child is able; introduce blowing games, bubble PEP and forced Expiration Technique (FET) “huffing” with the aim to progress to Active Cycle of Breathing Technique (ACBT) when able. Incorporate physical activity in the session. Variety is important in this age group to aid adherence. Positive Expiratory Pressure (PEP) and other oscillating PEP devices may be introduced as indicated.
- **From 8 years** – Encourage more independent treatments using a full variety of airway clearance devices and techniques as appropriate (with family support /supervision).

**Exercise:** The importance of exercise is highlighted as evidence links exercise capacity to improved survival, and therefore exercise should be incorporated in the patient’s life from an early age. Exercise has been shown to reduce sputum viscosity, improve ventilation and peak expiratory flow, and facilitate movement of mucus. Exercise prior to ACT has been shown to have an additive effect on sputum expectoration but must be combined with FET to clear sputum effectively. Current thinking is that exercise should be taken 3-5 times per week, lasting for a minimum of 30 minutes per session. Exercise needs to be consistent and varied and fit into family life with the aim of it becoming a family habit. Web based logs and digital software may be useful in motivating certain age groups,

The frequency and duration of ACT will alter depending on infective exacerbations, severity of disease and individual circumstances. In the majority of cases twice a day for 10-15 minutes is the minimum recommended.

Airway clearance techniques taught include:

- **Active Cycle of Breathing Techniques (ACBT)** – Combination of thoracic expansion exercises, breathing control, and forced expiration techniques.
- **Blowing games** including Bubble PEP – ideas include blow football, blow painting, bubbles and whistles. Bubble PEP requires the child to blow into a volume of water (10cms) via a 40cm tube (with washing up liquid) to create bubbles. The water provides resistance to expiration and therefore creates positive expiratory pressure and oscillation in the airways to mobilise secretions. Careful consideration should be given to age appropriate blowing toys, cost and infection control.
- **Positive Expiratory Pressure (PEP)** – Provides resistance to expiration through a mouthpiece or facemask, which temporarily increases functional residual capacity, encouraging collateral ventilation and alveolar interdependence, to recruit closed airways and get air behind secretions. This is followed by forced expirations.
- **Infant PEP** – PEP adapted for infants via a mask over the child's nose and mouth. Performed in the caregiver's arms or seated on their lap, bouncing on a gym ball (may be combined with assisted huffing).
- **High Pressure PEP** – 8-10 regular PEP breaths followed by forced expiration into the PEP mask. This creates pressures of 40-100 cmH<sub>2</sub>O and will therefore not be appropriate for all patients. Ask the physiotherapist for advice.
- **Oscillating PEP devices (e.g. Flutter<sup>®</sup>, Acapella<sup>®</sup> and Aerobika<sup>®</sup>)**. Create positive expiratory pressure and oscillation on exhalation to prevent premature airway closure, mobilise secretions, improve airway patency and reduce sputum viscosity.
- **Autogenic Drainage (AD)** – Uses controlled breathing which aims to attain the highest expiratory airflows to move secretions from peripheral to central airways while avoiding coughing and significant airway closure/or compression. Breathing is usually from low to high lung volume where secretions are expectorated.
- **Assisted Autogenic Drainage (AAD)** - Used for infants or non-cooperative patients. Manual pressure applied over the chest on inspiration which stimulates the patient to exhale slightly more with each breath and guides the patient towards the desired lung volume to mobilise secretions.
- **Positive Pressure (IPPB or NIPPV)** – Devices using positive pressure to augment tidal volume and reduce work of breathing. Useful in certain situations in hospital and occasionally home (iSleep 25<sup>®</sup>). Not to be commenced without discussion from team due to precautions and contraindications associated with positive pressure.
- **HFCWO (Vest)** – Many people ask about the Vest as an alternative treatment technique. Evidence shows that the Vest is less effective in amount of sputum cleared than other airway clearance techniques if used alone. In a long term study over 1 year comparing HFCWO to PEP mask therapy, PEP was associated with shorter treatment times and significantly fewer pulmonary exacerbations and antibiotic use than HFCWO. We will therefore only use the Vest in exceptional circumstances and always in combination with another airway clearance technique.

**Cleaning and disinfecting the airway clearance device is vitally important (refer to manufacturer's guidelines)**



Further information regarding use and evidence for the above ACT's please refer to Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis. Second edition. June 2011.

Other physiotherapy issues that may be discussed are:

- **Musculoskeletal issues and posture** – Screened at annual assessment; education and treatment is provided as required.
- **Urinary incontinence** – Stress incontinence can occur even in young children during activities such as coughing, laughing and exercise. The patient can be taught pelvic floor exercises and a technique known as 'the knack' (a pelvic floor contraction). Please consult the physiotherapist for advice.
- Upper Airway Clearance via nasal douching may also be taught where appropriate.

**The timing of inhaled medication around airway clearance** is important to optimise effectiveness:

- Bronchodilators - pre-physiotherapy if necessary and benefit shown. No need to do this routinely 10-15 mins before physiotherapy, effect can be quite fast so quicker for child if use it at time of physiotherapy session.
- Hypertonic Saline - Immediately pre-physiotherapy but post bronchodilator. Can also be given during airway clearance if combined with PEP or oscillating PEP. This can save the patient time, but although it improves peripheral deposition, the total lung deposition is reduced, and therefore it is often suggested that the dose should be increased e.g. to 5-6 mls (but not usually done in practice).
- DNase – Timing is decided on an individual basis. In most cases it is given at least 30 mins pre-physiotherapy. Cochrane review states "RhDNase can be administered before or after ACT to suit the individual, although in children with well-preserved lung function FEF<sub>25</sub> was improved if RhDNase was given prior to ACT. If RhDNase is given before ACT it should be a longer time interval than immediately before ACT"
- Steroid Inhalers – Usually taken post physiotherapy treatment. NB rinse mouth after taking a steroid or combination inhaler.
- Inhaled antibiotics - Post-physiotherapy. Either dry powder inhalers or nebulised. Appropriate nebuliser systems should be used.

### 6.15b Inhaled antibiotic bronchoconstrictor challenge (Drug Response Assessment)

See appendix 7 for details of Drug Response Assessment and pass/fail criteria.

For inhaled antibiotics (nebulised and dry powder) and hypertonic saline the child must always have a drug response assessment to detect any bronchoconstriction when the 1<sup>st</sup> dose is given. This should be done in hospital and requires the patient to perform pre and post dose spirometry. If the patient already always takes an inhaled bronchodilator before physiotherapy, then this should be taken before the baseline lung function.

If the patient fails the challenge, we will repeat it at a later date giving an inhaled short-acting bronchodilator with the inhaled antibiotic.

- We intend to use salbutamol before **all** doses of hypertonic saline, which can be given by a spacer device.

- We will only use salbutamol with nebulised antibiotics if they fail the challenge. Nebulised salbutamol can be added to colistin (but **not** tobramycin or aztreonam). Otherwise it should be given beforehand via a spacer.
- If they always take salbutamol before physiotherapy, they should still do this and it will still be active at the time they take the inhaled antibiotic which is done after physiotherapy.

If the child cannot perform spirometry then they should be observed having their first dose. SpO<sub>2</sub> and auscultation findings should be monitored throughout the test.

## 6.15c Nebulisers

Nebuliser systems available include Respironics Side Stream, Pari Sprint, Pari eFlow Rapid<sup>®</sup> and I-neb<sup>®</sup>.

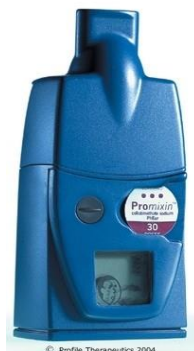
The I-neb<sup>®</sup> can be obtained if Promixin is prescribed and is a breath actuated device and only emits aerosol on inspiration (it is only appropriate if the child is able to use a mouthpiece). The breathing modes include tidal breathing mode and target inhalation mode which reduces nebulisation time (not to be used if FEV<sub>1</sub> is <1 litre).

- Once Promixin has been dispensed (the box of Promixin will contain a disc to make the I-neb work), the patient should contact Philips Respironics directly (08707703434) and a member of their team will arrange to visit the patient at home. They will personally deliver the device, teach the patient how to best use it for efficient nebulisation delivery, and provide details of cleaning instructions and the online download application. This enables the patient to download their I-neb regularly to view treatment times. It also alerts the company to when replacement parts may be required.
- **NOTE - 1 MU colistin in I-neb<sup>®</sup> delivers equivalent of 2MU via conventional nebuliser.**

Grey latched chamber -	Promixin <sup>®</sup> , bronchodilators (1ml fill volume)
Green latched chamber -	DNase (1ml fill volume)
Lilac latched chamber -	Tobi <sup>®</sup> (2.5 ml fill volume) and hypertonic saline (2ml fill volume). As the chamber takes a max of 2.5 mls, the dose has to be repeated to give the standard 5 mls TOBI and 4 mls hypertonic saline.

These devices may not be suitable for all patients so it is important to get advice from the physiotherapist. If nebulised antibiotics are required in a child under 5 years of age then we recommend wherever possible using a faster nebuliser device (such as the Pari eFlow Rapid). Nebulisers in this age group should be introduced carefully and a staged approach may be useful to reduce anxiety and ensure they are well tolerated in the long run (see appendix 8).

### PHILIPS RESPIRONICS I-neb<sup>®</sup>



© Profile Therapeutics 2004

**Advantages -**

- Fast nebulisation: Promixin<sup>®</sup> (colistin) 90s; and DNase 1min.
- Breath activated (inhalation only) AAD<sup>®</sup>.
- No filtering of antibiotics required.
- Device, maintenance and replacement parts free.
- **1 MU Colistin in I-neb<sup>®</sup> delivers equivalent of 2MU via conventional nebuliser**
- Can download usage data to review adherence

**Disadvantages -**

- Can only be used if can inhale through mouthpiece (>2 years).
- Only available if on Promixin<sup>®</sup>.

This table can be used when switching nebulised colistin from use via a conventional compressor to the I-Neb.

Colistin Dose	Conventional Compressor	I-neb <sup>®</sup> - Promixin <sup>®</sup>
2 MU	2MU	1MU (mix with 1ml saline)
1MU	1MU	1/2 MU (mix 1 MU vial with 2mls saline, draw out 1ml Discard remaining solution.

Tobramycin 300mg/4 or 5 mLs and hypertonic saline 7%/4mLs can be nebulised through the I-neb<sup>®</sup>. The table below may be useful to work out dosage and fill volume:

Device	Drug	I-neb Chamber	Fill Volume	Number of nebulisations
Conventional Nebuliser	Tobi <sup>®</sup> 300mg/5mL	N/A	5mL	1
<b>I-neb AAD</b>	<b>Tobi<sup>®</sup> 300mg/5ml</b>	<b>0.5mL (use lilac latched component) *</b>	<b>2.5mL</b>	<b>2</b>
<b>I-neb AAD</b>	<b>Bramitob<sup>®</sup> 300mg/4ml **</b>	<b>0.5mL (use lilac latched component) *</b>	<b>2.0mL</b>	<b>2</b>
Conventional Nebuliser	Hypertonic Saline 7%/4mL	N/A	4mL	1
<b>I-neb AAD</b>	<b>Hypertonic Saline 7%/4mL</b>	<b>0.5mL (use lilac latched component)</b>	<b>2mL</b>	<b>2</b>

\* This is a lilac coloured flap that covers the disc containing the drug when giving tobramycin.

\*\* Data of file (Profile Pharma)

### **PARI eFlow<sup>®</sup> rapid**



The PARI eFlow<sup>®</sup> rapid uses touch spray vibrating mesh technology and reduces inhalation time by 50% compared to the PARI LC Plus<sup>®</sup>

#### **Advantages**

- Fast nebulisation: TOBI<sup>®</sup> 6-8 mins, Colomycin<sup>®</sup> 3-4 mins, hypertonic saline and DNase 2-3 mins.
- Any age child can use it via mask or mouthpiece.

#### **Disadvantages**

- Annual cost of replacement parts.
- Some drug wasted as continuous nebulization.
- Antibiotics require filtering.

### **Drugs & their nebulisers –**

<b>I-neb</b>	<b>eFlow</b>	<b>Jet nebuliser (conventional)</b>
---	Amikacin (but slow)	Amikacin
---	---	Amphotericin
---	Aztreonam (Altera handset)	---
Bramitob* (lilac chamber)	Bramitob	Bramitob
---	---	Ceftazidime
---	Colistin	Colistin
Promixin (grey chamber)	---	---
---	Meropenem (but slow)	Meropenem
TOBI (lilac chamber)	TOBI	TOBI

---	---	Vancomycin
Hypertonic saline (lilac chamber)	Hypertonic saline	Hypertonic saline
DNase - Pulmozyme (green chamber)	DNase	DNase

\*Data on file (Profile Pharma)

**Cleaning and disinfection of the nebuliser devices is vitally important (follow manufacturer's advice).**

**In-Patients:** All children admitted will be assessed and physiotherapy requirements established. Treatment is also continued over the weekend as appropriate. If necessary, devices such as the Vest, Cough Assist, Intermittent Positive Pressure Breathing (IPPB), Non Invasive Positive Pressure ventilation (NIPPV) or ultrasonic nebulisation can be used. Children will also be seen pre- and post-general anaesthesia to ensure they can clear sputum effectively. Children will also be seen by the Therapy Assistant for regular exercise sessions on and off the ward. An exercise test may also be performed where indicated. Prior to discharge, the home regimen will be reviewed; as well as exercise and progression of treatment where appropriate. Liaison with homecare physiotherapy service occurs as required.

#### **6.15d Dry powder inhaled antibiotics (see also section 6.2a part 6.IIIi).**

##### **TOBI® Podhaler**

This is licensed in children 6 years and over with an FEV<sub>1</sub> of >25%. When trialling the drug for the first time (even if already on nebulised TOBI®) the patient must be assessed for bronchoconstriction to ensure it is well tolerated. They should be given an appointment for a Drug Response Assessment (see section 6.15b), and to learn how to use the device.

Each dose of Tobramycin inhalation powder is made up of 4 capsules. These are stored in blister packs clearly marked for morning and evening use. Doses are ideally taken 12 hours apart, but definitely not closer than 6 hours apart. As with most inhaled antibiotics it is recommended they are taken after chest physiotherapy. The blister packs are split up into weekly boxes (4 boxes for a 28 day supply), and each box comes with its own Podhaler and storage device. There is also a spare Podhaler and storage device.

Patient information and instruction for use can be found at:

[http://www.pharma.us.novartis.com/product/pi/pdf/tobipodhaler\\_ppi.pdf](http://www.pharma.us.novartis.com/product/pi/pdf/tobipodhaler_ppi.pdf)



It is important that the patient is taught the correct way to take the Podhaler. Ideally a 5 sec inspiration, with a flow of 30 l/min and 5 sec breath hold. We have found an in-check device (in-check™ m – Clement Clark International) useful to guide the patient in performing the optimum inhalation flow of 30 l/min. The child is instructed to perform at least 2 separate inhalations per capsule and following this, it is important to inspect the used capsule to ensure it is empty. If it isn't, it should be replaced in the device (pierced side first) and another inhalation performed. Wash mouth out after use to minimise risk of developing oral fungal infection.

Common side effects include cough (which in most cases tends to improve on the 2<sup>nd</sup> cycle of TOBI® Podhaler), sore throat, and changes to voice, fever, shortness of breath headache and haemoptysis.

### **Colobreathe® Turbospin.**

Colobreathe® is licensed in children 6 years and over and administered via a turbospin dry powder inhaler. The first dose should be trialled in hospital to assess for tolerability, bronchoconstriction (see section 6.15b), and for the patient to learn how to use the device.

Colobreathe® 1,662,500 IU inhalation powder is approximately equal to 125mg of colistimethate sodium. The dose for adults and children over 6 years is one capsule inhaled twice daily, ideally 12 hours apart and following chest physiotherapy. The hard capsules are stored in blister packs containing 14 capsules per strip (1 week supply). Each pack contains 4 strips of 14 capsules and 1 turbospin powder inhaler device (28 day supply). Store the capsules at room temperature and not above 25°C. It is recommended that when inserting the capsules into the device, the fat end goes in first, as there have been reports of the capsule breaking thus delivering all the powder in one go; also press the plunger slowly.

It is important that the patient is taught the correct way to take the inhaler. Ideally a 5 sec inspiration, with a flow of 30-40 l/min and 10 sec breath hold. The child is instructed to perform 2-3 separate inhalations for the one capsule, and following this it is important to inspect the used capsule to ensure it is empty. If it is not, it should be replaced in the device

and another inhalation performed. Wash mouth out after use to minimise risk of developing oral fungal infection.

Cough and bronchospasm may occur on inhalation but these reactions usually diminish with continued use. It is recommended to take a bronchodilator prior to its use. Most commonly reported adverse reactions include unpleasant taste, cough, throat irritation, dyspnoea, dysphonia and altered taste. Skin rash may indicate hypersensitivity and therefore treatment should be withdrawn. Less common adverse reactions include headache, haemoptysis, bronchospasm, nausea, vomiting, fever and reduced FEV.

### 6.15e Induced sputum

Isolation of bacteria from the lower airways is difficult in children who do not cough up sputum. Therefore sputum induction may be recommended for those who have declining lung function and are non-productive of sputum, with no significant bacterial growth, before resorting to a bronchoscopy.

We also consider it for children who have previously grown bacteria only on bronchoscopy, following eradication treatment when the child is not productive of sputum. In this case we perform it 2 weeks after the antibiotic eradication period ends.

We are now also doing this on all non-sputum producing children after eradication of a new *P aeruginosa* growth.

An appointment for sputum induction takes approximately 1 hour. It involves the child inhaling 7% hypertonic saline for 15 minutes via an ultrasonic nebuliser device. A cough swab is taken and a bronchodilator is administered prior to the test. In children over 5 years of age spirometry is performed to establish post-bronchodilator lung function. Spirometry is repeated at 5 minute intervals during the nebulisation to assess for bronchoconstriction. At these 5 minute intervals the child will be asked to huff and cough or will be guided to carry out airway clearance techniques to expectorate secretions.

The test can also be performed in younger children who cannot carry out spirometry; in this case oxygen saturations and auscultation is used to assess for tolerability. In children who cannot expectorate, a suction catheter, connected to a sputum trap, can be placed orally to suction secretions.

### 6.16 Oxygen

All children with CF admitted with a respiratory exacerbation should have a **continuous** overnight oxygen saturation performed on the first or second night (especially if FEV<sub>1</sub> <50% or resting SpO<sub>2</sub> <92%). The minimum is that every child admitted must have a spot SpO<sub>2</sub> on admission and during the first night. Oxygen therapy is usually given in hospital if saturations are <90% for >5% of the time, but this is not evidence-based. Oxygen, method of delivery and target saturations must be prescribed on the relevant section of the drug chart (Doctors) and changes to the flow documented in the relevant section by nursing staff.

If saturations were low and oxygen was required at the start of the admission then the overnight monitoring should be repeated at the end of the admission. If they remain low (**saturations <90% for >5% of the time**), then consideration should be given to providing oxygen at home, almost always only at night. When home oxygen is initiated, an overnight transcutaneous CO<sub>2</sub> should also be recorded, as it can rise slightly when oxygen therapy is initiated.

As this is for >8 hours then an oxygen concentrator is preferred to cylinders. The whole process is handled by the occupational therapy (OT) department. A Home Oxygen Order Form (HOOFF B) needs to be faxed to the relevant oxygen company, depending on the child's GP's address: Air Liquide (London, North West, East Midlands, South West); Air products (York & Humber, West Midlands, Wales); BOC (East of England, North East); Dolby Visiol (South East Coast, South Central, Scotland).

When ordering home oxygen, please also contact Andrew Montgomery in OT (ext. 4451, bleep 7755), who will help facilitate the process.

### **6.17 Non-Invasive Positive Pressure Ventilation (NIPPV)**

NIPPV has a number of uses:

- Nocturnal or daytime use of NIPPV is helpful in those with very advanced disease especially with CO<sub>2</sub> retention, and also patients requiring a 'bridge to transplantation'. It improves sputum clearance, reduces the work of breathing, may stabilise lung function and improve exercise capacity. Its requirement in children is most uncommon and needs prior sleep studies and careful evaluation.
- Occasionally, nocturnal NIPPV may be used during an in-patient exacerbation to improve sputum clearance in particularly those who are very tight and obstructed. A 2009 Cochrane review demonstrated few studies but some benefits especially in dyspnoea
- More commonly, the BIRD inspiratory positive pressure device can be used as an adjunct to chest physiotherapy for an inpatient – the principle being that positive pressure gets air 'behind the sputum', aiding its clearance and supporting the patient's work of breathing. In certain circumstances, where appropriate, an NIPPV device (iSleep<sup>®</sup>) can be loaned for home use so that positive pressure supported airway clearance can be continued after discharge.



## 7. Gastrointestinal & nutritional care

### 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) is common in CF.

- **All** children are supplemented from diagnosis.
- 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.

Vitamin levels are tested at annual assessment and dosages adjusted as necessary. (See section 11.2b on vitamin preparations).

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.

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 aged 5 years or less will be measured in their underwear, but those over 5 years can be measured in light clothing and do not need to undress completely. 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.

### Nutritional Assessment

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.
- All children with a BMI of <25<sup>th</sup> centile.
- Children that cross centile lines in a downward trend. This can be an acute picture or a longer, and potentially less noticeable, chronic change.

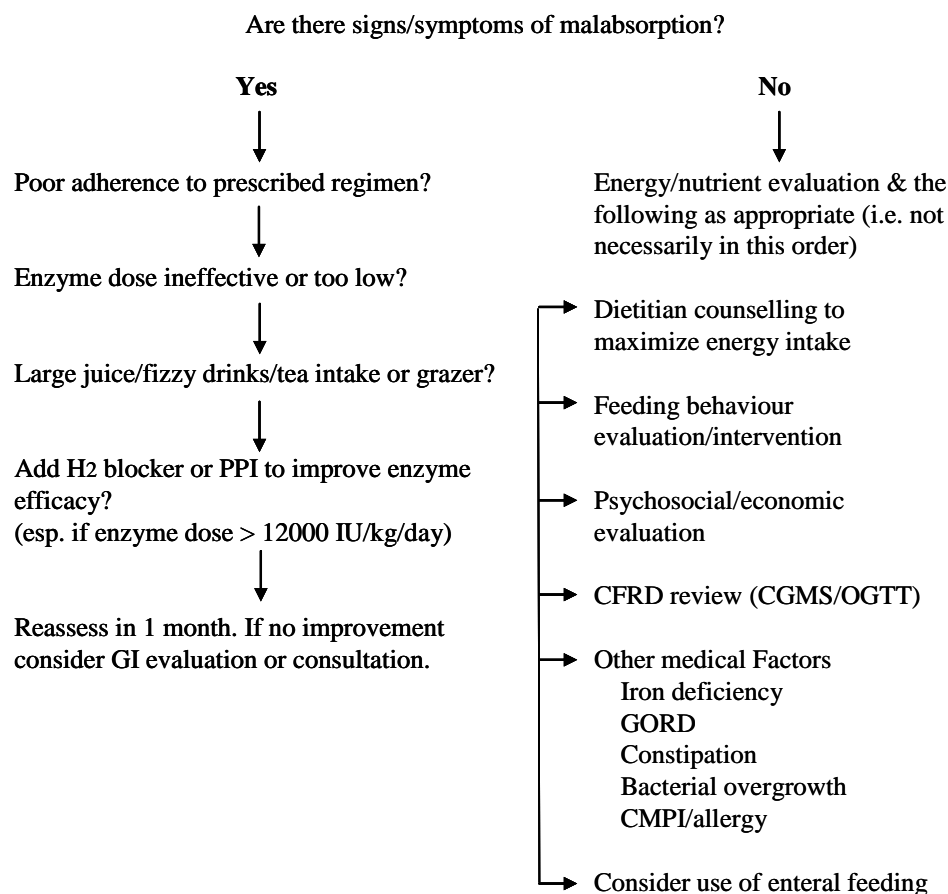
Clinical assessment of both height and weight centiles are analysed using UK WHO Growth Charts. This is monitored closely on a 1-2 monthly basis for infants and 2-3 monthly for older children and adolescents.

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.

**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 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 available on <http://dx.doi.org/10.1080/10640266.2014.1000111>.

**Algorithm for weight loss or lack of weight gain**

*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 1<sup>st</sup> 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). 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 capsules at the 1<sup>st</sup> 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: ½-1 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

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. When a child is on a particularly high dose, (*e.g.* >15,000 IU lipase/kg) 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<sub>2</sub> 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 or periods of ill health. They are susceptible to more rapidly depleting stores and therefore should be encouraged to include extra salt in the 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 in 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 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. This provides 12mmol NaCl 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 NaCl/tablet. However Dioralyte can be a more ideal 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<sup>®</sup> (sodium chloride MR) 600mg (10mmol) tablets; 1-3 / day). This is also necessary in very hot weather in the UK. See Appendix 12.

## 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 regards 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)	<ul style="list-style-type: none"> <li>• SMA High Energy (SMA)</li> <li>• Infatrini (Nutricia)</li> <li>• Similac High Energy (Abbott)</li> <li>• Concentrated Standard infant formula – <i>must</i> be supervised by the Dietitian</li> </ul>
	Paediatric	<ul style="list-style-type: none"> <li>• Paediasure Plus (Abbott)</li> <li>• Fortini &amp; Fortini smoothies (Nutricia)</li> <li>• Frebini Energy (Fresenius Kabi)</li> </ul>
	Adolescent	<ul style="list-style-type: none"> <li>• Ensure Plus (Abbott) - Also available in yoghurt style flavour</li> <li>• Ensure TwoCal (Abbott)</li> <li>• Scandishake (Nutricia)</li> <li>• Calshake (Fresenius Kabi)</li> <li>• Enshake (Abbott)</li> <li>• Fortisip and Fortisip Compact (Nutricia)</li> <li>• Fresubin Energy (Fresenius Kabi)</li> </ul>
Juice Based Supplements	Paediatric	<ul style="list-style-type: none"> <li>• Paediasure Plus Juce [spelt correctly!] (Abbott)*</li> </ul>
	Adolescents	<ul style="list-style-type: none"> <li>• Ensure Plus Juice (Abbott)*</li> <li>• Fortijuice (Nutricia)*</li> </ul>

Powder and liquid polymers to add to foods	Carbohydrate	<ul style="list-style-type: none"> <li>• Maxijul (SHS)*</li> <li>• Polycal (Nutricia)*</li> </ul>
	Fat emulsions	<ul style="list-style-type: none"> <li>• Calogen (Nutricia)</li> <li>• Liquigen – MCT fat (Nutricia) *</li> <li>• Fresubin 5kcal shot (Fresenius)</li> </ul>
	Mixed macronutrients	<ul style="list-style-type: none"> <li>• Duocal (Nutricia) *</li> <li>• Procal Powder (VitaFlo)</li> <li>• Procal Shot (VitaFlo)</li> </ul>

\* *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. 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 will only 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, and this may be done as part of the challenging CF protocol (section 6.13):

- CGMS
- Urinary sodium
- Serum electrolytes
- 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; that is, 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 carefully introduced to the concept of a gastrostomy. It is important that education about the potential effects a gastrostomy tube is discussed. 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. 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 Hayley Strowger, Surgical Clinical Nurse Specialist at C&W on 0203 315 8627 or 0203 315 8000 bleep 4988; or via [hayley.strowger@chelwest.nhs.uk](mailto:hayley.strowger@chelwest.nhs.uk) or [cw.gastrostomy@nhs.net](mailto: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 9)**

- 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

Adolescents feeds Adult feeds (>20kg)	Peptamen Junior Advance (Nestle)			✓	1.5 kcal/ml
	MCT Peptide 1+ (SHS)		✓		0.91 kcal/ml (Can be made-up more concentrated)
	Nutrini Peptisorb			✓	1.0 kcal/ml
	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; 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.

The following principles are encouraged to reduce behavioural feeding problems:

- Creating a relaxed and enjoyable feeding environment *e.g.* avoiding distractions such as the television.
- Give age appropriate portions and offering second helpings if desired
- Giving *gentle* encouragement to eat and positive feedback for good behaviour.
- Ignore feeding behaviour that is not acceptable.
- A structured meal and snack pattern appropriate to the child's age and lifestyle.
- Limiting mealtimes to maximum 30 minutes (meals that last longer than this rarely result in higher calorie consumption.)
- Not offering alternative meals or snacks if the first meal is refused.
- Engaging children at meal times (for example 'messy play', self-feeding and simple food preparation).

- Where possible dining with family members or peers.
- Having a consistent approach from all adults at meal times.

## 7.8 Gastro-oesophageal reflux

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, possetting 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<sub>2</sub> 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 failure to thrive.

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.

There are no research proven motility drugs for use in GOR, however we will use domperidone if a PPI is not working. An ECG must be done prior to use to make sure there is no evidence of a prolonged QT interval. Another motility drug we sometimes use is erythromycin (see BNFc for doses).

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.

## 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 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

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

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

### Management of DIOS

**1. Acute** – a stepwise process although always includes hydration.

- **Rehydration** - patient must be **well hydrated** before and during treatment, and it is critical if gastrografin is used.

If there is complete obstruction an NG tube is needed to empty the stomach and prevent bilious aspiration, and IV fluids are given ('drip and suck').

- **Movicol** – for *mild DIOS*.  
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.
- **Oral gastrografin**  
Hydration is very important if gastrografin is used as it is highly osmotic. This is often done as an in-patient, 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 paediatric Movicol for several weeks and review chronic management below.
  - *Contraindicated if complete bowel obstruction.*
- **Klean-prep** is used for *severe DIOS*.
  - Admit patient.
  - Aim is to take solution until clear fluid is passed PR. 1 sachet dissolves in 1 litre and 2 sachets are used in a day.
  - NG tube is usually required as volume is so large but occasionally some patients will prefer to drink it (more palatable if cool).
- **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 -

- **Oral N-acetylcysteine**- a di-sulphide 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.
- 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.
- Paediatric Movicol 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 Wednesday morning on Rose Ward) 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 or Lactulose may be used (see formulary 11.2f).
- Paediatric Movicol dose can be adjusted up and down to produce regular soft stools, usually no need for more than 4 sachets a day.
- 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% 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  $\alpha$ 1-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 this doesn't always correlate with the presence or severity of CF related liver disease.

### **Steatosis (Fatty liver)**

This is a relatively common CF finding, occurring in 23-75% of patients. 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 Kings is that in the absence of hepato- or splenomegaly, and with normal liver function, they would not start ursodeoxycholic acid 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 shear 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.

### **Standard treatment**

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

- Ursodeoxycholic acid (increases bile flow). It is well tolerated with main side effect of diarrhoea, in which case reduce the dose. This reverses markers of CF liver disease but it is unclear whether it can delay or reverse fibrosis.
- Vitamin K (if prothrombin time prolonged) – If PTT corrects then continue with daily oral vitamin K (see section 11.2b). Occasionally 2 IV stat doses are required.
- Avoid aspirin and NSAIDs in those with documented cirrhosis.
- Care with fusidic acid, minocycline, rifampicin, azithromycin, itraconazole, posaconazole and voriconazole (If in doubt consult with BNFC).

## 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 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  $\beta$ -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.
  - 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).
- 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 transferrin 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 iso-ferritins 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 have therefore lowered our threshold for starting iron therapy. **We now 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 1<sup>st</sup> 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 and eggs.

	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
<b>Iron stores</b>					
Serum ferritin	↓	↓	↓	↓↑ or N	N or ↑
<b>Transport iron / iron supply</b>					
Hypochromic red cells	N	↑	↑	N or ↑	N or ↑
<b>Functional iron</b>					
Hb	N	N	↓	↓	↓
MCV	N	↓	↓	N or ↓	N or ↓
<b>Approach to management</b>	Increase dietary iron	Iron supplementation	Iron supplementation	Address underlying inflammation	

## 8. Other non-pulmonary complications of CF

### 8.1 Cystic Fibrosis-Related Diabetes

#### Contacts

Consultant Paediatric Endocrinologists, Chelsea & Westminster Hospital  
Dr Nicola Bridges  
Dr Saji Alexander

Diabetes Nurse Specialist, Chelsea & Westminster Hospital  
Ms Karen Spowart

#### Background

All CF individuals with exocrine pancreatic insufficiency have insulin deficiency, which worsens with increasing age. Insulin secretion is reduced even in individuals with normal glucose tolerance. There is an increase with age in the prevalence of impaired glucose tolerance and diabetes. CF related diabetes (CFRD) is not common in those under 10 years although up to a third of this age group will already have impaired glucose tolerance. The reported prevalence of CFRD depends on the diagnostic criteria used and screening methods, but approximately 50% of individuals with CF will have CFRD by 30 years of age. CFRD is distinct from either type 1 or type II diabetes mellitus and we have different approaches to diagnosis and management.

In CF the insulin response to a glucose load or a meal is reduced in amplitude and delayed compared to normal individuals, but basal insulin secretion is relatively preserved. The typical pattern in the early stages is for fasting glucose to be normal with elevated glucose levels after meals.

**WHO criteria** for diabetes and prediabetes (2006 and 2011).

#### Diabetes- any of these

- Fasting glucose  $\geq 7.0$  mmol/L.
- Two-hour post glucose challenge value  $\geq 11.1$  mmol/L.
- HbA1C value of  $\geq 6.5\%$  (48 mmol/mol) can be used as a diagnostic test for type 2 diabetes.

#### Impaired glucose tolerance (IGT)

- Fasting glucose  $< 7.0$  mmol/L **and** a two-hour glucose post glucose challenge of  $\geq 7.8$  mmol/L but  $< 11.05$  mmol/L.

#### Impaired fasting glucose (IFG)

- Fasting glucose of 6.1 - 6.9 mmol/L.

#### Why we treat CF related diabetes and impaired glucose tolerance

CFRD reduces life expectancy and there is evidence that management of diabetes improves outcome, so CFRD has become an important aspect of CF management. Individuals with CF who have diabetes or impaired glucose tolerance have worse outcomes (lung function,

nutritional status, reduced survival) compared with those with normal glucose tolerance. Insulin treatment has been demonstrated to improve these clinical markers. Diabetes in CF is caused by insulin deficiency, so insulin is the logical choice for treatment. Oral hypoglycaemic agents have not been shown to give the same benefits to clinical status as insulin. The risk of microvascular complications in diabetes is related to control (measured by HbA1c) and the duration of diabetes, and appears to be the same in CF as in other forms of diabetes.

The adverse impact of insulin deficiency is associated with loss of the anabolic effect of insulin, loss of nutrition related to glycosuria and possibly increased infection risk with elevated glucose.

The WHO diagnostic categories for diabetes and prediabetes based on oral glucose tolerance tests or fasting glucose (see above) are based on the risk factors for cardiovascular disease in type 2 diabetes. In CFRD there is evidence of clinical impact from glucose abnormalities which do not meet the criteria for a diagnosis of diabetes, and also evidence of benefit from treatment of impaired glucose tolerance. Most clinicians use these standard definitions for diabetes in CF but because the clinical situation is different treatment may be given to individuals who do not meet the criteria for diabetes.

### **Screening for abnormal glucose tolerance and diabetes in CF**

#### *Available tests of glucose status in CF*

- Continuous Glucose Monitoring System (CGMS)
- Oral glucose tolerance test
- Random glucose tests
- HbA1c

#### *When to test for glucose status in CF:*

Current CF Trust recommendation is for OGTT once yearly in all CF patients over 12 years. There have been significant changes in our knowledge about CFRD since these guidelines, and our new policy is to routinely carry out **CGMS in 10 & 14 year olds** (it used to be at 12 & 15 yrs) around the time of their annual reviews and to screen with CGMS at other times based on clinical concerns. OGTT is only used if CGMS is refused or not possible.

#### **Consider doing a CGMS in a child of any age if:**

- There is poor weight gain or decline in lung function with no other obvious cause.
- Finding of high random glucoses in any individual (most normal individuals can maintain their glucose <7.8 mmol/l, whatever they eat). Formal assessment is required if there are repeated glucose levels >8.0 mmol/l or a single level >11.0 mmol/l.
- HbA1c on annual review or at other times >**6.5%** (IFCC HbA1c >**48** mmol/mol).
- Symptoms of hyperglycaemia, including increased thirst, polyuria, blurred vision, constipation and candida infections.
- Before high dose steroids, starting overnight feeds, or before major surgery.
- If there are documented hypoglycaemic episodes or symptoms suggesting this.

## CGMS

*How it works* - A subcutaneous sensor measures the glucose in the interstitial fluid and gives a continuous profile of glucose levels for up to 6 days. The sensor needs to be calibrated with blood glucose measurements at least **twice daily** for as long as sensor is in place, and the profile can be downloaded at the end of the study. The equipment gives a profile and statistical breakdown of the glucose levels.

### *Advantages*

- CGMS gives a better picture of glucose status in CF than either OGTT or random glucoses and can demonstrate glucose abnormalities that would not otherwise be detected.
- The effect of food, exercise and treatment on glucose levels can be assessed.
- It may be a better guide than OGTT as to when to start insulin treatment in CF but data are limited.

### *Disadvantages*

- The sensor is sometimes uncomfortable and some individuals cannot tolerate it.
- Blood glucose still needs to be measured 4-6 times in 24 hour period which can be a problem with needle anxiety.
- Clear guidelines as to when to treat on the basis of CGMS are not available.
- The sensors are relatively expensive (£35-44 each).

## Oral glucose tolerance test

*How it works* - Glucose levels are measured before and after a standard oral glucose load.

- *Preparation*  
The child is fasted from midnight although drinks of plain water are allowed.
- *Dose of glucose*  
1.75 g/kg glucose to a maximum of 75 g, as glucose monohydrate diluted in water (200-300 mls).

A glucose drink giving the same dose of glucose can be substituted, such as Lucozade. The glucose content varies with the type but is clearly printed on the label, so calculate a volume to give the equivalent amount of glucose. Lucozade Energy “original” contains 17.2g glucose/100ml and the dose of this is 10.2 ml/kg to a maximum of 436 mls.

- *Samples*
  - Take blood for glucose at 0 mins (fasting) and give the glucose drink.
  - Take blood for glucose at 60 + 120 minutes.
  - A sample at 30, 60, 90 and 150 minutes will add further diagnostic information, take these samples if there is a cannula in place. These measurements are not required for the diagnosis of diabetes.

**The diagnostic guidelines are based on venous blood samples and not fingerprick samples. The accuracy of bedside blood glucose meters is good but only do this if you are forced to because of needle phobia.**

*When to use an OGTT*

- If it is not possible to get CGMS.
- OGTT is not needed if the diagnosis of diabetes is already established with CGMS or random glucose levels.

*Advantages of OGTT -*

- Easy to carry out and only takes 2 hours.

*Disadvantages*

- In CF because individuals with impaired glucose tolerance get benefit from treatment OGTT is not a clear guide as to when to treat.
- The OGTT will miss a significant number of individuals with abnormal glucose tolerance in CF, particularly if only baseline and 120 minute tests are done.

**Profile of random glucose tests**

Checking random glucose levels over a few weeks can give a good picture of glucose status. Draw up a clear plan of how many tests are needed (ideally 3- 4/day) and when to do them. Testing should be before and also 1-2 hours after meals. The most likely time for glucose to be high is about 2 hours after the evening meal. In CF fasting (pre breakfast) glucose levels can be normal even if the glucose levels later in the day are very high.

*When to use random glucose profile*

- If CGMS is not possible, or as an outpatient screen for glucose status.

*Advantages*

- Easy to arrange as an outpatient.
- Most people tolerate this well.

*Disadvantages*

- Choice of time to test can mean that you do not get a clear picture, accidentally or deliberately.

**Interpretation of screening results:****CGMS**

There are no fixed criteria for treatment with insulin based on CGMS. However CGMS gives an accurate reflection of glucose levels during the test so it is acceptable to make management decisions based on this. For an individual with completely normal insulin secretion the CGMS will show that glucose is held steady within the normal range through the whole day.

Current management strategy is to divide CGMS results into 4 groups:

Diagnostic category	CGM values	Treatment
CFRD	2 x peaks >11.1nmol/l and >10% of time >7.8	Start insulin
Impaired glucose tolerance	No more than 1 peak >11.1nmol/l and/or >10% of time >7.8nmol/l	Consider insulin Repeat CGM in 6 months
Indeterminate glucose homeostasis	4.5-10% of time >7.8nmol/l or hypoglycaemia	Close monitoring Dietary modification for hypoglycaemia Repeat CGM in 12 months
Normal	No peaks >11.1nmol/l and <4.5% of time >7.8nmol/l	Nil Repeat CGM when indicated

Insulin treatment should be started for those in the CFRD group (based on CGMS criteria) and considered for those in the “impaired glucose tolerance” category if weight gain or lung function is poor.

CGMS results can be affected by a variety of circumstances and will be lower than normal if the subject does not eat during the profile or higher if they are unwell or on steroids.

### OGTT

Two-hour post glucose challenge value  $\geq 11.1$  mmol/L (or fasting glucose  $\geq 7.0$  mmol/L) confirms diabetes and treatment should be started. In CF, individuals who do not reach the diagnostic criteria for diabetes based on OGTT can still benefit from treatment. Insulin has been shown to benefit individuals who fall into the “impaired glucose tolerance” category as well as those with diabetes. If CGMS is not possible treatment should be considered for individuals with impaired glucose tolerance if they have poor clinical status.

### Random blood glucoses

Multiple blood random glucose levels over 11.0mmol/l will confirm a diagnosis of diabetes, but further tests such as CGMS may be helpful before starting insulin.

### HbA1c

The value as a screening test for diabetes in CF is not clear. However HbA1c is an accurate reflection of average glucose in CF, and if the HbA1c is over 48mmol/mol (6.5%) average glucose levels are over 8 mmol/L and further investigations are needed.

### Treatment of diabetes and abnormal glucose tolerance in CF

The primary cause of the abnormal glucose tolerance in CF is insulin deficiency so the treatment for this is insulin. Insulin has been shown to improve lung function and nutritional



status in CF. Oral hypoglycaemic agents can control glucose levels in some individuals but there is no sustained benefit to clinical state, **so we do not use them.**

### **Who should be treated?**

- Everyone who meets the criteria for a diagnosis of diabetes or falls into the CFRD category on CGMS, unless there are overwhelming clinical or psychological reasons preventing this.
- Everyone with symptomatic hyperglycaemia.

Consider treatment for those who have abnormal results (impaired glucose tolerance on CGMS or OGTT) which do not meet the criteria for diabetes but:

- There is declining lung function or nutritional status with no other cause found.
- Nutritional concerns, for example on overnight feeds or supplements and not gaining weight.

### **What insulin to start**

Discuss treatment with one of the paediatric diabetes team - these decisions are not made by the respiratory team.

Many individuals with CF can manage on one type of insulin, either once daily Levemir (long acting) or Novorapid (short acting) with meals. It is helpful to look at the CGMS before starting. If there are peaks of high glucose through the day start on Levemir before breakfast. If there is a single peak around the evening meal, start once daily Novorapid, given just before the evening meal.

#### *Starting doses of insulin -*

- Levemir- use 2-8 units depending on weight of the individual. Start at a low dose and gradually increase.
- Novorapid – use 2-4 units to cover meals. The insulin dose depends on the carbohydrate content of the meal and so a larger dose is needed for a larger meal.

### **Monitoring after starting insulin**

Glucose should be checked 4-6 times per day for the first few days, varying the time to check before and 2 hours after meals. Everyone on insulin treatment should monitor blood glucoses regularly, once a day (varying the time of day) is sufficient for those on once daily insulin but individuals on multiple dose regimens should monitor more frequently (4-6 times a day ideally).

HbA1c accurately reflects glucose levels in CFRD but is a less helpful guide to control than in type 1 diabetes. Measure HbA1c when a child with diabetes is admitted, and when they come to clinic unless it has been checked in the last 2 months.

Repeat CGMS is not needed routinely for children on insulin but can be helpful:

- If control is persistently poor despite adjustment
- To check that overnight feeds are adequately covered
- If blood glucose measurements do not fit with the HbA1c levels

### **Adjusting insulin doses after starting**

- Ideally only change one thing at a time.
- Go up by 1 to 2 units at a time
- The effect of a change in long acting insulin may take several days to be clear.
- For individuals on once daily Levemir, if levels after meals remain high despite increasing Levemir dose, consider adding in Novorapid.
- Remember the time course of the insulin- Novorapid lasts 2-4 hours, Levemir 16-20 hours and Glargine up to 24 hours.

### **Adjusting for steroid treatment**

- Steroid treatment will usually increase glucose levels and oral steroid taken in the morning will result in highest blood glucoses in the late afternoon.
- The effect of steroids on blood glucose can take several days to develop and will take time to wear off after stopping.
- Start by increasing the morning Levemir dose with the option of adding in an evening dose of Levemir if needed.
- Novorapid doses may need to be increased or added in. Aim to use the Novorapid to cover the post meal rise in glucose, but if the glucose is elevated through the day it is better to increase the Levemir.

### **Covering overnight feeds**

- Give Levemir to cover overnight feeds, injecting 1 hour before the start of the feed. Adjust the dose, looking at glucose in the middle of the feed and at the end. Mixed insulins or isophane insulin are options if this is not successful.
- If feeds are not given every night, specify a dose for the nights with feed and nights without.
- It is important to get reasonable glucose control while the feed is going in- if the glucose is high during the feed, the calories in the feed will be lost in the urine.

### **Dietary advice**

The family should have input from the dietitian at RBH. It is important that they understand that the dietary management is not the same as in other forms of diabetes and they do not need to adopt a “diabetic” diet. Families should be discouraged from reducing calorie intake to avoid starting insulin treatment.

Calorie intake In CFRD maintaining adequate nutrition remains the priority and a high calorie and high fat diet must continue. Older children should avoid high sugar snacks and drinks between meals (i.e. regular fizzy drinks, juices and squashes, jellied sweets etc.) and substitute no-sugar-added drinks (i.e. diet fizzy drinks and squashes).

Regular eating. Encourage regular meals and snacks (including breakfast if possible) because this makes the diabetes easier to control and improves weight gain. Food intake should not be reduced to try to control glucose levels; meals and snacks must be given whatever the blood glucose.

**Psychology** referral is suggested as this is a stressful time for the child and family with added treatment burden and possibly anxiety about the needles.

## Hypoglycaemia

Hypoglycaemia is a blood glucose  $<4.0$  mmol/L and any glucose lower than this should be treated even if the child feels well.

Symptoms of hypoglycaemia include confusion, irritability, pallor, fatigue, dizziness, and a “wobbly” or “funny” feeling, and many children can easily identify if they are low blood glucose.

Caregivers and schools should be given information about hypoglycaemia (e.g. the JDRF or Diabetes UK schools leaflet). Hypoglycaemia can be caused by a number of factors- too much or wrongly timed insulin dose, insufficient carbohydrate intake, exercise, missed enzyme doses, diarrhoea and vomiting leading to poor absorption of food, alcohol consumption.

**Treatment:** Give a rapidly-absorbed carbohydrate followed by a complex-carbohydrate snack. There is an understandable tendency to overtreat hypoglycaemia, which can result in hyperglycaemia later on. Chocolate and sweets are not a good alternative for the initial treatment of hypoglycaemia- they are not as rapidly absorbed as glucose, and it gives the wrong psychological message to reward hypoglycaemic episodes. If the test before a dose of insulin shows hypoglycaemia, treat the hypoglycaemia and then go ahead with the meal and give the normal insulin. Do not treat as hypoglycaemia unless glucose levels  $<4$  mmol/L.

- If hypoglycaemia is suspected test the blood glucose if possible.
- Treat hypoglycaemia with 10g of rapidly absorbed carbohydrate (50 ml of Lucozade, 100 ml of Coca-Cola, 3 glucose tablets, 2 tsp. of jam/honey/syrup).
- Wait 15 minutes and test blood sugars again. If  $< 4.0$  mmol/L, repeat step 2. If  $> 4.0$  mmol/L, give a complex-carbohydrate snack (such as a sandwich, crisps or 3-4 biscuits).
- Think about what caused the hypoglycaemia.
- Spontaneous hypoglycaemias (from endogenous insulin production) are also seen in CFRD and glucose intolerance. Typically this is after meals and can be improved by avoiding very sugary meals.

## Equipment

Ideally patients should go home with spares of pens and glucose meters. Remember to contact the GP to make sure that supplies of insulin, pen needles, lancets and strips for the meter are added to the regular prescription. Pharmacy at RBH does not keep glucose meters. Most children will need 4 mm needles for their pens. Never use needle and syringe for insulin and always use an appropriate device for pricking fingers.

## Outpatient follow up

*Royal Brompton Hospital*

Nicola Bridges or Saji Alexander comes to the CF clinic on the 3<sup>rd</sup> Friday afternoon of each month. If possible arrange follow up in this clinic.

*Chelsea and Westminster Hospital*

There is a diabetes clinic every Tuesday morning, and patients can be reviewed here. If you want an urgent appointment please phone or e mail.

Some patients will have diabetes follow up arranged in their local hospital. It is important that all of the local team are aware of the management of CFRD. Nicola Bridges or Saji Alexander are always happy to discuss these patients and ideally we should review them at the Brompton as well. We give families our contact details and they can phone or e mail with problems.

*Transition clinic*

There is a regular diabetes clinic in adult outpatients at the Royal Brompton with Dr Kevin Shotliff and Nicola Bridges. Follow up in this clinic is discussed and arranged when they attend their transition appointment.

*Monitoring*

A realistic plan for monitoring blood glucose levels at home should be discussed. Children on insulin once a day should be encouraged to test at least once a day, varying the time. HbA1c should be checked every 3-4 months. Individuals with CFRD are not at increased risk of thyroid disease or coeliac disease (compared to a CF child without CFRD) so this is not screened for, but regular eye screening and checks for urine albumin should be started in everyone over 12 years. CFRD gives the same risks of microvascular complications as any other type of diabetes and adults with CFRD should be regularly screened.

**If a child with diabetes is admitted to the ward**

- Please call Nicola Bridges or Saji Alexander to review the patient, even if things appear to be going well.
- Insulin injection and blood testing must be supervised.
- Encourage good habits- blood testing at appropriate times, eating snacks and meals on time and not omitting insulin.
- Make sure you have the right equipment- the right strips for the meter, the right pen for the cartridges.

**Prescribing insulin***Safe use of insulin*

All health care professionals prescribing or administering insulin should have had training in safe use of insulin. There are many clinical incidents in the UK each year related to insulin prescription and administration. Common incidents include giving the wrong insulin, lack of clarity in prescriptions, and drawing up or giving insulin with the wrong type of syringe.

*Safe insulin prescriptions*

- Get the correct insulin name (there are some insulins with similar names) but also the presentation, e.g. cartridges, disposable pen.
- State when the insulin is to be given. For short acting insulin this will be before a meal and not at a particular time of day.
- If the dose is variable (for example short acting insulin for meals) you must make it clear how the dose will be decided.

- For paper prescriptions the word “units” must be written in full and never “u” or ”iu”. This is a cause of drug errors because a badly written “u” can be taken to be a zero.

#### *Safe insulin administration*

- Even if the patient has been having insulin treatment for a long time it is important to check the dose, administration technique and the injection sites.
- The person signing for the insulin dose takes responsibility that the correct dose is given. Even if the parent or patient is giving the insulin, check the dose and injection technique.
- Always use an insulin syringe to draw up insulin for an insulin infusion

#### **Surgery**

Prior to any general anaesthetic a plan must be made to reduce the insulin while the child is fasting. Make sure anaesthetists are informed in advance.

#### **Diabetic ketoacidosis (DKA)**

DKA is rare in CFRD but it can still happen. DKA should be managed according to national consensus guidelines (these can be found on the BSPED website: [www.bsped.org.uk](http://www.bsped.org.uk)).

#### **Other practical aspects**

*Schools.* The school will need information. A healthcare plan needs to be made if blood testing or injections are occurring during school. Legally, schools must provide support for children with medical needs. It is possible for school staff to check glucoses or give insulin if they have training and a healthcare plan. Even if insulin is not given during school times, blood glucose monitoring must be facilitated at school. Lunchtime doses of insulin can easily be forgotten and so an arrangement for a member of school staff to supervise and support is usually helpful

*Travel.* If a child with diabetes is travelling abroad they need a letter saying that they are travelling with insulin, needles and glucose testing equipment (see appendix 13). All equipment and insulin must be in their hand luggage.

*Driving.* There are strict rules covering driving and diabetes which change from time to time. Some types of licence cannot be obtained if you have diabetes (some classes of HGVs). Currently everyone with diabetes must renew their licence every 3 years. Patients applying for a licence must declare their diabetes and must get medical confirmation that they are well controlled and are testing glucose regularly.

#### **Useful links**

The CF Trust guidance –

<http://www.cftrust.org.uk/scope/documentlibrary/Publications/diabetes.pdf>

Other diabetes websites:

The Juvenile diabetes research foundation (JDRF) - [www.jdrf.org.uk](http://www.jdrf.org.uk)

The Diabetes UK website - [www.diabetes.org.uk](http://www.diabetes.org.uk)

The information is not all relevant to CF. The school information leaflet from the JDRF is very good.

## 8.2 Growth

Average birth weight and length is slightly reduced in CF compared to unaffected infants. In unscreened infants growth rate (weight and length) is reduced in the first year of life, mainly because of impaired nutrition. Once the diagnosis is made and nutrition is improved, catch up growth usually occurs. Individuals diagnosed after newborn screening are taller in childhood than unscreened children picked up later on clinical grounds.

Improvement in the treatment of CF over time has resulted in the patterns of growth in childhood moving nearer to that of unaffected children. There still appears to be a small height deficit in childhood related to CF. Up to 15% of children with CF were less than 5<sup>th</sup> percentile for height on US CF registry study. Height velocity in childhood is within normal limits. The height deficit can increase further in adolescence because of delay in puberty and in some cases, worsening clinical status. Adult height is usually within the normal range for the population but reduced compared to mid-parental height.

Pituitary function (growth hormone (GH), gonadotrophins, & ACTH) is normal in CF. Chronic infection/ inflammation, nutritional factors, abnormal glucose levels and steroid treatment result in GH resistance and can also reduce GH secretion.

### Normal growth

Movement across height and weight centiles (up or down) is common in the first 2 years of life and does not necessarily represent a problem. Our data show nutritional status should be normal by 1 year. Most children will settle onto a height centile by 2-3 years of age and after this a child who is growing normally will maintain a height velocity sufficient to keep on the same centile, and will carry on growing along this centile until they commence their pubertal growth spurt. A child with late puberty will have a fall in height centile position and also feel relatively shorter compared to their peers, until they start their pubertal growth spurt. 98% of normal girls have started pubertal development (Tanner breast stage 2) by 13.7 years and 98% of boys have started development (testicular volume over 4 mls) by 14.2 years.

### Patient monitoring

Height (measured with a stadiometer) and weight should be recorded at every clinic visit (minimum interval between measurements should be 3 months) and plotted on the standard growth centile charts. In children under 1 year, head circumference (OFC) should be plotted. Mid parental height and parental target centiles should be calculated as shown on the growth chart.

### Further assessment is required for children who:

- Are falling from their centile position- they have a poor height velocity over a reasonable period of time (6 months to a year).
- Are very short (below 0.4<sup>th</sup> centile) even if they are growing at a normal height velocity.
- Are very short for their mid-parental height.
- Have significant pubertal delay (see puberty section 8.3).

## Assessment

Look for factors related to CF which may impact on growth.

- Nutrition - intake or malabsorption. Feeding behaviour problems are common in younger children (see section 7.6).
- Chronic infection
- Impaired glucose tolerance or CF related diabetes
- Steroid treatment.
- Pubertal delay.

Consider checking for non CF related causes:

- Coeliac disease.
- Hypothyroidism.
- Turner syndrome (this is not always associated with clinical features and it is worth checking karyotype if a girl is very short).

Patients can be discussed with Dr Bridges or Dr Alexander at any stage. They are happy to look at growth charts or assess bone ages for patients.

## Investigations which can be done before referral

- Thyroid function, coeliac antibodies and karyotype in girls.
- Bone age (x-ray of the non-dominant wrist and hand) is a way of looking at how much growth there is still to come. Bone age is not likely to be helpful in children under 4 years. Assessment of bone age is operator-dependent and results are more likely to be helpful if the score is assessed by someone with experience.
- One off measurements of GH are not helpful. IGF1 and IGFBP3 are helpful in assessing GH activity but do not distinguish between defects of GH secretion (pituitary problems) and GH action (inflammation, infection, steroids).
- For pubertal delay it may be helpful to check LH, FSH and sex steroid levels although these are likely to be low until mid-puberty.

## Consider referral to paediatric endocrinology for the following reasons:

- Pubertal delay (see puberty section 8.3).
- Reduced height velocity or short stature, which does not seem to be caused by CF related problems.
- Concerns by family or child about height.
- Assessment may be of value if there is persistent poor growth velocity even if there are medical factors sufficient to completely explain the situation (nutritional issues, inflammation, reduced lung function, high dose steroids, etc.). There may not be any intervention to improve things but an assessment and explanation may help.

## Growth hormone

GH deficiency is a rare cause of short stature in the general population. It can occur in CF but the prevalence is not increased. GH deficiency should be considered in short children with persistent poor growth velocity where other causes have been ruled out. Diagnosis requires a stimulation test.

There have been a number of studies of the use of GH in CF patients (without GH deficiency) which have demonstrated short term anabolic, pulmonary function and bone health benefits. However, the impact of GH on longer term clinical status is not known, and there is no evidence that GH given in this situation increases adult height. GH is not licensed for use in CF without GH deficiency.

Weak androgens like Oxandrolone have been shown to improve short term prepubertal growth velocity in children but are not routinely used.

## 8.3. Puberty

Pubertal delay remains a problem in CF although the improved clinical status of those entering adolescence has made this less common. Delayed pubertal development has been found to contribute significantly to the psychological problems suffered by adolescents with CF. Presentation may be with short stature or with concerns about development.

Gonadotrophin and sex steroid secretion is normal during puberty in CF and adult sex steroid levels are usually within the normal range. Boys reach normal testicular volumes in puberty despite the majority having azoospermia.

Mean age of menarche is delayed in CF by up to 1.5 years (14.5 years compared to 12.9 years). Menstrual irregularities may also be relatively more common in CF adolescents.

### Assessment of pubertal delay

- Height & weight.
- Tanner staging. (these are printed on growth charts).
- Bone age if there are concerns about height.
- LH, FSH and sex steroid levels although these are likely to be low until mid-puberty.

In girls:

- The first sign of puberty is breast development (Breast stage 2).
- The pubertal growth spurt starts as puberty commences (Breast stage 2).
- Periods occur relatively late in development, at Breast stage 4 or 5.
- Growth slows after menarche, with about 4-5cms remaining.

Ask if pubic hair is present.

Is there any breast development (part of chest examination).

Ask whether periods have started.



In boys:

- The first sign of puberty is an increase in testicular volume (4mls and over). This means that the start of pubertal development may be overlooked if testicular volumes are not assessed (and may not be noticed by the individual themselves).
- The pubertal growth spurt in boys does not start until mid-puberty (10-12mls testicular volume).
- The voice breaks towards the end of puberty.

Ask if pubic hair is present.

Has voice broken?

### **Treatment of pubertal delay**

Individuals with the most significant medical problems are the most likely to be delayed. Any nutritional problems should be addressed, and CF-related diabetes should be excluded as a contributory factor. Growth during puberty can be adversely affected by nutritional problems, infection and steroid treatment; all of which can reduce the increment in height achieved during this phase of growth. It may be appropriate to delay treatment if there is a realistic chance that medical status can be improved thus allowing growth without adverse effects. If it is unlikely that any significant change will occur (and things might get worse), it is then reasonable to go ahead with treatment to induce puberty even if optimum growth may not be achieved.

### **Potential benefits of treatment**

- Psychological and social.
- Height.
- Bone density - Bone density increases during puberty and peaks in the years after the end of puberty, as a result of sex steroid action. CF patients are at increased risk of low bone density and it makes sense to optimise it at this point.

### **Treatments available**

Patients should be referred to Dr Bridges or Dr Alexander. Treatment to induce puberty mimics the gradual rise in sex steroids during normal puberty and aims to complete growth and development over about 2 years. Many individuals start to develop spontaneous puberty after a few months of treatment and medication can be stopped. There is no harm in stopping treatment at any point but if spontaneous puberty does not occur, it usually makes sense to take the individual to nearly adult height and development before stopping and reassessing endogenous function. Given in these doses treatment does not have an adverse effect on adult height.

### Steroid treatment for induction of puberty

#### *Females*

Increasing doses of oral ethinyloestradiol:

- 2 or 2.5 micrograms ethinyloestradiol daily for 6 months (either 2 microgram tablets or one quarter of a 10 microgram tablet)
- 5 micrograms ethinyloestradiol daily for 6 month

- 10 micrograms ethinyloestradiol daily for 6 months
- 15 micrograms ethinyloestradiol daily for 6 months
- 20 micrograms ethinyloestradiol daily for 6 months

Adding in progesterone when 15 micrograms ethinyloestradiol is given or before this if there is any vaginal bleed, using -  
levonorgestrel 30 micrograms daily or norethisterone 5mg daily for 7 days out of each 28 day cycle.

### *Males*

Increasing doses of intramuscular depot testosterone esters as Sustanon (250mg in 1ml)

- 50 mg IM every 4-6 weeks for 6 months
- 100 mg IM every 4 weeks for 6 months
- 100 mg IM every 3 weeks for 6 months
- 100 mg IM every 2 weeks for 6 months

### *Topical sex steroids to induce puberty*

There are very few published data on preparations or doses. There is one published study using “Evoral 25” oestrogen patches, (one eighth or one quarter of a patch every 48 hours) in girls. “Tostran” metered dose topical testosterone is a possible option for boys but there are no supporting publications.

## **8.4 Bone Metabolism**

### **Bone density in CF**

Approximately 25% of adults with CF have osteoporosis and there is an increased risk of vertebral and non-vertebral fractures, which is significantly worse in individuals post-transplant. The aim of monitoring and therapy is to reduce the morbidity related to fractures. Bone density increases during puberty under the influence of sex steroids, peaks in early adult life and falls after this, so in children and adolescents with CF it seems logical to try to get the best bone density possible in the hope of reducing problems which may occur many years later. In general, bone mineral content and density are normal in children with a good nutritional status and preserved lung function.

### **Investigation of bone mineralisation by DEXA scans**

Dual energy X ray absorptiometry (DEXA) is the commonest way of examining bone density in children and adolescents, looking at the spine and upper femur. Bone mineral density (BMD) is calculated from the bone mineral content (BMC) measured by DEXA and the 2 dimensional area of the bone calculated during the scan. The measured BMD of larger bones will be greater without the actual density of the bone being more because the beam will pass through a bone of greater dimensions. This makes assessment of BMD in growing children complex. Bone mineral apparent density (BMAD) is a correction factor aimed at overcoming this problem. There are normal ranges for bone density in healthy children and the measured BMD will be compared with this (z score). Interpretation of the z score may be difficult if the child is very short (and compared with children with larger bones) or delayed in puberty (and

compared with children with normally timed puberty). The trend between repeated measurements may be more helpful than comparing with the normal range.

### **Risk factors for reduced bone mineral density**

- **Steroids** Frequent courses of oral or intravenous steroids and those on high dose inhaled corticosteroids.
- **Vitamin D and Calcium** are vital in bone growth. **Everyone** with CF (including pancreatic sufficient) should take vitamin D supplements, (see below for management of deficiency). Encourage intake of dairy products and consider supplements in those who do not. **A negative calcium balance adversely affects bone health.**
- **Nutritional status-** nutrition apart from calcium and vitamins influences bone growth. CFRD can contribute to reduced bone density.
- **Vitamin K** is a fat soluble vitamin vital for the function of osteocalcin and other bone related proteins, and may be low in CF patients, including those who are pancreatic sufficient. Vitamin K in multivitamin preparations is minimal and so we recommend oral water soluble vitamin K (menadiol) at a dose of 10mg/day for ALL CF children when 6 years old (it can be dissolved in water if necessary). We are also starting ALL newborn screened babies (including pancreatic sufficient babies) on DEKAs plus or Aquadeks which contains a small amount of vitamin K.
- **Infection-** chronic inflammation can inhibit bone formation.
- **Endocrine issues** - sex steroids are vital in the attainment of adult bone density during puberty and adult levels of sex steroids are required to prevent osteoporosis in adults.
- **Physical activity** -exercise, particularly weight bearing is needed for normal bone growth and children who do not move much will have reduced bone density.
- **CFTR** is expressed in bones and mutations in CF may contribute to reduced bone density.
- **CFRD** may be a potential risk factor for reduced bone density.

### **Screening of bone density**

Bone densitometry (DEXA scans of lumbar spine and femur) is measured in all patients from age 8 years every 2 years at annual review. Look at the vertebrae on chest x-rays for any evidence of injury/crush fractures.

Repeat the scan after 12 months if:

- BMD z score is  $\leq -2.0$ .
- The child has had fractures which do not seem to be related to sufficient trauma.
- They are in a very high risk group for osteoporosis (high dose steroids, poor nutritional status, long periods of inactivity).

Abnormal scans can be discussed with Dr Nicola Bridges or Dr Saji Alexander (Chelsea and Westminster). They will be repeated in 1 year.

### **Prevention of osteoporosis- everyone with CF**

- Vitamin D supplements and treatment of Vitamin D deficiency
- Monitoring and treatment of pubertal delay
- Assessment of sex steroid levels in adults
- Encouragement of weight bearing exercise

### **Management of reduced bone density and osteoporosis**

Consider the following factors if BMD z score is  $\leq -2.0$ . If the BMD is low on repeated DEXA scans or the child has had fractures which do not seem to be related to sufficient trauma, a more formal assessment of bone health or a referral are required.

- *Pubertal delay and hypogonadism* Consider treatment with sex steroids if bone density is reduced in an adolescent with pubertal delay and assess whether adult levels of sex steroids have been achieved in post pubertal individuals.
- *Clinical factors* - CFRD, reduced lung function ( $FEV_1 < 50\%$  predicted), nutrition, immobility.
- *Vitamin D and calcium status.*

#### *Bisphosphonate treatment*

Bisphosphonates reduce turnover and result in increased bone density. There have been a number of studies of bisphosphonates in adults and young people with CF demonstrating increased bone density with treatment. Bisphosphonates have been demonstrated to decrease fracture risk in a range of other clinical situations but data in CF is lacking. Intravenous formulations include pamidronate, usually given as a 3 monthly IV infusion, and zoledronic acid, given once or twice a year. There are a number of oral formulations, but there are significant cautions about how the tablets should be taken, and there are no liquid preparations:

- tablets should be swallowed whole with at least 200 ml of water on an empty stomach immediately after getting up in the morning
- patients should stay fully upright for at least 30 minutes or one hour after taking the tablet and before taking any food, drink or other medicine

In children and adolescents bisphosphonate treatment should be considered if all of these apply:

- After other contributory issues (as above) have been addressed.
- Serial BMD z score is -2.0 or less in total body or lumbar spine.
- There is a history of low trauma fractures in limbs or vertebrae.
- Requiring continuous glucocorticoid treatment, e.g. post-transplant

Potential side effects of bisphosphonates:

- Osteonecrosis of the jaw can occur and those with poor dental hygiene are at most risk. A dental check is mandatory prior to start of bisphosphonates.

- There is an increased risk of atypical fractures of the femur.
- Bone pain and flu like symptoms - studies using IV bisphosphonates suggest these may be more common in CF.
- Calcium and Vitamin D status should be replete.
- Bisphosphonates are teratogenic in animal studies and are contraindicated in pregnancy. Because they bind to bone and are then leached out over a long period there is a theoretical risk that a fetus could be exposed if the mother had treatment in the years before pregnancy. Outcomes of a very small number of pregnancies where the mother has taken bisphosphonates have not demonstrated serious adverse effects.

Bisphosphonates are unlicensed for this indication and treatment should be discussed on an individual basis in conjunction with Dr Bridges or Dr Alexander.

### **Vitamin D status**

We measure total 25 hydroxy-vitamin D levels annually. Because a large proportion of vitamin D comes from sunlight, levels are lower in winter and spring. Low vitamin D levels are very common in the general population (poor diet, pigmented skin and covering clothing are risk factors). Aim to maintain a serum 25 hydroxy-vitamin D level over 75nmol/l to optimise bone health.

Optimal levels vitamin D	> 75 nmol/L
Vitamin D adequate -	50 -75 nmol/L
Vitamin D insufficient -	25 -50 nmol/L
Vitamin D deficient -	< 25 nmol/L

- We treat all children with vitamin D supplements (colecalciferol) if levels are <50.
- If levels are 50-75, we would increase their daily vitamin A&D (or dalivit) assuming vitamin A levels allow that (i.e. vitamin A is not high). Clearly there is a spectrum so that we might chose to give full treatment dose if levels are in 50s, especially if the DxA scan shows reduced BMD.

### **Prophylaxis to prevent deficiency**

400 IU of vitamin D daily should prevent deficiency in most infants and 800 IU in older children. This can be given as Vitamin A and D capsules (5000 IU of Vitamin A and 400 IU Vitamin D). Most ordinary multivitamin preparations contain 400 IU Vitamin D.

10 mcg of colecalciferol is equivalent to 400 units.

All newborn screened babies (pancreatic insufficient and sufficient) are being started on DEKAs plus or Aquadeks which contains vitamin D.

### **Treatment of vitamin D deficiency see formulary (section 11.2b)**

*Anyone with a vitamin D level below 50nmol/l should be treated.*

**Stoss therapy** will now be our principle way of treating vitamin D deficiency. It involves oral administration of the total treatment dose of vitamin D given in a single dose. Ideally this

is given in clinic. An alternative is the whole dose as a single intramuscular injection. This may need to be repeated (usually every 3 months), if poor compliance persists with maintenance dosing. However the Sydney paper (Shepherd et al, JCF 2012) showed this regimen maintained vitamin D levels for a year. See section 11.2b for doses.

Oral colecalciferol can still be given daily for 3 months but stoss therapy is likely to be more effective.

Check total 25 hydroxy-vitamin D levels after 3 months, if  $> 75\text{nmol/l}$  and alkaline phosphatase normal, put child back on to prophylaxis. If not corrected, give another 3 months treatment.

Do not increase the dose of Vitamin A+D capsules too much because there is a risk of Vitamin A toxicity. Vitamin D toxicity is rare and usually only occurs following massive miscalculations of the dose- individuals who are getting vitamin D from a number of sources such as supplements and fortified feeds are not going to develop toxicity. Combined calcium and vitamin D preparations are very difficult to take and the dose required to treat Vitamin D deficiency would be unlikely to be tolerated. Do not treat vitamin D deficiency with alfacalcidol.

## 8.5 ENT complications

### 8.5a Nasal polyps

- Are rarely seen in children other than in cystic fibrosis and may occur in up to 45% of adults and children with CF. In children, about half of these will be asymptomatic.
- Aetiology is unclear but is associated with chronic inflammation and may be related to infection, allergy, immune factors, altered secretions and abnormal cilia.
- Can result in chronic nasal obstruction, which increases airway resistance and may lead to mouth-breathing and obstructive sleep apnoea syndrome.
- Can also cause headaches and impair smell and taste.

Diagnosis is made by simply examining the nasal cavities with a light but sometimes it is difficult to differentiate polyps from inflamed turbinates.

If troublesome:

- Initial treatment is usually with a nasal steroid spray such as fluticasone (Flixonase or Avamys) or mometasone (Nasonex); see BNFC for dosages. Use of drops in the form of betamethasone or fluticasone (Flixonase Nasules) for periods of up to several weeks at a time often reduces nasal polyposis significantly. Note though that adrenal suppression and growth failure has been reported with protracted use of betamethasone nose drops.
- Saline douching is usually helpful, with Sterimar or NeilMed sinus rinse, which should be used before topical steroid administration.
- Anti-histamines are of no value unless co-existing allergy.
- If persistent severe obstructive symptoms or headache, surgery should be considered, but due to the high recurrence rate (60-90%), multiple procedures may be necessary. Surgery may also be considered if chronic rhinosinusitis with polyposis felt to be a source of respiratory tract reinfection with *Pseudomonas*.
- Oral steroid courses are occasionally used for severe multiple recurrent polyps.

If conservative therapy is failing, refer to Mr William Grant (who has a particular specialisation in paediatric nasal problems), Consultant ENT Surgeon at Chelsea & Westminster Hospital (020 3315 7972). Mr Jonny Harcourt is present in Brompton clinic on the 2<sup>nd</sup> Friday of every month from 11am-1pm, and can see the children by agreement with him or his SpR, if there is an acute complication in an In-patient.

### 8.5b Sinusitis

- Although almost all children with CF have chronic paranasal sinus retention of secretions and mucosal inflammation, many are asymptomatic.
- X-ray of the sinuses is of little value, as over 92% of all children with CF will have opacification of the maxillary, ethmoid and sphenoid sinuses. Initially, opacity is due to retention of thick secretions but later it may be due to polyposis within the sinuses. The frontal sinuses rarely develop in children with CF, probably due to early onset of sinusitis, which prevents pneumatization. CT scans are the investigation of choice (not MRI) but should only be considered if it a complication (such as a mucocoele) is considered or if the patient is failing conservative treatment and surgery is a possibility.
- Nasal swabs are extremely useful as a wide spectrum of bacteria may be involved.
- Chronic sinus infection, with associated upper airways obstruction, may worsen lower respiratory tract health.
- Chronic sinusitis is commonly associated with nasal polyposis.
- Sinusitis may cause headaches, which are persistent and localised. Other symptoms are related to chronic nasal obstruction (mouth-breathing, snoring, loss of sense of smell and taste) and purulent drainage (postnasal drip, cacosmia – foul smells in the nose, constant throat-clearing, halitosis).
- Long-term oral antibiotics, usually in the form of a macrolide, or based on sensitivity studies, may be of value (3-6 weeks), and oral metronidazole may improve halitosis.
- Invasive sinus washout (needle inserted into maxillary antrum) is not recommended, unless to provide a sample for culture, as it has no long term benefit. However a nasal douche may give symptomatic relief.
- In a minority endoscopic sinus surgery is appropriate if persistent sinus distribution localised headaches, usually combined with persistent offensive nasal discharge persists despite initial medical treatment with antibiotics and steroids. Persistent Pseudomonal infection may warrant surgical intervention.
- Mucocoeles may occur as a complication of CF in the sinuses. A single air cell becomes blocked, retains its secretions and becomes slowly enlarged. This may be a painless process though maybe complicated by an acute infection. If advanced the condition can cause proptosis or hypertelorism. Surgery is highly effective in draining the chronic infection and preventing further expansion of the paranasal sinuses.

### 8.5c Hearing and tinnitus

There is no known connection between deafness and the basic CFTR mutation. However, hearing loss and tinnitus are reported in people with CF usually secondary to aminoglycoside use. The hearing loss can be attributable to high levels of aminoglycoside or the accumulative use of aminoglycosides over time. This appears to be more common with the use of IV amikacin which is one of the principle drugs used for *M abscessus* complex treatment; we no

longer use IV gentamicin which was particularly associated with hearing loss. Some reports of tinnitus do happen with nebulised aminoglycosides but it is usually attributable to intravenous aminoglycoside use hence the recommendation to regularly monitor blood trough levels for aminoglycosides.

If there is a family history of deafness, genetic mutation screening for m.1555A>G, which predisposes to aminoglycoside ototoxicity is recommended. Prevalence of this is estimated at 1 in 520, it is a mitochondrial mutation. Aminoglycoside use should be avoided if a carrier of this mutation.

Audiometry should be performed:

- as a baseline at the start of commencing treatment for NTM and repeated after 1 year.
- in all children starting on regular 3 monthly IV antibiotics and will be repeated yearly.
- if a child ever has a high aminoglycoside trough level.

Audiology should be arranged by referral to the child's local audiology clinic.

If any hearing deficit is detected or tinnitus is reported then consideration of stopping aminoglycoside therapy and switching to alternative treatments should be made.

A systematic review has shown that the antioxidant N-acetylcysteine (NAC) has a protective effect against aminoglycoside-induced hearing loss, reducing the risk of ototoxicity by 80% (Kranzer et al, Thorax 2015). We will use oral N-acetylcysteine at the time of IV aminoglycoside therapy for (a) those receiving IV amikacin (for NTM) and (b) 3-monthly antibiotics. We are starting this new policy for the most at risk group, and will see how the children tolerate the NAC. In time we may decide to use this for all courses of IV aminoglycosides. There are no data on its use with nebulised amikacin and we are not using this currently. See formulary for doses.

## 8.6 Arthropathy

Arthropathy may occur in up to 10% of children with CF and the mean age of onset is 13-20 years (depending on the series). **Cystic fibrosis arthropathy** (CFA) is a specific condition, which may be immune-complex mediated and related to chronic pulmonary infection and inflammation. Typically, the children have an episodic arthritis with pain and swelling, usually of large joints such as knees and ankles and wrists. It is often accompanied by low-grade fever and there may be erythema nodosum or an erythematous rash or purpura. Joint x-rays are usually normal. Episodes tend to settle spontaneously after 3-4 days and respond well to non-steroidal anti-inflammatory drugs (e.g. ibuprofen). Intensification of chest therapy may also help control joint symptoms. Beware renal toxicity when using IV aminoglycosides in those on regular ibuprofen. There are still no published randomised controlled trials according to 2016 Cochrane review.

Some of the children with arthritis and advanced lung disease have features of **hypertrophic pulmonary osteoarthropathy** (HPOA), this occurs in 2-7% of CF patients with a median age of onset of 20 years. In this condition, as well as arthritis, which is often accompanied by joint effusions, there are features of periostitis. The latter consists of tenderness and pain over the long bones with periosteal elevation on x-ray. Periosteal changes may also be noted on radioisotope bone scan. HPOA is seen in patients with more severe lung disease and worsens during chest exacerbations. Anti-inflammatory drugs may be necessary.



Occasionally, sero-positive **rheumatoid arthritis** occurs in CF. It may require treatment with anti-inflammatory agents, steroids and regular infusions of immunoglobulin (see section 6.12) re approval and funding). Finally, it must be remembered that **ciprofloxacin** can cause arthropathy in both children and adults with CF. Onset of symptoms may occur between three weeks and two months but tend to respond within two weeks once the drug is stopped.

If there is doubt over diagnosis or management, refer to Dr Clarissa Pilkington (tel 0207 829 7887) at Great Ormond Street Hospital for Children.

### 8.7 Pseudo-Bartter's syndrome

An uncommon cause of metabolic alkalosis that has been seen as a presenting feature of CF as well as a complication in those with known disease. It is accompanied by chronic salt depletion and sometimes failure to thrive without severe dehydration. It can also present acutely often as part of heat stroke so is commoner in hot weather when there has been inadequate salt and fluid replacement with dehydration. Principal findings are *hypokalaemic hypochloraemic metabolic alkalosis, sometimes with hyponatraemia*. This may be preceded by anorexia, nausea, vomiting, fever and weight loss, in the acute setting this can be mistaken for infective gastroenteritis. Judging degree of dehydration in an acute presentation can be hard, the classic clinical signs of dehydration (sunken eyes, loss of skin turgor) are not always apparent and a comparison of acute presentation weight with last clinic weight is helpful.

Check venous sample in blood gas machine for bicarbonate, or venous blood for Cl, Na and K. Acutely oral rehydration solution (Dioralyte or equivalent) or sometimes IV fluids (normal saline +/- potassium chloride) is required. In the more chronic, indolent presentation treatment is with sodium +/- potassium chloride supplements, which may be required for many months or long term. After salt replacement, the metabolic abnormality resolves and weight gain follows rapidly.

Unexplained failure to thrive should always have urinary electrolytes checked, a spot urine  $\text{Na}^+ < 20 \text{ mmol/l}$  indicates low total body sodium that needs correcting. A serum potassium at the lower end of the normal range may still be associated with body depletion.

It is quite usual for a newborn screened infant under 3 months to have low urine Na levels and normal range is less well defined, so it should **not** be used to guide sodium supplementation in this age group (see salt supplement recommendations in section 7.3).

### 8.8 Fertility

Although it should be assumed that all males are infertile, this is not necessarily the case and so male contraception must be strongly encouraged, with the additional benefit of adhering to 'safe sex'. Condoms are mandatory! It is our duty to ensure that all boys are aware of this issue. The age of telling them may vary and occasionally is problematic if parents are reluctant for the issue to be discussed. We would encourage parents to tell their sons as early as possible, and we would wish to ensure they are informed by 8-12 years. The annual review is often a good time to do this. It is important to stress to them that infertility is not the same as impotence and that sexual performance is unaffected (although the volume of ejaculate is

reduced). There are successful reports of CF men having children after microsurgical epididymal sperm aspiration and intracytoplasmic sperm injection (ICSI). It is important to reassure families that men with CF can father a baby.

Girls are not infertile so again contraception must be encouraged. Useful information on types of contraception is available in a booklet entitled 'Cystic fibrosis and relationships' available via CF Trust website (see appendix 19). Care must be taken with oral contraception due to effect of short term courses of antibiotics, but long term ones (e.g. azithromycin) do not effect the Pill once the treatment is established (care again is necessary when they are started). Antibiotics for treating NTM, especially rifampicin can reduce the effectiveness of the Pill.

Female fertility may be reduced due to thickened cervical mucus (note that women who are on ivacaftor have had their fertility improved), and the issue of pregnancy and CF can be discussed with Mr Guy Thorpe-Beeston, Consultant Gynaecologist at Chelsea & Westminster Hospital (0203 315 8000). Generally women with CF need to be relatively healthy when planning a pregnancy.

## **8.9 Stress incontinence**

Urinary incontinence is a condition where certain activities e.g coughing, laughing, jumping etc. leads to a leak of urine. This can be anything from a slight dribble to a complete emptying of the bladder. It is known that many women with CF are affected by urinary incontinence and it has become increasingly recognised that young girls may also be affected. This has been highlighted by the survey carried out at the Brompton, Great Ormond Street and Royal London hospitals, where we found 1 in 3 girls aged 11-17 years answering the survey had a problem at times. For many (if not all) girls this is rather embarrassing and many do not want to talk to their parents about it, and especially not to male doctors! It is more likely they will discuss this with female members of the team (nurse specialists, physiotherapists). We can arrange for the girls to be seen by a gynaecologist and/or women's health physiotherapist, but initially they are seen by one of our physiotherapists, as sometimes simple 'pelvic floor exercises' and a technique known as 'the knack' (a pelvic floor contraction) can be quite helpful.

Please note that, although it is less common, stress urinary incontinence may also occur in males and for some patients (boys and girls) faecal incontinence may be an issue.

## 9. Transplant assessment

Almost all assessments are now carried out at Great Ormond Street Hospital for Children and referrals should be made to Drs Helen Spencer or Paul Aurora. A referral proforma is available from Great Ormond Street Hospital (see below). An exception would occur in the case of an adolescent approaching transition to the adult service, in which case, the assessment should be done here, liaising with the adult team. Contact Dr Su Madge, Nurse Consultant, extension 4053 at Royal Brompton Hospital, for the booklet listing investigations. Once complete, return these to Dr Martin Carby or Dr Anna Reed, Consultants in Respiratory & Transplant Medicine, at Harefield Hospital.

Over the years, most transplants performed in CF children were heart / lung (HLT) with the CF patient's heart being used in a domino procedure for another patient. More recently, bilateral lung transplant are being done more often. Although living lobar transplants (a lobe each from two relatives, most commonly parents) have been performed in adults and some paediatric centres abroad, they are not yet performed in paediatric practice in the UK.

Consideration of a child for HLT assessment should be based on the individual patient, and is best performed in a multi-disciplinary fashion.

### Criteria for Transplant Referral

- Significantly reduced lung function, usually with FEV<sub>1</sub> <30% predicted. May include rapidly declining FEV<sub>1</sub> even if still >30% predicted.
- Severely impaired quality of life.
- Oxygen-dependent (resting SpO<sub>2</sub> < 90%).
- Exacerbation of pulmonary disease requiring PICU/HDU stay.
- Pneumothorax in advanced disease especially if recurrent.
- Severe haemoptysis not controlled by embolisation.
- Child and family committed to the idea.

Traditionally, children fulfilling these criteria would be likely to have a median life expectancy of 2 years, but this may not be the case anymore.

### Contra-indications

The following contra-indications differ between centres, and may be subject to change over time with the availability of e.g. newer antibiotics and increasing surgical expertise. The decision will be influenced by the presence of multiple problems within an individual child.

#### 1. Major

- Other organ failure (excluding hepatic when a lung/liver transplant could be considered).
- Untreated *Mycobacteria tuberculosis*.
- Invasive pulmonary aspergillosis.
- Malignancy in the last 2 years.
- Unstable critical clinical condition (e.g., shock, mechanical ventilation or extra-corporeal membrane oxygenation).
- Colonisation with *Burkholderia cenocepacia* and *Mycobacterium abscessus subspecies abscessus*. Note *M abscessus* complex is NEW major criterion.

- Child does not want the procedure despite receiving information.

## 2. Relative

- Long term corticosteroids > 20mg/day.
- Non-pulmonary infections e.g. Hepatitis B or C, HIV.
- Previous thoracic surgery - pleurodesis will make the procedure more difficult and should be discussed with the surgical team.
- Multi-resistant organisms e.g. NTM (esp. *M abscessus* complex), some genomovars of *B cepacia* complex, *MRSA*, panresistant *P aeruginosa*.
- Severe osteoporosis.
- Some extreme psycho-social issues, for example, long standing and entrenched non adherence to treatments; lack of family support.

Transplantation is so familiar to many people now from TV, newspapers etc, most of which tend to be biased towards successful outcomes, that it is often perceived as a miracle cure. It is therefore important when discussing the issues with the family and child, that as well as the potential benefits, the following negative points should be addressed (these will be addressed at the assessment meetings, but should be raised early with families):

1. Acceptance onto the waiting list does not guarantee a transplant. Due to a shortage of donors about 30% of patients will die before organs become available. The time spent waiting for organs will be extremely stressful (uncertainty, false alarms etc).
2. Heart/lung or lung transplantation is not a complete cure for CF, it is palliative. After the operation, invasive procedures including bronchoscopy and biopsies are likely to be required. In addition, unless complete eradication of reservoirs of infection has been successful (which almost never occurs due to chronic infection of sinuses), there is potential for bacterial infection of the transplanted lungs, which may make ongoing antibiotic therapy and physiotherapy necessary.
3. Transplantation has little impact on the non-pulmonary manifestations of the disease (ie, enzyme replacement and other therapies need to be continued), although there may be nutritional benefits in the medium term. CF-related diabetes may worsen.
4. Problems associated with transplantation include early rejection, severe sepsis related to immunosuppression and later development of obliterative bronchiolitis (OB). OB can eventually lead to severe respiratory impairment, and is difficult to treat successfully.

# UK Paediatric Lung and Heart-Lung Transplantation

## Referral Proforma

*STRICTLY CONFIDENTIAL*

**THIS FORM MAY BE USED TO REFER TO ANY OF THE UK  
CENTRES THAT PERFORM LUNG & HEART-LUNG  
TRANSPLANTATION. PLEASE RETURN THE FORM TO THE  
CENTRE OF YOUR CHOICE:**

### **GREAT ORMOND STREET**

Dr Paul Aurora and Dr Helen Spencer  
Cardiothoracic Transplant Office  
Great Ormond Street Hospital  
Great Ormond Street  
London  
WC1N 3JH

Tel: 020 7813 8563  
Fax: 020 7813 8440

### **NEWCASTLE**

Dr Malcolm Brodlie  
Cardiopulmonary Transplant Unit  
Freeman Hospital  
High Heaton  
Newcastle upon Tyne  
NE7 7DN

Office: 0191 223 1132  
Fax: 0191 223 1439

## **GUIDANCE NOTES FOR COMPLETION OF REFERRAL PROFORMA**

**This proforma has been designed to streamline the referral process for potential lung and heart-lung transplant recipients. As a result potential transplant candidates can be identified more easily, be formally assessed more quickly and duplication of investigations will be avoided. The information required has been agreed by all UK lung transplant centres and this form can be used to refer to any UK centre.**

**Thank you for your co-operation.**

### **KEY POINTS**

**Please complete all sections - any questions which are not applicable should be marked as N/A.**

When specific results are not available but have been requested please mark as **awaited**.

**Copies of Imaging (CT, coronary angiography, etc) should be sent on CD with this form**

Copies of complete reports of investigations can be appended to this proforma, but the clinical summary should be completed by a member of the multidisciplinary team in the appropriate proforma section. Serial lung function tests are very helpful and should be included when available.

Any questions about this proforma or its use can be addressed by contacting the transplant co-ordinators at the hospital to which you intend to send the referral.

## PERSONAL DETAILS

PATIENT NAME: .....

NHS Number:.....

AGE: .....

DOB: .....

ELIGIBILITY FOR NHS CARE:.....

NEED FOR INTERPRETER: YES / NO LANGUAGE:.....

ADDRESS: .....

(Include Postcode) .....

.....

TELEPHONE NUMBER .....MOBILE: .....

REFERRING CONSULTANT:.....

REFERRING CENTRE:.....

(Include Postcode) .....

.....

TELEPHONE NUMBER .....FAX: .....

PCT: .....

GP NAME: .....

GP ADDRESS: .....

(Include Postcode) .....

.....

GP TELEPHONE NUMBER .....FAX: .....

IS PATIENT AWARE OF REFERRAL FOR TRANSPLANT ASSESSMENT?

YES NO (please circle)

## RESPIRATORY HISTORY

Primary Diagnosis: .....

Secondary Diagnoses      Respiratory.....

Non respiratory      1.....

2.....

3.....

Respiratory Diagnoses made by: Clinical /CT chest/Histology/Genotype/ Sweat Test  
Details.....

Any household members smoke? :    YES                      NO                      (Please Circle)

Microbiology:              Have these organisms ever been isolated?

*Burkholderia cepacia*                      YES    NO    specimen.....date.....

*Pan-resistant Pseudomonas*                      YES    NO    specimen.....date.....

*MRSA*                      YES    NO    specimen.....date.....

*Mycobacteria (TB or atypicals)*                      YES    NO    specimen.....date.....

*Aspergillus*                      YES    NO    specimen.....date.....

If YES, please give further details.....

.....

Oxygen at home      YES                      NO                      (Please Circle)

Amount .....L/min      Average daily use ..... hrs

### Respiratory Past History

Haemoptysis              YES                      NO                      (Please Circle)

Details:                      .....

Pneumothorax:              YES                      NO                      (Please Circle)

Details:                      .....

Thoracic Surgery:              YES                      NO                      (Please Circle)

Details:                      .....

Has the patient ever required ventilation?    YES                      NO    (Please Circle)



If yes                      NIV / formal ventilation in ITU                      (duration .....days)

Details:.....

### Current Exercise Capacity

Exercise tolerance ..... (distance)

Formal 6 minute walk test performed?                      YES                      NO                      (Please Circle)

If yes                      Max distance ..... metres                      Lowest saturation.....%

Performed on air / oxygen at ..... litres per minute

Wheelchair                      YES                      NO

### Progress pre and post diagnosis (Free Text)

Include details on rate of decline, life threatening exacerbations, frequency of IV antibiotics, etc

Is family aware of prognosis?                      YES / NO

Is patient aware of prognosis?                      YES / NO

## PAST MEDICAL HISTORY

Current or previous :

Details:

Heart Disease	YES	NO	.....
Renal Disease	YES	NO	.....
Liver Disease	YES	NO	.....
Diabetes	YES	NO	.....
Malignancy	YES	NO	.....
GI problems	YES	NO	.....
Portacath	YES	NO	.....
Gastrostomy	YES	NO	.....

### Current Medication

1.....	Dose	Frequency
2.....	Dose	Frequency
3.....	Dose	Frequency
4.....	Dose	Frequency
6.....	Dose	Frequency
7.....	Dose	Frequency
8.....	Dose	Frequency
9.....	Dose	Frequency
10.....	Dose	Frequency

**ALLERGIES:** YES NO (Please Circle)

1.....

2.....

Oral Corticosteroids? YES NO (Please Circle)

Date commenced

Max dose

Current dose

Date stopped

Response.....

## Family and Social History

Adherence Good                      YES                      NO                      (Please Circle)

Attendance Record Good      YES                      NO                      (Please Circle)

Family support available:.....

Social Services input:                                      YES                      NO

Details.....

School details:.....

School attendance:.....

Siblings?.....

Relevant Family Medical or Social History:.....

.....

.....

.....

.....

.....

## Psychological assessment

Current or Previous History of:

Depression:                                      YES                      NO

Panic attacks:                                      YES                      NO

Anxiety:                                      YES                      NO

Needle phobia:                                      YES                      NO

Other psychological concerns?:                      YES                      NO

Details .....

.....

.....

.....

.....

.....

## CLINICAL INVESTIGATIONS

Weight.....kgs                      Height.....m                      BMI.....

ECG                      Date performed:

Result.....

Echocardiogram                      Date performed:

Result.....

Chest x-ray                      Last performed:

Result.....

HRCT Thorax Date performed

Result.....

.....

Arterial/Capillary/Venous (please circle) Blood Gas (ON AIR)

pH .....      pO<sub>2</sub> .....      pCO<sub>2</sub> .....      BXS .....      HCO<sub>3</sub> .....      Sats .....

Others (if available)

Bone Densitometry                      Spine Z score = .....      Femur Z score = .....

Abdominal ultrasound                      .....

Coronary angiography                      .....

Right heart catheter                      .....

GORD Testing                      .....

Glomerular Filtration Rate                      .....

## Respiratory Function Tests (attach trend values if possible)

Date	.....	.....
	Value	%
FEV1	.....	.....
FVC	.....	.....
FEV1/FVC	.....	.....
TLC	.....	.....
FRC	.....	.....
RV	.....	.....
TLCO	.....	.....
KCO	.....	.....

Haematology	
Date:	
Na	
K	
Urea	
Creatinine	
eGFR	
Bilirubin	
ALT	
ALP	
GGT	
Glucose (fasting)	
Chol (fasting)	
Trig (fasting)	
Total Calcium	
CRP	

Biochemistry	
Date:	
Hb	
WCC	
Platelets	
PT	
APTT	
Fibrinogen	
ESR	

Virology	
Date:	
HIV	
CMV	
Hepatitis B	
Hepatitis C	
Immunology	
IgE	

Additional Microbiology	
	Date & Details
MRSA screen	
Asp. precipitins	
Asp. culture	

Blood group (if known) .....

Anti crossmatch antibodies (if known) YES NO

Details .....

ANY OTHER COMMENTS

Signed..... NAME:.....

POSITION:..... DATE:.....

## 10. Miscellaneous

### 10.1 Preparation for surgery

It is important to ensure that BOTH the parents and child/young person have a clear understanding of what the surgery is for, and what the outcome of surgery will be. Consent will be obtained by the surgeon.

*Pre-op nil by mouth -*

6 hrs food and bottle milk

4 hrs breast milk

2 hrs water

General anaesthesia commonly leads to lung atelectasis (hence post-operative fever), even in healthy patients, a situation which is exacerbated in children with CF. We therefore routinely give peri-operative antibiotics to **all CF children** undergoing general anaesthesia, however good their lung function. This includes portacath insertion, gastrostomy insertion/changes, ENT surgery such as polypectomy, tonsillectomy and also gastrointestinal endoscopy. Many of these procedures are carried out at Chelsea & Westminster Hospital but it is still important to ensure the surgeons and gastroenterologists are aware of this when arranging the procedure – always give antibiotic recommendations (IV *vs* oral, and choice of drug) in the referral letter.

- Minimal and moderate lung disease - (especially for minor surgery) can usually receive high dose oral antibiotics for 48 hours pre- and 48 hours post-op.
- Severe lung disease may need 7-14 days IV antibiotics pre-surgery and 7 days post-operatively, and these would usually be given at the Brompton. Choice of drug is determined by the latest sputum or cough swab culture. The on-call paediatric respiratory SpR at Royal Brompton Hospital will advise over the exact choice, which is usually ceftazidime and tobramycin. It is also important that chest physiotherapy is strictly adhered to during the admission.
- Children with severe lung disease ( $FEV_1 < 40\%$ , or oxygen-dependent) can be at high risk from anaesthesia and surgery, so the risk benefit of the procedure must be carefully considered, and pre-op assessment by the anaesthetist should be carried out. Their health status must be optimised prior to the operation.
- **Pre-op plan** for those with significant disease – IV antibiotic course, IV fluids when NBM, see Pain Team for planning, organise postop on call physiotherapy, consider NIV post op, early mobilisation.
- Children with CFRD – Discuss management prior to admission with Dr Nicola Bridges or Dr Saji Alexander.
- Beware dehydration or opiates post-operatively leading to DIOS.
- In a non-sputum producing child see if a blind BAL can be performed by the anaesthetist if we are not bronchoscoping the child as well.

*Bronchoscopy* – no antibiotics beforehand but minimum 48 hours IVABs post-procedure if **significant** secretions are seen. In practice, bronchoscopy is often done at start of 14 day IVAB course when patient not doing well and no microbiology available or nothing ever grown. For newly diagnosed newborn screened babies, if the bronchoscopy is clear they need not stay afterwards for IVABs.

All CF patients undergoing general anaesthesia must be discussed with Prof Jane Davies re inclusion in research studies.

## 10.2 Immunisation

We strongly recommend that all **routine childhood vaccinations** are given at the usual times and should be arranged by the general practitioner.

**Influenza** immunisation for children over 6 months of age is mandatory and is also arranged by GPs. However families must be reminded and it is also useful to put a reminder in to the clinic letters to GPs in early autumn. The vaccines are usually available in October each year. We follow the NHS policy –

Under 6 months	No vaccine	
6m – 2yrs	Inactivated injected vaccine	<ul style="list-style-type: none"> <li>• Deep subcutaneous or intramuscular injection.</li> <li>• If never had before (and &lt;9yrs old), they get 2 doses 4 weeks apart.</li> </ul>
2 yrs and above	Live attenuated nasal spray vaccine - (Fluenz®).	<ul style="list-style-type: none"> <li>• If never had before (and &lt;9yrs old), they get 2 doses 4 weeks apart.</li> <li>• Not to be given if large bilateral nasal polyps.</li> <li>• Contraindicated if severely asthmatic.</li> </ul>

Egg hypersensitivity with evidence of **previous anaphylaxis** is a contraindication, although NHS guidance suggests children with milder egg allergy can receive the nasal vaccine. Parents should also receive the vaccine (but we do not routinely give to siblings).

Further information is available on:

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/456568/2904394\\_Green\\_Book\\_Chapter\\_19\\_v10\\_0.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/456568/2904394_Green_Book_Chapter_19_v10_0.pdf)

**Pneumococcal vaccine** - Prevenar is given as part of national immunisation policy, and Prevenar 13 covering 13 serotypes was introduced in April 2010. In older children who did not receive Prevenar, if the parents are keen, we would have no objection to them having the vaccination, although it is not routinely recommended, as Pneumococcus is not an organism particularly associated with CF. Pneumovax is used for children >5 years. It is of course mandatory for children who have had a splenectomy.

**Palivizumab (Synagis)** is a monoclonal antibody available as passive immunisation against respiratory syncytial virus (RSV). It is given as 5x monthly intramuscular injections. There is no good evidence for benefit in CF and we do not routinely recommend it.

## 10.3 Chicken pox

Although the literature is scarce, it has been documented that varicella-zoster infection can lead to infective pulmonary exacerbations and that early treatment with aciclovir may prevent pulmonary deterioration.



**Children who are not on oral corticosteroids.** If the diagnosis of chicken pox is confirmed and we are contacted early in the course of the illness, we suggest a one week course of oral aciclovir in those children who are unwell and particularly those who are known to have significant chest disease (see BNFC for dose).

If however we are informed late in the course of the illness or the child really has mild chicken pox only with a few spots then aciclovir is not warranted. This is particularly the case in CF children who are well from the CF point of view.

**If children are on oral corticosteroids** or have recently been on them, then the Guidelines as outlined in the BNFC should be followed:

Chicken pox contacts should only receive **Varicella-Zoster Immunoglobulin (VZIG)** if:

- they have not had chicken pox previously.
- and*
- are currently taking oral steroids.
- or*
- within the last 3 months have been taking the equivalent of 2 mg/kg/day prednisolone (or >40mg/day) for 1 week *or*
- within the last 3 months have been taking the equivalent of 1 mg/kg/day prednisolone for 4 weeks.

VZIG is given by deep intramuscular injection at the following doses:

<6 years 250mg; 6-11 years 500mg; 11-15 years 750 mg; 15 years and over 1000mg.

VZIG is available directly through the Health Protection Agency (tel. 0208 200 6868).

We would also recommend that we see those children and if a chicken pox rash still develops in these children who are at risk of serious disease, IV aciclovir is indicated for at least 7 days; total 10 days treatment.

At the 6<sup>th</sup> birthday annual review, we measure varicella antibodies, and if negative, we will offer **varicella immunisation** (even if there is a history of having had chicken pox). This is to ensure that we reduce the risk of a child contracting chicken pox while they are on a course of oral steroids for ABPA when older.

## 10.4 Travel abroad

Patients will need:

1. An information fact sheet which is available from the CF Trust (020 3795 1555).
2. Advice is also available in the BTS guidelines with an updated guideline published 2011. <http://www.brit-thoracic.org.uk/Portals/0/Guidelines/AirTravelGuidelines/BTS%20Air%20travel%20recommendations%20September%202011.pdf>
3. Adequate travel insurance. They need to be advised to fill in the medical information in great detail so that there is no risk of the company not reimbursing a potential claim. They also need to check that the policy does not exclude pre-existing illness. CF Trust fact

sheet has a list of suitable travel insurance companies. Everyone needs a European Health Insurance Card (EHIC) in order to receive free emergency care in EU countries. Information is available on <http://www.dh.gov.uk/travellers>.

4. All their medications (including for an extra week) plus suitable stand-by course of oral antibiotics. Remember to keep some medication in hand luggage in case of delays in airports. DNase will need to be carried in a cool bag.
5. Sunblock is needed if taking ciprofloxacin, doxycycline or voriconazole (and for 4 weeks after course has finished).
6. 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<sup>®</sup> (sodium chloride MR) 600mg (10mmol) tablets; 1 – 3 / day). This is also necessary in very hot weather in the UK.
7. In Europe (except for Cyprus, Gibraltar), the voltage for the nebuliser is not a problem (220v) and a standard travel plug adapter is all that is needed. If travelling to USA, South America, Caribbean, Cyprus, & Gibraltar, you will need a 110v nebuliser e.g. Port-a-Neb. A plug adapter is not enough. Discuss this with our Physiotherapy Department (extension 8088) well in advance of the holiday. A refundable deposit of £50 is required to borrow a nebuliser for a holiday. (A charge may be introduced at a later date).
8. Letter for customs explaining the need for all the drugs and equipment – available in clinic or from the CF secretary (appendix 13). Separate letter available for those with CF related diabetes.
9. Fitness to fly test needs to be considered. This consists of breathing 15% O<sub>2</sub> at sea level which is the equivalent O<sub>2</sub> concentration in the plane at altitude. It should be performed in patients with:
  - a history of oxygen requirement during chest exacerbations.
  - resting oxygen saturation < 94%.
  - FEV<sub>1</sub> < 50% predicted.
  - If on home oxygen, it will definitely be needed on the airplane, but a test can be used to determine flow rate necessary on the plane.

It is arranged with lung function laboratory (extension 8910). Patients who desaturate to less than 85% during the test (or who have baseline FEV<sub>1</sub> < 50% predicted) will need oxygen available during the flight. This is especially important during long haul flights when the children are likely to sleep. Patients whose SpO<sub>2</sub> is normally < 92% will definitely need oxygen, and those usually on home oxygen will need an increased flow rate. Oxygen is usually available at a flow rate 2 or 4 l/min and is not humidified, arrangements can be made through the travel agents, but adequate time is needed to do so. Costs vary between airlines (usually free of charge now). Signing the letter to say a patient is fit to travel must not be undertaken lightly – it is a disaster if a plane has to be diverted if the patient was not fit! If in doubt, check with a consultant.

Different airlines have different charges for providing on-board oxygen and these are available on the Pulmonary Hypertension Association website – [http://www.phassociation.uk.com/living\\_with\\_ph/airline\\_rules\\_on\\_oxygen.php](http://www.phassociation.uk.com/living_with_ph/airline_rules_on_oxygen.php)

Remember that oxygen for the airport itself is not part of the airline's responsibility.

10. Additional advice to drink plenty before & during flights. Chest physiotherapy should not be forgotten during long flights.

11. Check-up in clinic prior to departure may be necessary.

### 10.5 Palliative Care

Death in childhood is a very unusual event amongst our CF population, and tends to happen in the hospital rather than at home. The overriding principal is that the child's comfort and wishes must come first followed closely by those of the immediate family. The management of a dying child needs to be flexible so as to cater for individual family needs and reviewed at least twice daily to accommodate changes in needs. We believe that communication amongst the CF team and ward staff is critical and must be consistent so as not to confuse the family (or the staff).

End of life care will be discussed with the parents by the child's consultant. These discussions, where possible and appropriate, should include the child. We would encourage an honest and open approach at all times, although we would also consider the wishes of the child and his or her family about sharing information. It is important that a child on the transplant waiting list receives appropriate end of life care, and is not disadvantaged by false hopes of a last minute donor organ becoming available.

Children and families should be given a choice as to where their child receives care. This can include staying at the tertiary centre, going to a hospital locally, a hospice or home. Informed discussions about the provisions available (including support and expertise) should be openly discussed with the family.

**Specialist Paediatric Palliative care services** are available to provide symptom management, support advance care planning and end of life care. All services offer a 24-hour telephone advice service for families and professionals:

1. The PATCH (Paediatric Palliative Care) service (based at Royal Marsden Hospital - RMH) Contact: 0208 661-3625 (Mon-Fri daytime) and out of RMH via Switch board (0208 642-6011) and ask operator for the PATCH service.

2. The GOSH palliative care team  
Contact: 020 7829 8678 (Mon- Fri daytime) and out of hours via Switchboard 0207 405 9200 and ask to be put through to the palliative care team

Additionally: The adult Palliative care team (Royal Marsden) provides a specialist adult service at the Brompton. Their service may be more appropriate in the older teenager and young adult population.

### End of life care – the process

Please also refer to the Royal Brompton & Harefield NHS Foundation Trust policy document - "Guidelines for the management of patients and families during death and bereavement"

available on the Trust Intranet; and NICE guidance for End of life care in children and young people.

- An advance care plan including symptom plan, preferred place of care and death, wishes, tissue donation, and emergency resuscitation plan should ideally be in place prior to, or at the start of, the end of life phase, (e.g. Wishes document - [http://www.kidshealth.org.nz/sites/kidshealth/files/images/Child%20%20Family%20Wishes%20advance%20care%20plan\\_v3.pdf](http://www.kidshealth.org.nz/sites/kidshealth/files/images/Child%20%20Family%20Wishes%20advance%20care%20plan_v3.pdf)).
- Clear and open discussions about the appropriateness and need for specific observations, interventions and treatments should be discussed with the family and documented in the medical records for staff. This could include blood sampling and routine basic observations e.g. blood pressure monitoring. Intravenous access is usually unnecessary, since symptoms can often be managed via buccal, transdermal, enteral or subcutaneous routes.
- Regular review by the child's lead Consultant and Specialist nurses should continue and local services and involved professionals should be updated on any changes in the child's condition.
- Some of the medications should be continued, although only those offering symptomatic relief e.g. bronchodilators, enzymes supplements, humidified oxygen. Drugs such as antibiotics, vitamins, calorie supplements may offer no benefit at this stage.
- Gentle physiotherapy may be continued if it is giving symptomatic relief. It is such a way of life for most families that they may wish to continue it so that the child does not feel abandoned. The same may be true for some of the other therapies, so an individualised care plan should be agreed.
- Psychosocial support by the psychosocial team including the CF clinical nurse specialists, family liaison team, psychology, play specialists and chaplaincy team) is offered to the patient with CF and their family. This is closely planned and offered to the family to prevent them feeling overwhelmed with support at such a difficult time.
- Each child and their family have specific cultural and religious needs, these should be sensitively explored. There is a hospital chaplain (020 73528121 Ext 4736), who leads a team of various faith representatives available both for consultation with staff members as well as to the child and their family. The child and families local faith leader is welcomed if preferred by the family.
- Support for RBH staff both formal and informal is offered and all team members are encouraged to participate in treatment (or non-treatment) planning at all times.

**Do-not-resuscitate (DNR)** recommendations (decisions about the level of active resuscitation to be taken) must be discussed with the family (and when appropriate the child as well) by the consultant. Conclusions of the discussion must be documented clearly in the notes.

Please refer to the Royal Brompton & Harefield NHS Trust policy document - "Do not attempt to resuscitation order in children and young people, the policy for the use of advanced statements and policy for the obtaining of consents" available on the Trust Intranet.

Emergency care and resuscitation plans are replacing DNR forms in many services. They provide a more comprehensive and detailed account of the levels of intervention offered to a child experiencing various clinical scenarios.

### Care at home

Should the family have decided to care for their child at home the local Paediatric & community teams will take the lead role in the child's care, with support from specialist palliative care services, and the CF community outreach team. The Specialist palliative care service will help facilitate the transfer of care and support the child and their family in all settings.

### Medication for symptom relief

*'APPM Formulary' provides up to date guidance on medication for children in the palliative care setting in the UK (it is also used throughout the world). This formulary is available free online and is regularly updated. The formulary is written from best evidence and expert advice - [www.appm.org.uk/10.html](http://www.appm.org.uk/10.html).*

*'Prescribing in palliative care' in British National Formulary for Children (BNFc) also provides advice around prescribing and drug doses.*

#### 1. Analgesia

- Paracetamol - oral.
- NSAIDs e.g. Ibuprofen- oral.  
can be given with paracetamol.
- Short acting (immediate release):
  - Morphine: Oromorph (liquid) or Sevredol (tablet)
  - Oxycodone: Oxynorm (liquid or tablet)
  - Fentanyl: Fentanyl buccal or sublingual or intranasal spray

Each drug has a different time to onset of action and clearance. The decision of which opiate to use should be based on the prescriber's experience with the opiate and the preference of the child.

In opiate naïve the child should start on a standard starting dose of an immediate release (IR) preparation. Even if the opiate requirement is determined and a long acting opiate is commenced. The child may still experience breakthrough or incidental pain and require IR doses. The ongoing IR dose is 1/10<sup>th</sup> of the total 24hour background (long acting) opiate. Ensure constipation is avoided by a regular laxative when a child is commenced on Opiates.

- Long acting (modified release) opiates:

Once the opiate requirement has been established the child could start a long acting opiate. The drug of choice will depend on the breakthrough opiate used e.g. Oromorph (breakthrough pain) and MST (long- acting agent) as well as the preferred route and preference of the child.

- Morphine: MST or Zomorph (oral)
- Oxycodone: Oxycontin (oral)

- Fentanyl: Fentanyl patches (topical)
- Buprenorphine: BuTrans patches (topical)
- Opiate (IV/Subcut) infusions (e.g. Morphine, Diamorphine and Oxycodone) may be required especially if rapid pain controlled is required or gut absorption is poor. PCA(Patient controlled analgesia) may also be an effective means of pain control offering both a background Opiate dose and bolus sc/iv doses for breakthrough pain. PCA is offered in the community by both specialist palliative care services.

## 2. Anxiolytic

- Midazolam buccal or lorazepam sublingual for acute anxiety or longer-acting benzodiazepine e.g. Diazepam or Clonazepam may also be effective for frequent or persistent anxiety.
- Midazolam - (IV/Subcut)- Sedating and amnesic effect as well.
- Nozinan (levopromazine) – (Oral /IV/Subcut)

## 3. Anti-emetic

- Cyclizine – (Oral /IV/Subcut)  
May be 1<sup>st</sup> line if central element to nausea. It may also be given as a subcutaneous infusion using the total daily dose over 24 hours.
- Ondansetron – (Oral /IV/Subcut)
- Haloperidol -(Oral /IV/Subcut)
- Domperidone – (Oral)
- Lorazepam S/L for anticipatory nausea/vomiting.
- Nozinan (levomepromazine) – (Oral /IV/Subcut)  
If no response to cyclizine, but useful as can be given subcutaneously, and has additional anxiolytic effect. May cause some sedation as well.
- Dexamethasone may help with nausea.

## 4. Cough

- Low dose long-acting Opiates e.g. Morphine (MST/Zomorph) or Oxycodone (Oxycontin) may relieve intractable cough.

## 5. Dyspnoea

- Humidified oxygen may help.
- Opiates (Morphine/Diamorphine/Oxycodone) may also help with dyspnoea.
- Midazolam buccal for agitation or distress.
- Dexamethasone (Oral /IV/Subcut) may help bronchospasm / airway obstruction.

## 6. Respiratory secretions

- Hyoscine patches can help but a dry mouth is unpleasant, so good mouth care is essential.
- Glycopyrronium(Oral /IV/Subcut) may also be useful.

## 7. Restlessness / confusion / hallucinations

- Haloperidol –(Oral /IV/Subcut)
- Nozinan (Levomepromazine) – (Oral /IV/Subcut)
- Midazolam (buccal) for acute agitation

## 8. Syringe driver mixing and compatibility

See APPM Formulary or BNFC for more details.

### Once the child has died

More information is available on the Bereavement portal on the Trust's intranet

- The family should be given the opportunity to be alone with their child for as long as they want. Alternatively they may require the presence of a member of the CF Team should they wish. It is worth gently encouraging the family to hold their child if they wish.
- The on-call doctor will need to confirm death. This is done by looking for pupil reaction to light, feeling for a central pulse for 1 minute, listening for heart sounds for 1 minute, then listening to breath sounds for 1 minute.
- Inform the on-call consultant immediately unless they are there anyway, which is inevitably the situation.
- Inform the Bereavement team (ext. 2268) indicating that a child has died, giving their name, time of death and patient hospital number and ward.
- A bereavement pack must be given to the family (available on all wards and PALS office). They should also be given the Hospital Trust leaflet entitled 'When Your Child Dies'.
- The doctor will then need to write a medical certificate confirming the cause of death (MCCD) and this book is available on the PICU and Sydney Street reception, or in the PALS office. It is advisable for the doctor completing the MCCD to ensure they have seen the patient after death; this is because it is a compulsory requirement for completing a cremation form. If the death is 'Unexpected' (this is most unlikely with an expected death of a CF patient) then discuss with the on-call consultant. A discussion may be required with the coroner before the medical certificate is written. This discussion should take place in the presence of the bereavement officer.
- The family may wish to take the child home after death, or transfer the child to a children's hospice local to their home. An advantage of the hospice is that the child can stay in a cooled bedroom and parents can visit freely or even stay with their child until the funeral. If going home, particularly during hot weather, it may be necessary for the family to get air cooling units or mattress. A local funeral director will discuss this with the family or the team can contact the local hospice who may be able to provide this equipment. This cannot happen until the MCCD has been completed and handed to the family.
- The doctor or a member of the CF team must phone the GP and local paediatrician as soon as possible and record the time this is done in the notes.
- The CF nurse specialist is responsible for ensuring all members of the CF team at RBH and the local hospital are informed the child has died. The nurse will also ensure Out-patient Administrators are informed so that appointments are no longer sent to the family. Other health and allied services should also be informed.

- During normal working hours, either the paediatric family liaison team and/or the RBH Bereavement Officer (ext. 2268, bleep 7701) will help provide information (including written literature) for the family. The CF CNS and/or family liaison team will be the main contact with the family once the child's body is no longer on the inpatient unit.
- Mandatory reporting. If a death is unexpected contact the local SUDI paediatricians - Dr Paul Hargreaves or Dr Kingi Aminu at Chelsea & Westminster Hospital. Far more likely is that deaths are anticipated, in which case no need to inform them. But we still fill in Initial Notification Forms A & B ensuring the box 'expected' is ticked, and send to the single point of contact.
- Parents will need to make an appointment at Chelsea Old Town Hall (0207 351 3941) to register the death. They will need the death certificate in order to do this. The family will receive their child's 'Death certificate' from the Registrar at the Town Hall.
- They should be given the Hospital Trust leaflet entitled 'When Your Child Dies'.
- If a child has an expected death at home and the parents ring the ward, they must be told to phone their GP or community nurse when they feel able. If it is during the night they may want to wait until morning when the surgery opens. A death certificate will usually only be issued by their own GP or a doctor who has cared for the child during their last illness, the next working day. If they want a funeral director to move the child before a death certificate is issued, they need written confirmation of death from a doctor (usually the duty GP if out-of-hours) or a nurse (trained in confirmation of death). The on-call consultant must be informed immediately.

## After care

### 1. Transport Home of a Child's Body from RBH

A child's body can be removed from the hospital at any time if it is an 'Expected' death and the MCCD has been completed by a doctor who has cared for the patient. The family may wish for the child to go home, to a relative's house or to a hospice. The documentation of death by a doctor is called the 'Medical certificate of Cause of Death (MCCD)'. The 'Death certificate' is the document issued by the Local Registry Office. According to the Child Death Review process all 'Unexpected deaths' should be discussed with the Coroner prior to any discussion or consideration about transfer of the body out of the hospital.

**A parent can take a child's body home.**  
**A hospital MCCD must be given to the family before they leave.**  
**A covering letter from a doctor or another medical member of staff is required.**  
**The exception to this is if the child is travelling outside England or Wales where the Coroner must provide an Out of England Certificate prior to travel.**

The family may wish to move the child themselves. If so:

1. Ensure they are given the MCCD.
2. Give them a letter (written by a doctor or nurse) stating



- a. Date
  - b. Child's name, date of birth and that the child has died
  - c. Address they are travelling from
  - d. Address they are travelling to
  - e. Contact details of the doctor or nurse in the case the family are stopped on route by police.
3. Legally, a body must be transported "in a suitable container". We interpret this as meaning that children must be safely secured in a car seat, as they would be if alive (to prevent injury to other passengers in a collision)

If parents want the child to go home or to a hospice, but are unable to transport the child themselves, there are several options:

1. Contact a funeral director (either local to the family or local to the hospital). They will be able to arrange transfer of the child and can usually act fairly quickly. Normally parents bear the cost of transport of their child's body as part of the bill for the funeral, if a Funeral Director is used.
2. The hospice may be able to advise on a local funeral directors
3. The family may have a friend/relative who can help
4. See if hospital transport can assist
5. NB. London Ambulance Service DOES NOT perform this service

## 2. Bereavement support

- Parents will be invited (by letter) to come back to discuss any issues with a consultant 4-6 weeks after the child's death.
- Bereavement counselling is available to families at the Brompton or we can help the family to try to access support in the community. There are various on line support forums/sites including:
  - [www.childbereavementuk.org](http://www.childbereavementuk.org)
  - [www.togetherforshortlives.org.uk/families/familys\\_journey/bereavement\\_support](http://www.togetherforshortlives.org.uk/families/familys_journey/bereavement_support)
  - [www.cruse.org.uk](http://www.cruse.org.uk)
- The CF team should signpost the family to local bereavement services. This can be supported by the specialist palliative care team.
- Another invitation given routinely is to the hospital commemorative ceremony for children who have died. This is an annual event (late Oct/early Nov), comprised of words and music, open to those of any or no religion. Although the hospital chaplaincy and other religious leaders attend, there is no overt religious content. Parents chose music their child loved, or a reading, or ask for a poem they have themselves written. The reading may be given by the parents themselves, by a sibling or a friend or staff member. A brief talk is given by a senior member of staff, and a brief closing ceremony such as the release of balloons ends the occasion. Refreshments are served.
- Staff 'debrief' meetings, facilitated by representatives from the paediatric clinical psychology team, are offered to all involved. Additional support is offered to staff as requested.

## 11. Drug Formulary

### 11.1 DRUGS FOR THE RESPIRATORY TRACT

In CF, doses of antibiotics are usually given at a higher dose and for a longer period than in non-CF children, for reasons of pharmacokinetic differences as well as the presence of underlying lung disease. See section 6.2a for antibiotic prescribing policies.

NOTE: **od** = once daily; **bd** = twice daily; **tds** = 3 times daily; **qds** = 4 times daily

#### 11.1a ORAL ANTIBIOTICS - PROPHYLACTIC DOSES

##### Oral

Azithromycin	Oral	<15kg: 10mg/kg od  15-40 kg: 250mg od  >40kg: 500mg od	<b>Consultant decision.</b>	Potential for hepato- and ototoxicity but usually <i>very</i> well tolerated. Can cause tooth and tongue discolouration. For anti-inflammatory effect see section 11.1f other respiratory treatments.
Co-amoxiclav <b>400/57</b> (Augmentin duo)	Oral Susp	2 months – 2 yrs: 0.15 ml/kg bd;  2-6 yrs: 2.5 ml bd  7-12 yrs: 5 ml bd	Use if flucloxacillin not tolerated or regularly grows <i>H influenzae</i> . Tastes better than flucloxacillin but may discolour teeth.	
Co-amoxiclav <b>125/31</b>	Oral Susp	<1 yr: 0.25ml/kg (max 5ml) bd	<b>Clean teeth after dose</b>	
Co-amoxiclav <b>250/62</b>	Oral Susp	1-<6 yrs: 2.5ml bd 6-12 yrs: 5ml bd		
Co-amoxiclav 250/125	Oral tabs	>6 yrs: 1x (375 mg) tab bd		
Flucloxacillin	Oral	3-5kg: 125mg bd  5-9kg: 175mg bd  9-15kg: 250mg bd  Older children: 25 mg/kg bd (usual max 1 gm bd)	Give 1 hour BEFORE meals or on an empty stomach. Liquid tastes awful – different brands may be tolerated better than others.	If <i>S aureus</i> a troublesome, regular problem can use up to 2 g bd – <b>Consultant decision.</b>

**11.1b ORAL ANTIBIOTICS – TREATMENT DOSES**

See section 6.2a for antibiotic prescribing policies. Decision depends on:

- Current clinical state.
- Current and past organisms and their antibiotic sensitivities.
- Past history of individual.
- Known ‘allergies’ or intolerance.

Azithromycin	Oral	10 mg/kg od max 500 mg  NOTE dose differs from prophylactic and long term use	<i>S aureus</i> , <i>H influenzae</i> and <i>mycoplasma</i>	For anti-inflammatory effect see section 11.1f other respiratory treatments.	Ten days gives about 1 month's coverage.
Chloramphenicol	Oral	>1 month: 12.5 mg/kg qds.  Occasionally use 25 mg/kg qds (Max 4 gms/day).	Consider with <i>S maltophilia</i> , <i>P aeruginosa</i> , <i>B cepacia</i> , <i>S aureus</i> and desperation.	Needs full blood count at day 21 if course longer than 3 weeks.  Very expensive (£450 - £1700 per two week course)  Preferably round dose to the nearest whole capsule. Capsules can be opened and the contents mixed with water or orange juice and given immediately.	2-3 weeks

Ciprofloxacin	Oral	<p>&lt;1 month: 15 mg/kg bd</p> <p>≥1 month: 20 mg/kg bd (max 750mg) bd.</p> <p>Care should be taken if previously used within previous 3 months because of risks of resistance.</p>	<p><b>First line</b> oral antipseudomonal agent. Photosensitising so warn patient re sunlight. High strength sunblock should be used in summer or on holidays for 4 weeks after course finished. Joint pains occasionally – risk of tendonitis and tendon rupture – consider withdrawing treatment. <b>Milk will</b> reduce absorption. Avoid milk for at least 30 mins before and after taking ciprofloxacin.</p>	<p><b>3 weeks for 1<sup>st</sup> isolation.</b></p> <p><i>Consultant decision</i> to exceed this period.</p> <p>Also used for NTM treatment – <i>consultant decision</i>. See appendix 2.</p>	
Clarithromycin	Oral	<p>&lt;8 kg - 7.5mg/kg bd</p> <p>8 – 11kg – 62.5 mg bd</p> <p>12 – 19kg – 125 mg bd</p> <p>20 – 29kg – 187.5 mg bd</p> <p>30 – 40kg – 250 mg bd</p> <p>(if &gt;12 years old can increase to 500mg bd if necessary)</p>	<p>Cheaper alternative to azithromycin. Can cause tooth and tongue discolouration. Part of NTM protocol.</p>	<p>One month</p> <p>Care needed as interacts with some drugs e.g. itraconazole, rifabutin – check BNFc</p>	

Clofazamine	Oral	1-2 mg/kg (max 100mg) od	<i>Consultant decision</i> – reserved for the treatment of NTM. See appendix 2.	<p>Take with or just after food.</p> <p>May cause a discoloration of the skin from red to brownish-black, as well as red staining of sweat, sputum urine, faeces, tears and saliva.</p> <p>Patient/carer should be advised that skin discoloration, although reversible, may take several months or years to disappear after the stopping therapy.</p> <p>Advise patient/carer to seek medical advice if persistent abdominal symptoms develop (pain, diarrhoea, nausea, vomiting).</p>	See appendix 2.
Co-amoxiclav <b>400/57</b> (Augmentin-Duo)	Oral susp	2 months – 2 yrs: 0.3 ml/kg bd; 2-6 yrs: 5 ml bd 7-12 yrs: 10 ml bd	For <i>S aureus</i> and <i>H influenzae</i>  Care with CF liver disease	Co-amoxiclav 625mg tabs are to be used in preference to 2 x 375mg tabs to reduce clavulanic acid intake.	One month
Co-amoxiclav <b>250/62</b>	Oral Susp	1-<6 yrs: 5ml tds 6-12 yrs: 10ml tds			
Co-amoxiclav <b>500/125</b>	Oral tablets	>6 yrs: (625mg tabs) 1 tab TDS			
Co-trimoxazole	Oral	6 weeks–5 months: 120 mg bd 6 months–5 years: 240 mg bd 6–11 years: 480 mg bd 12–18 years: 960 mg bd		Use mainly for <i>S maltophilia</i> & MRSA. Maintain adequate fluid intake Treatment should be stopped if blood disorders or rashes develop. Advise patient/carer to report all rashes, sore throats and fevers. Avoid in severe liver disease.	One month

Doxycycline	Oral	>12 years: 200 mg <b>once daily</b> on day 1 then 100 mg once daily thereafter (can increase to 200 mg daily if required).	Can be useful for <i>S maltophilia</i> and <i>B cepacia</i> , and MRSA <b>Consultant decision.</b>	Patient <b>MUST</b> be > 12 years (due to discoloration of growing teeth and bone). Take standing or sitting upright with 200 ml water (to avoid oesophageal irritation). Photosensitivity (see ciprofloxacin).	2-4 weeks (can be used long term)
Ethambutol	Oral	15mg/kg od (max 1.5g od)		<i>Consultant decision</i> – reserved for the treatment of NTM. See appendix 2.  Monitoring - Visual acuity & colour vision, peripheral neuropathy. Advise patients to report visual changes if possible.	
Flucloxacillin	Oral	30-35 mg/kg TDS  MAX 4 gms/day	Give 1 hour <b>BEFORE</b> meals or on an empty stomach. Liquid tastes awful – different brands may be tolerated better than others.		One month
Fusidic acid	Oral	<1 yr: 15mg/kg tds  1-4 yrs: 250 mg tds (5 ml)  5-12 yrs: 500 mg tds (10 mls)  > 12 yrs: 750 mg tds (15mls) <b>or</b> 500mg sodium fusidate tablets tds		See rifampicin. Caution in CF liver disease. Liquid should be taken with or after food Should always be prescribed with additional anti-staphylococcal agent Higher dose of fusidic acid liquid needed as incomplete absorption compared to sodium fusidate tablets.	Two weeks

Linezolid	Oral	<12 yrs: 10mg/kg (max 600mg) <b>tds</b> .  ≥12 yrs: 600 mg bd	Last line for <i>MRSA</i> or <i>S aureus</i> where patients have not responded to conventional agents e.g. high dose flucloxacillin, rifampicin, fusidic acid.  Occasionally used for NTM, consider use of pyridoxine (B <sub>6</sub> ) to reduce risk of cytopenias. See appendix 2.  <b>Consultant decision.</b> Courses >28 days leads to risk of optic neuropathy so patients having 4 week or repeated courses should have ophthalmic exam before starting first course and every 2 months after. Aim for 2 week courses. Where possible patients should be warned to immediately report any visual changes, regardless of treatment duration.  Monitor FBC weekly.		Two weeks
Minocycline	Oral	>12 yrs: 100mg <b>bd</b>	Can be useful for <i>S maltophilia</i> . <b>Consultant decision.</b>	Patient <b>MUST</b> be > 12 years (due to discoloration of growing teeth and bone). Caution in CF liver disease. Take standing or sitting upright with plenty of water (see doxycycline).	Two weeks
Moxifloxacin	Oral	7.5 – 10mg/kg (max 400mg) od	<i>Consultant decision</i> – reserved for the treatment of NTM. See appendix 2.  <b>Not</b> active against <i>P. aeruginosa</i> or <i>MRSA</i>	Has been associated with QT interval prolongation. The manufacturer advises should not be used concurrently with other drugs that prolong the QT interval: risks and benefits must be considered if this is deemed necessary.  Caution in CF liver disease.	See appendix 2.

Rifampicin	Oral	<p><i>S aureus</i> treatment: 10 mg/kg (max 600mg) bd.</p> <p>NTM treatment: 10 - 20 mg/kg (max 600mg) <b>od.</b></p>	<p>Second line for <i>S aureus</i>. Usually give with fusidic acid.</p> <p>Occasionally used for NTM. See appendix 2.</p>	<p>Give 30 – 60 minutes <b>before</b> food. <b>Consultant decision.</b> Caution in CF liver disease.</p> <p>Please note rifampicin interacts with many drugs (including itraconazole, voriconazole, posaconazole, chloramphenicol) so always check in BNFc.</p> <p>Check re oral contraceptive interactions.</p> <p>Can cause red staining of urine, tears and saliva.</p>	<p>Two weeks</p> <p>See appendix 2.</p>
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### 11.1c INHALED ANTIBIOTICS

See NHSE Clinical Commissioning Policy for inhaled therapy first published Dec 2014.

<https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/01/a01-policy-inhld-therapy-cf.pdf>

Amikacin (from IV solution)	Nebulised	6-12 years: 250mg bd (add 2ml 0.9% saline to 1ml of 250mg/ml amikacin).  >12 years: 500mg bd (add 1ml 0.9% saline to 2ml of 250mg/ml amikacin).	Usually for NTM. See appendix 2.	Can further dilute injection with 0.9% sodium chloride.  Suitable for jet nebuliser. Can use e- flow rapid but might be slow. Can't use I- neb. Avoid using ear bud headphones for increased risk of hearing problems.
Amphotericin (Fungizone)	Nebulised	<10 years: 5 mg bd  >10 years: 10 mg bd  Dilution: 50 mg in 10ml of water. For a 5 mg dose, use 1ml of this solution and dilute further with 2ml of water (minimum volume of 3ml for nebulisation).	For chronic aspergillus.	<b>Consultant decision.</b> Use 1 vial per day, keep remaining solution in the fridge. No need to use expensive liposomal preparation unless cannot tolerate standard preparation which tastes awful.  Only suitable for Jet nebuliser. Can't use e- flow or I-neb.
Aztreonam Lysine (Cayston)	Nebulised	75 mg tds during alternate months  Mix with 1ml 0.17% saline (diluent comes with drug).  Licensed >6 years Not commissioned for continuous use (only for alternate month).	3 <sup>rd</sup> line for chronic <i>P aeruginosa</i> .  Doses should be taken at least 4 hours apart.  Pre dose with bronchodilator	<b>Consultant decision.</b>  Colistin or tobramycin usually given during the intervening month  Should ideally be stored 2-8°C. but can be kept out of the fridge, but below 25°C, for up to 28 days.  Used via e-flow but must use special Altera handset which nebulises to dry.

Ceftazidime	Nebulised	1 gm bd Reconstitute 1 gram injection with 3ml water for injection	For <i>B cepacia</i> . Tastes awful.	<b>Consultant decision</b> Only suitable for Jet nebuliser. Can't use e-flow or I-neb.
Colomycin® (Colistin)	Nebulised	<8 yrs: 1,000,000 Units bd >8 yrs: 2,000,000 Units bd  Mix with 3ml 0.9% saline.  1,000,000 units = 1 megaunit (Mu)	1 <sup>st</sup> line for chronic <i>P aeruginosa</i> .  Bronchospasm can be reduced by i) pre-dose with bronchodilator. and ii) diluting with salbutamol.	Nebulise in Jet nebuliser or e-flow. <b>Not</b> I-neb.
Promixin® (Colistin)	Nebulised via I-Neb	< 8 years: 500,000 units bd >8 years: 1,000,000 units bd		I-neb only. Use Grey I-neb Chamber.  For 500,000 unit doses: the reconstituted solution may be kept for up to 24 hours in the fridge.
Colobreathe® turbospin (Colistin)	Inhaled (dry powder inhaler)	1 capsule (1.66 MU) bd via Turbospin powder inhaler  Licensed >6 years only	Doses should be inhaled as close as possible to 12 hours apart.	Put fat end of capsule into inhaler first to minimise capsule shattering when capsule is pierced.
Meropenem (from IV solution)	Nebulised	6-12 years: 125mg bd >12 years: 250mg bd	Usually for NTM. See appendix 2.  Also used for <i>B cepacia</i> chronic therapy.	Reconstitute 500mg vial with 10ml 0.9% sodium chloride (keep remainder of vial in fridge for up to 18 hours).  For a 250mg dose: use 5mls of reconstituted solution. For a 125mg dose: use 2.5mls of reconstituted solution and add 0.5mls of 0.9% saline  Nebulise in e-flow or Jet nebuliser.

Tobramycin – Bramitob® or TOBI®	Nebulised	300 mg bd during <b>ALTERNATE MONTHS</b>  Licensed >6 years only	1 <sup>st</sup> line for eradication of <i>P aeruginosa</i> .  2 <sup>nd</sup> line for chronic <i>P aeruginosa</i> .	<p><b>Consultant decision.</b></p> <p>Colistin will usually be given in the month off tobramycin.</p> <p>Use Jet nebuliser, E-flow or I-neb (lilac chamber); TOBI® &amp; Bramitob® need to be nebulised twice if given via an I-neb (lilac chamber).</p> <p>After removal from refrigerator, TOBI® pouches (intact or opened) may be stored at up to 25°C for up to 28 days.</p> <p>In our experience Bramitob® tends to be better tolerated in pre-school children and best given via a jet nebuliser.</p> <p>After removal from refrigerator, Bramitob® pouches (intact or opened) may be stored at up to 25°C for up to 3 months.</p>
Tobramycin – TOBI Podhaler®	Inhaled (dry powder inhaler)	112mg (4 x 28mg capsules) bd via podhaler during  <b>ALTERNATE MONTHS</b>  Licensed >6 years only		Doses should be inhaled as close as possible to 12 hours apart and not less than 6 hours.
Vancomycin	Nebulised	4mg/kg (maximum 200mg) qds for 5 days for eradication  May be used bd for chronic suppression.  <i>Consultant decision</i>	MRSA	<p>Reconstitute according to manufacturer's instruction (take into account displacement volume). Draw up required dose and make up to a total of 4ml with sodium chloride 0.9%.</p> <p>Use jet nebuliser. Pre-dose with nebulised salbutamol.</p>

## 11.1d INTRAVENOUS ANTIBIOTICS

See section 6.2a for antibiotic prescribing policies. Decision depends on:

- Current and past organisms and their antibiotic sensitivities.
- Past history of the individual patient.
- Known 'allergies' or intolerance.

### NOTE

- i) Two antipseudomonal antibiotics from different classes are ALWAYS given – consultants only for exceptions.
- ii) High dose flucloxacillin is no longer used accompanying IVABs but we add in IV teicoplanin if *S aureus* has been grown in the past year.
- iii) Preferred *blind* starting combination is meropenem (better Staph cover) or ceftazidime (or aztreonam) **plus** tobramycin (gentamicin is never used due to increased renal toxicity and less favourable MIC).
- iv) Course length is **always** a minimum two weeks.
- v) Take care with first doses as unexpected, severe hypersensitivity does occur.
- vi) Antibiotics can impair liver and renal function. Take care with drug dosing with underlying impairment – refer to BNFC or the pharmacy team for more information.

### CIVAS (Centralised Intravenous Additives Service)

CIVAS is now outsourced to an external provider so we no longer use banding tables to round off doses.

Since most patients come in for admission during the daytime, the dose for that night and the next morning is made up by the nurses in the usual way on the ward. Admissions from Friday daytime, Saturday & Sunday (and bank holidays) will receive drugs made up on the ward until evening of next midweek working day.

Amikacin	IV	30 mg/kg od (max 1.5g od)	Infuse over 30 mins. Levels at 23 hours after 1 <sup>st</sup> dose (ie <b>before</b> 2 <sup>nd</sup> dose) must be < 3mg/l. Repeat at least every 7 days. If level raised, OMIT next dose and re-measure, reduce dose by 20%. See section 6.2a	Aminoglycoside	Only use if resistant to tobramycin or gentamicin. Dilution: 0.9% sodium chloride.  Used for initiation of NTM treatment – <i>consultant decision</i>  Audiology at baseline.
Aztreonam	IV	50 mg/kg tds (Max 2 gms tds).	No gram-positive activity.	Monobactam	Usual reconstitution: water for injections.
Cefoxitin	IV	50mg/kg tds (Max 12g /day).	Can give as a slow bolus or infusion over 30 minutes.	Cephalosporin	Reserved for treatment of NTM – <i>consultant decision</i> . See appendix 2.  NOT active against <i>P aeruginosa</i> .
Ceftazidime	IV	50 mg/kg tds (Max 9 gms /day).	Unexpected hypersensitivity on first exposure.	Cephalosporin	Usual reconstitution: water for injections.
Colistin	IV	20,000-25,000 units/kg <b>tds</b> .  <b>Long term use at home:</b> Use above total daily dose divided into 2 doses i.e. (30,000-38,000 units/kg <b>bd</b> )	Slow infusion over 30 mins. Max concentration is 40,000 units/ml.  Boluses can be used for <b>Portacaths</b> only – not PICC lines. <12 yrs: dilute to 90,000 units/ml. ≥12 yrs: dilute to 200,000 units/ml.  Measure renal function once a week.	Polymyxin	Not a first line agent. <b>Avoid using with IV amphotericin</b> (renal toxicity).  Usual reconstitution: 0.9% sodium chloride

Co-trimoxazole	IV	>6 weeks old: 60 mg/kg BD  (no upper dose limit)	Infuse over 60-90 minutes.		Useful for <i>A xylosoxidans</i> & <i>S maltophilia</i> – <i>consultant decision</i>  Maintain adequate fluid intake.  Treatment should be stopped if blood disorders or rashes develop. Advise patient/carer to report all rashes, sore throats and fevers. Avoid in severe liver disease.
Linezolid	IV	<12 years: 10mg/kg  (max 600mg) tds  ≥12 years: 600mg bd	Infuse over 30 – 120 mins. Monitor FBC weekly. <b><i>Consultant decision only as courses &gt;28 days leads to risk of optic neuropathy so patients having alternate monthly Linezolid should have ophthalmic exam before starting first course and every 2 months after.</i></b> Where possible patients should be warned to immediately report any visual changes, regardless of treatment duration.	Oxazolidinone	Use oral route wherever possible. Otherwise convert to oral route as soon as clinically indicated. Last line for <i>MRSA</i> or <i>S aureus</i> where patients have not responded to conventional agents.
Meropenem	IV	20 – 40 mg/kg tds.  (Max 2g tds)	Headache common.	Carbapenem	Usual dilution: water for injections.
Piperacillin / Tazobactam	IV	>1 month: 90mg/kg qds  (Max 4.5g qds)		Ureidopenicillin	<b><i>Consultant decision.</i></b> Not used unless we are desperate due to rashes and hypersensitivity.

Teicoplanin	IV	>1 month 10mg/kg (max 400 mg) 12 hourly for 3 doses (loading dose)  followed 24 hours later by 10mg/kg (max 400 mg) od.	Can give as a slow bolus or infusion over 30 minutes	Glycopeptide	<i>Consultant decision</i>
Temocillin	IV	25mg/kg bd  (Max dose 2g bd)	Slow bolus over 3 – 5 minutes	Penicillin	<i>Consultant decision.</i> 3 <sup>rd</sup> line Dilution: water
Tigecycline	IV	8 – 11 years: 1.2mg/kg (max 50mg) bd  ≥12 years: 100mg loading dose then 50mg bd, reduced to 50mg od if not tolerated	Infusion over 60 minutes.  Nausea/vomiting a real problem. Use regular oral Ondansetron – ensure that patient receives anti-emetics <b>before</b> commencing treatment.	Tetracycline	Before using in children <12 years old, please confirm with dental professional all 'adult' teeth in place (due to discolouration of growing teeth/bone).  Reserved for treatment of NTM. See appendix 2. <i>consultant decision.</i>
Tobramycin	IV	10mg/kg/day in ONE DOSE  (Max 660mg/day)  If previous course had raised trough level reduce dose by 20%	Infuse over 30 mins. Levels at 23 hours after 1 <sup>st</sup> dose (ie <b>before</b> 2 <sup>nd</sup> dose) must be <1 mg/l) Repeat at least every 7 days. If level raised, OMIT next dose and re-measure. See section 6.2a	Aminoglycoside	Usual dilution: 0.9% sodium chloride.  <b>DO NOT PRESCRIBE THIS DOSE FOR NON-CF CHILDREN.</b>

We RARELY use:

- i) Imipenem - too many side effects and spectrum no different from meropenem.
- ii) Piperacillin/tazobactam (Tazocin®, piptazobactam) is rarely used because there is a high incidence of allergy.



**11.1e ANTIFUNGAL ANTIBIOTICS**

Itraconazole	Oral	<p>1month – 12 yrs: 5 mg/kg twice daily</p> <p>(max 200mg bd)</p> <p>&gt;12yrs 200 mg twice daily</p>	<p>Must be used when treating ABPA with steroids, when taking steroids for whatever reason if aspergillus isolated, and for symptomatic aspergillus infection. See section 6.9.</p> <p>Poorly absorbed, use liquid, on empty stomach if possible. Capsules should be taken with acidic liquid e.g. <b>coca-cola</b> and <b>food</b>. Stop antacids if possible.</p> <p>Headaches seem commonest problem but in theory hepatotoxic. Adrenal suppression also been seen when combined with budesonide. Do liver function tests if taken for longer than 1 month or if known liver dysfunction.</p> <p>Note interaction with rifampicin.</p>	See <b>section 6.9</b> for length of courses.
Terbinafine	Oral	<p>10 – 19kg: 62.5mg od</p> <p>20 – 39kg: 125mg od</p> <p>40kg +: 250mg od</p>	<p>For use in combination with an azole antifungal for <i>Lomentospora prolificans</i>. Consultant decision.</p> <p>Monitor liver function tests and FBC monthly when given in combination with an azole.</p>	

Posaconazole	Oral suspension	<p>&gt;8 years: 400mg BD</p> <p>Monitor levels.</p> <p>Monitor liver function tests monthly.</p>	<p>2<sup>nd</sup> line for Aspergillus/ABPA where patients have not responded to or are intolerant of itraconazole. <b>Consultant decision (not licensed in &lt;18 years old).</b></p> <p><b>The tablet and oral suspension are not to be used interchangeably due to the differences in the dosing of each formulation.</b> Tablets should be used preferentially as in our experience more consistent levels are obtained.</p>	See section 6.9 for length of courses.
	Oral tablets	<p>&gt;8 years: 300mg BD on day 1, then 300mg OD thereafter</p> <p>Monitor levels.</p> <p>Monitor liver function tests monthly.</p>	<p><b>Suspension</b> should be taken immediately following a meal (preferably fatty meal) to enhance absorption. If this is not possible, may need to use 200mg QDS dosing. <b>Tablets</b> can be taken with or without a meal.</p> <p>Levels should be monitored on initiation, on amendment of dosage, if an interacting drug is commenced or efficacy is not observed. Pre-dose samples (if not possible then a random sample) taken after at least 1 week on therapy. Aim: 1 - 5mg/L For levels &gt;5mg/L review dose with consultant and pharmacist.</p> <p>Note interaction with rifampicin. Levels <b>when using suspension</b> reduced by ranitidine and proton pump inhibitors which should be stopped if possible.</p>	

Voriconazole	Oral	<b>2 – 11 years:</b> 9mg/kg (max 350mg) bd (Liquid preferred)	May be used for ABPA (3 <sup>rd</sup> line) where patients have not responded to or are intolerant of itraconazole or posaconazole. <b>Consultant decision.</b> See section 6.9.  Take on an empty stomach.	See <b>section 6.9</b> for length of courses
		<b>12 - 14 years:</b> <50kg 9mg/kg (max 350mg) bd  >50kg 400mg bd for 2 doses then 200mg bd (max 300mg bd).	<b>Highly photosensitising</b> so warn patient re sunlight. High strength sunblock should be used in summer or on holidays for 4 weeks after course finished. Refer to dermatologist if photosensitivity reaction occurs. Risk of squamous cell carcinoma of the skin has been reported in long term use in patients with photosensitivity and other risk factors.	
		<b>15 years +:</b> <40kg: 200mg bd for 2 doses then 100mg bd (max 150mg bd)  >40kg: 400mg bd for 2 doses then 200mg bd (max 300mg bd).	Adrenal suppression has been reported in patients also taking inhaled corticosteroids.  Levels should be monitored on initiation, on amendment of dosage, if an interacting drug is commenced or efficacy is not observed. Pre-dose samples taken after at least 3 days on therapy. Aim: 1.3 - 5.7mg/L  Monitor liver function tests + U&E's weekly for first month then monthly thereafter.	
Liposomal amphotericin (Ambisome)	IV	5 mg/kg od  Start at 1 mg/kg once daily then increase to 5 mg/kg od over 3 days.  Give test <b>dose</b> of 100 mcg/kg (max 1mg) over 10 mins. Observe for 30 mins then continue Treatment.	For invasive or troublesome aspergillus. Check <b>renal/liver function and U&amp;Es at least 3/week. Use with caution with other nephrotoxic antibiotics</b> e.g. aminoglycosides, colistin.  We DO NOT use the standard amphotericin preparation (fungizone) for IV use.	<b>Consultant decision.</b> Administer over 30 mins. Compatible with 5% Dextrose only. Flush pre & post dose with 5% dextrose. Final concentration of the solution should be 0.2 – 2 mg/ml.

Caspofungin	IV	<p>&lt;3 months: 25 mg/m<sup>2</sup> od</p> <p>3months - 1yr: 50 mg/m<sup>2</sup> od</p> <p>&gt;1 yr: 70 mg/m<sup>2</sup> (max 70mg) on day 1 then 50 mg/m<sup>2</sup> (max 70mg) od.</p> <p>This can be increased to 70 mg/m<sup>2</sup> (max 70mg) od if lower dose is tolerated but inadequate response</p>	<p>For invasive or troublesome aspergillosis.</p> <p>Reduce dose in liver impairment (see BNFc).</p>	<p><b>Consultant decision.</b></p> <p>Infuse over 60 mins.</p> <p>Dilute to concentration not exceeding 500 mcg/ml with 0.9% sodium chloride.</p> <p>Incompatible with glucose solutions.</p>
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**11.1f OTHER RESPIRATORY TREATMENTS**

Aminophylline	IV	<b>Load:</b> 5mg/kg (max 500mg) over at least 20 minutes, then –  <b>IV infusion:</b> <12 years: 1mg/kg/hour  >12 years: 0.5 – 0.7mg/kg/hour	<b>Consultant decision</b>	Do not use loading dose if already receiving oral theophylline or aminophylline.  Measure levels 4- 6 hours after starting infusion, and daily thereafter. Do not exceed 20mg/l.  Care needed as interacts with some drugs e.g. clarithromycin, erythromycin, fluconazole, ciprofloxacin – check BNFc
Azithromycin  (see 11.1a & 11.1b for standard antibiotic doses)	Oral	<15kg: 10mg/kg od 3/week  15-40 kg: 250 mg od 3/week  >40kg: 500 mg od 3/week  Mon/Wed/Fri	Potential long-term treatment as anti- inflammatory. <b>Consultant decision</b>	<i>Potential</i> for hepato- and ototoxicity but usually <i>very</i> well tolerated.  <b>Avoid</b> long term concurrent use with erythromycin
DNase (Dornase alpha)  Homecare delivery	Nebulised	2.5 mg once daily  Consideration of alternate day after 6 months if well or treatment burden an issue.	In afternoon, usually at least 30 mins pre- physiotherapy.  See section 6.4 for more details of variation of timing.	Occasionally use twice daily - <b>consultant            decision.</b>
Hypertonic saline 3 or 7%	Nebulised	4 mls up to twice a day  Immediately before or during physiotherapy.	Pre-treat with bronchodilator. (see section 6.5).	

Ivacaftor	Oral	<p>2 years and above : &lt;14kg: 50mg granules bd</p> <p>≥14kg - &lt;25kg: 75mg granules bd</p> <p>≥25kg: 150mg tablet bd</p>	<p>For children with one of the following gating mutations- G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R.</p> <p>-Liver function tests 3 monthly for 1<sup>st</sup> year then yearly (annual review).</p> <p>-Sweat chloride 6-8 weeks after starting, at 6 months, then annually.</p> <p>-Eye exams before starting then annually in &lt;12 yr olds.</p> <p>-Stool elastase in 2-5 yr olds pre- and 6 months after starting.</p>	<p>Take with fat containing food.</p> <p>Avoid food containing grapefruit or Seville oranges.</p> <p>See section 6.8 for specific drug interactions.</p> <p>Always check for interactions when initiating treatment with Ivacaftor or whenever new medicines are prescribed. Refer to the paediatric pharmacy team for information.</p>
Mannitol	Inhaled	<p>Initiation dose assessment: see details in Summary of Product Characteristics on <a href="http://www.medicines.org.uk">www.medicines.org.uk</a></p> <p>Therapeutic dose regimen: 400mg (10 x 40mg capsules) bd via inhaler supplied</p> <p>Licensed for &gt;18 years only</p>	<p><b>Consultant decision</b></p> <p>Not currently commissioned for use in children, and funding should be sought before initiation of treatment.</p>	<p>Doses should be taken morning and evening with evening dose taken 2 – 3 hours before bedtime.</p>
N-acetylcysteine (NAC)	Oral	<p>&lt; 12 years: 300mg BD</p> <p>≥12 years: 600mg BD</p>	<p>Given for the duration of the IV aminoglycoside course. For the prevention of ototoxicity in patients receiving IV aminoglycosides as part of NTM treatment and 3-monthly IV's only.</p>	<p>600mg tablets (unlicensed brand ACC® from Hexal) are scored and halve easily and for children unable to take a tablet they disperse in a small amount of water.</p>

## 11.2 DRUGS FOR THE GASTROINTESTINAL TRACT

### 11.2a Pancreatic Enzymes

- Get to know one preparation properly. This clinic uses **Creon Micro (for infants) or Creon 10,000** for all children except under exceptional circumstances. See section 7.2 on PERT.
- Both creon preparations are porcine (pig) origin.
- Dose for a child established on pancreatic enzymes is *approximately* 1 capsule per 3-5 grams of fat.
- In babies, start with ½ scoop per feed (average fat content of 150ml standard infant milk is 5g) mixed with small amount of expressed breast milk, infant formula or apple puree\*, just before feeds and increase in half scoop steps (quarters is too fiddly). Do not put Creon granules into the bottle.
- Enzymes may not be chewed or *mixed into* food, do not mix into hot foods
  - Dose should not exceed 10,000 units/kg/day of lipase without considering why needed.

Creon Micro	=	5,000 units of lipase per scoop
Pancorex V powder	=	25,000 units of lipase per gram
Creon 10,000	=	10,000 units of lipase per capsule
Creon 25,000	=	25,000 units of lipase per capsule

**\*NOTE:** At RBH we use apple puree to provide enzymes from birth as the puree keeps the enterically coated enzyme spheres in a suspension. This ensures that the child takes in the entire dose, and minimizes the chance of gum breakdown caused by trapped enterically coated spheres in the mouth. If apple is not available, other fruit purees may be used. If apple purees for enzyme administration are introduced from birth, they must be done so carefully as it contradicts the WHO and Department of Health recommendations on the age that solids should be introduced to infants.

**Patient/Parent/Carer advice available at -**

**<http://www.medicinesforchildren.org.uk/pancreatin-pancreatic-insufficiency>**

### 11.2b Fat soluble vitamins

Empirically, the aim is to have plasma levels of vitamins A and E at upper limit of normal range. Daily recommendations from the CF Trust Nutrition Working Party are:

Age	Vitamin A <i>1 mcg = 3.3 IU</i>	Vitamin D <i>1 mcg = 40 IU</i>	Vitamin E <i>1mg = 1.5 IU</i>
< 1 Year	1200 mcg (4000 IU)	10 mcg (400 IU)	10 - 50 mg
> 1 Year	1200 - 3000 mcg (4000 - 10,000 IU)	10 - 20 mcg (400 - 800 IU)	50 - 100 mg
Adults	1200 - 3000 mcg (4000 - 10,000 IU)	20 - 50 mcg (800 - 2000 IU)	100-200 mg

**Preparations:**

- **DEKAs<sup>®</sup> Plus** are a brand of all-in-one multivitamins designed for people with CF. 1ml of Paediatric Liquid contains 1,725 mcg of Vitamin A, 750 units of vitamin D, 33.6mg Vitamin E, and 0.5mg of Vitamin K. One Softgel or one chewable tablet contains 5505mcg of Vitamin A, 3000 units of vitamin D (2000 units in chewable tab), 101mg Vitamin E (67 mg in chewable tab), and 1mg of Vitamin K. All contain a number of other vitamins and trace elements, and have the advantage of containing both vitamin E and vitamin K.
- **AquADEKs<sup>™</sup>** are a brand of all-in-one multivitamins designed for people with CF but currently unavailable. 1ml of Paediatric Liquid contains 1,743 mcg of Vitamin A, 10mcg of vitamin D, 48mg Vitamin E, and 0.4mg of Vitamin K. **One Softgel or two chewable tablets** contains 5505mcg of Vitamin A, 20mcg of vitamin D, 180mg (softgel)/97mg (chewable tablets) Vitamin E, and 0.7mg of Vitamin K. All contain a number of other vitamins and trace elements. Note if aquadeks is spilt it can stain clothes yellow.

We offer DEKAs Plus or Aquadeks to all newborn screened children (including those who are pancreatic sufficient). If children will not tolerate it, or if GPs are unable to continue supplies, then we will use standard dalivit and vitamin E. All patients will be supplied with a supply letter outlining information about the preparation for the GP and community pharmacist.

- **Dalivit:** 1.2 ml supplies 3000 mcg of vitamin A, 20 mcg of vitamin D, and **no** vitamin E.
- Abidec: not usually given due to low vitamin A content however may be a suitable alternative if Dalivit unavailable.
- One **vitamin A+D capsule BPC** contains – vitamin A 1200 mcg, vitamin D 10 mcg
- **Vita-E gel capsules:**
  - 75 unit capsule  $\approx$  50 mg vitamin E
  - 400 unit capsule  $\approx$  268 mg vitamin E

(Note that 200iu capsules no longer available from GPs)

**Recommended dosing (empirical):**Birth to 12 months:

- Either **DEKAs<sup>®</sup> Plus Liquid** 1ml od
- Or **AquADEKs<sup>™</sup> Paediatric Liquid** 1ml od
- Or **Dalivit** 0.6 ml + **Vitamin E Liquid** 50 mg (0.5ml) od

1 to 4 years:

- Either **DEKAs<sup>®</sup> Plus Liquid** 2ml od
- Or **AquADEKs<sup>™</sup> Paediatric Liquid** 2ml od
- Or **Dalivit** 1.2 ml + **Vitamin E Liquid** 100 mg (1ml) od

5- 8 years:

- Either **DEKAs<sup>®</sup> Plus Liquid** 2ml od or **DEKAs<sup>®</sup> Plus softgel or chewable tablet** 1 od
- Or **AquADEKs<sup>™</sup> Paediatric Liquid** 2ml od or 1 **AquADEKs<sup>™</sup> softgel or 2 chewable tablets** od
- Or **Dalivit** 1.8 ml + **Vitamin E Liquid** 100 mg (1ml) od



9 years and above:

- Either 2-3 **Vitamin A&D capsules + Vitamin E (Vita-E Gel 75iu/400iu Caps)** 150 - 400iu.
- Or 1 - 2 **DEKAs<sup>®</sup>** Plus softgels or 1-2 chewable tablets od
- Or 1 - 2 **AquADEKs<sup>™</sup>** softgels or 2-4 chewable tablets od

Note: annual review blood levels may not reflect dosages prescribed as low levels may simply reflect poor adherence.

**Vitamin D deficiency** (see section 8.4)

*Any one with a vitamin D level below 50nmol/l should be treated.*

Stoss therapy will be the default therapy. It involves a single oral administration of the total treatment dose of vitamin D. An alternative is the whole dose as a single intramuscular injection but there is no reason to use this. This may need to be repeated, if poor compliance persists with maintenance dosing. However the Sydney paper (Shepherd et al, JCF 2012) showed this regimen maintained vitamin D levels for a year.

**Oral colecalciferol single dose:**

- 1 - 12 months 150,000 units
- 1 - 12 years 300,000 units
- $\geq 12$  years 500,000 units

The previous regimen can still be used if there are difficulties with prescribing high dose stoss therapy –

**Oral colecalciferol for 3 months:**

- Infant 1 - 6 months 3000 units daily
- 6 months - 12 years 6000 units daily
- $\geq 12$  years 6000 - 10,000 units daily
- Alternative for older children – colecalciferol 20,000 units 3 times a week; or colecalciferol 50,000 units once a week.

This can be as

- colecalciferol liquid 3000 units/ml.
- colecalciferol capsules or dispersible tablets 1000 units
- colecalciferol capsules 10,000 or 20,000 units
- colecalciferol liquid 50,000 unit/1ml

## Vitamin K

Offered to all children aged 6 years (including pancreatic sufficient) and mandatory for those with liver disease (with or without clotting abnormalities).

Use **water-soluble** preparation: **Menadiol phosphate** tablet. Tablet can be swallowed or dissolved.

- 6 years & above: 10 mg od.

Newborn screened children will receive a small amount of vitamin K from diagnosis contained within DEKAs plus or Aquadeks.

## 11.2 c ‘Antacids’

If enzyme dose high and compliance and diet etc have been considered then consider:

- **Ranitidine:**
  - <1 month: 2 mg/kg tds (max 3 mg/kg tds)
  - 1 – 6 months: 1 mg/kg tds (max 3 mg/kg tds)
  - >6 months: 2-4 mg/kg bd (max 150 mg bd)
  - small risk of headache.

- **Omeprazole:**

	Once daily dose	Maximum daily dose
<2.5kg	0.7 - 1.4mg/kg	3 mg/kg/day
2.5 – 7kg	5mg	3mg/kg/day (max 10mg/day)
7-15 kg	10mg	20 mg daily
>15kg	20mg	40 mg daily

- Doses may divided and given twice daily if required.
- If using dispersible ‘MUPS’ tablets:
  - Round to nearest 5mg (half of a tablet).
  - Tablet can be cut in half but should not be crushed or chewed. Do not try to give a fraction of a tablet by dispersing it – it does not disperse evenly!
  - Allow tablet (or portion of) to dissolve on the tongue or disperse in water/juice/yoghurt and give the whole amount.
- Alternatively, patients can open the capsule and swallow the contents with half a glass of water or after mixing the contents in a slightly acidic fluid *e.g.*, fruit juice or applesauce, or in non-carbonated water. If using this method then doses should be rounded to nearest 10mg (whole capsule).
- For administration through an *enteral feeding tube*, use Aclomep® oral liquid or the contents of a Losec® capsule dispersed in 10 mL Sodium Bicarbonate 8.4% (1 mmol Na<sup>+</sup>/mL).
- If unable to tolerate omeprazole – lansoprazole can be tried as an alternative – see BNFC for doses.

### 11.2d Gastro-oesophageal reflux

Very common in CF.

- **Omeprazole:** see above (11.2c) for doses

**OR**

- **Ranitidine** see above (11.2c) for doses

Consider: **Infant gaviscon**, <4.5kg: Half Dual sachet per feed; >4.5kg: one dual sachet per feed.

**Erythromycin** dose for gastric stasis is: 3 mg/kg tds

### 11.2e Distal Intestinal Obstruction Syndrome (DIOS)

Old name meconium ileus equivalent (MIE). See **section 7.7**. All therapies are osmotic in action therefore fluid support is CRUCIAL, if necessary, intravenously.

- **Oral Gastrografin:**
  - <15 kg, 25 ml BD with 75 ml flavoured juice / water
  - 15-25 kg, 50 ml BD with 150 ml flavoured juice / water
  - >25 kg, 100 ml BD with 200 ml flavoured juice / water

Use for up to 3 days if no response in first 24 hours (but not if symptoms worsen).

**Do NOT give in the presence of bile stained vomiting or bowel obstruction.**

- **Rectal Gastrografin:** Use same doses as oral.
  - <5yrs: Dilute to 5 times its volume with water
  - >5yrs: Dilute to 4 times the volume with water
  - Requires IV line for IV fluids.
- **Oral N-acetylcysteine** - tastes like rotten eggs – The 200mg/ml injection can be given orally and should be mixed with water, orange juice, blackcurrant juice or coke to a concentration of 50mg/ml. Alternatively 200mg sachets or 600mg tablets are available.
 

1 month – 2 years	0.4 - 3g STAT
2 – 6 year	2 – 3g STAT
≥7 years	4 – 6g STAT
- **Polyethylene glycol (Klean-prep)**
  - **Do NOT give in the presence of bile stained vomiting.**
  - Solid food should not be given for at least 2 hours before starting treatment.
  - Add contents of 1 sachet to 1 litre water – can be flavoured with a clear fruit cordial. After reconstitution the solution can be kept in a refrigerator and discarded if unused after 24 hours.

- Can be given orally or via NG tube (usually latter) and a single dose of domperidone 30 minutes before starting can increase gastric emptying.
- Do not administer just before bedtime due to risk of aspiration.
- Start at 10ml/kg/hour for 30 mins then 20 ml/kg/hour for 30 mins.
- If well tolerated rate can go up to 25 ml/kg/hour.
- Maximum volume is 100 ml/kg or 4 litres (whichever is smaller) over 4 hours.
- Patients must be reviewed after 1<sup>st</sup> 4 hours.
- If not passing essentially clear fluid per rectum then a further 4 hours treatment can be given.
- Monitor for hypoglycaemia, which can occur with CF diabetics undergoing this regimen.

#### **N-acetylcysteine (oral) - Prevention of DIOS:**

<2 years: 100 – 200mg tds

2 – 11 years: 200mg tds

≤12 years: 200 – 400mg tds

### **11.2f Constipation**

Ensure fluid intake is adequate.

#### **Lactulose**

<1 year            2.5 ml bd

1-5 years:        5 ml bd

5-10 years:      10 ml bd

>10 years:      15-20 ml bd

then adjust dose according to response.

#### **Movicol**

Chronic constipation, prevention of faecal impaction:

1 - 5 years: 1 sachet of Movicol **Paediatric** OD.

Adjust dose accordingly - maximum 4 sachets daily.

6 - 11 years: 2 sachets of Movicol **Paediatric** OD.

Adjust dose accordingly - maximum 4 sachets daily.

12 - 17 years: Initially 1 - 3 sachets of Movicol per day in divided doses for up to 2 weeks. Maintenance dose 1-2 sachets daily.

Mix contents of each Movicol **Paediatric** sachet in 1/4 of a glass (60-65ml) water and each Movicol sachet in 1/2 of a glass (125ml) water

### **11.2g Liver disease**

- **Ursodeoxycholic acid:**            10 – 15mg/kg bd

- Commonest side effect is diarrhoea (rare though), in which case, reduce dose. Last dose should be taken in late evening.
- **Vitamin K** - Menadiol phosphate 10 mg once daily.

### 11.3 Home delivery of medicines

NHS England Prescribed Specialised Services Commissioning Intentions (2014) has stated that responsibility for the ongoing prescription of high cost inhaled medicines (dornase, tobramycin, colistin, aztreonam, mannitol) for cystic fibrosis should defer to the Hospital Trust (GPs currently prescribed the majority of these medicines). A homecare delivery service to supply these medicines directly to patients is already in use, as responsibility for any **new** prescriptions of these medicines (aside from those already prescribed by GPs) transferred to the Trust in 2014. However, the repatriation of those medicines currently being prescribed by GPs, to the trust is expected to take place imminently.

This homecare service enables these medicines that are not able to be prescribed by the patient's GP, to be prescribed by the CF team at RBH, and then delivered directly to the patient at home by the hospital's chosen homecare provider, for as long as is required. The default for prescribing and supply of **all other** CF medicines except the ones listed above should be from the GP.

If homecare is required then please contact a member of the paediatric pharmacy team as soon as possible (Bleeps 7403/7410/7425/7428 or ext. 4375; [paedpharmacy@rbht.nhs.uk](mailto:paedpharmacy@rbht.nhs.uk); [rbh-tr.paediatricpharmacy@nhs.net](mailto:rbh-tr.paediatricpharmacy@nhs.net)) who will then advise on the process to be followed. The paediatric pharmacy team should also be informed if there are ANY CHANGES to patient medicines that are supplied via homecare *i.e.* dose changes or discontinuations. Where possible copy the paediatric pharmacist into correspondence detailing such changes.

## Appendix 1 - Transition Integrated Care Pathway

### TRANSITION OF CARE FROM THE PAEDIATRIC SERVICE TO THE ADULT SERVICE

Name:

Referring consultant:

CRN or referring hospital:

Please attach a referral letter if outside the Royal Brompton Hospital.

**Transition:** Is the planned process of changing from paediatric family centred care to a more independent adult service. This process usually starts during the latter stages of paediatric care and ends in the early years of attendance in the adult service. It is a process that fully involves the young adult, their parents, and both the paediatric and adult Cystic Fibrosis (CF) teams.

### INTEGRATED CARE PATHWAY

The aim of this document is to improve the process of transition from paediatric to adult care. Please see: [www.rbht.nhs.uk/cf-transition/](http://www.rbht.nhs.uk/cf-transition/)

Date ICP started:

Date ICP ended:

This ICP will start in the paediatric CF service and end after transition to the adult CF service. It must be kept at the front of the medical notes throughout this time. Please initial and date the YES/NO boxes.

This ICP is for adolescents with CF who are 14-17 years old and planning their move to adult care. Transition from the paediatric to adult clinic may take place over a period of up to three years.

- Patients will be contacted by the paediatric nurse specialist with an appointment for both the Pre-transition and Transition clinics.
- Both paediatric and adult CF teams are informed of the dates.
- Information will be provided and arrangements made for patients and families in advance of the clinic.

a. 14<sup>th</sup> Birthday Letter sent: Yes ☐ No ☐

b. Pre-Transition Clinic Date ...../...../..... Attended: Yes ☐ No ☐  
i. If NO, action taken:

c. Transition Clinic Date ...../...../..... Attended: Yes ☐ No ☐  
i. If NO, action taken:

d. 1<sup>st</sup> Adult CF Clinic ...../...../..... Attended: Yes ☐ No ☐  
i. If NO, action taken:

Please ensure that the Family & Social Information Form is attached before sending to the adult team

	PLANNING TRANSITION	YES	NO	VARIANCE AND/OR ACTION TAKEN
1	<p>Has transition been discussed with the patient?</p> <p>Has transition been discussed with parents / caregiver?</p> <p>Are there any concerns?</p>			<p>If NO reasons why:</p> <p>If NO reasons why:</p>
2	Has the patient been given a Family & Social Information form to complete?			If NO reasons why:
3	Has the form been returned			If NO reasons why:
4	Has the pre-transition ICP data been fully completed?			If NO reasons why:
5	Is the transition ICP available for the adult team to review?			If NO reasons why:
<b>CLINICAL DATA</b>				
6	<p>Age at diagnosis:</p> <p>Presentation at diagnosis:</p>			<p>Genotype:</p> <p>1:</p> <p>2:</p>
7	<p><b>CURRENT CLINICAL STATUS</b></p> <p>Date of measurements:</p> <p>Height:                      cm                      Weight:                      kg                      BMI:</p> <p>Lung function: FEV<sub>1</sub>:                      (    %)                      FVC:                      (    %)                      MEF 25-75:                      (    %)</p> <p>SaO<sub>2</sub>:                      %</p>			
8	<p><b>INTRAVENOUS ACCESS</b></p> <p>What type of access is usually used?</p> <p>Are there any problems associated with this (seen psychology)?</p> <p>Portacath:                      Date inserted:                      Type:</p> <p><b>Any problems?</b></p>			

CLINICAL DATA		YES	NO	VARIANCE AND/OR ACTION TAKEN		
9	<p>Has fertility been discussed?</p> <p>What contraception advice has been given?</p> <p>Is the patient using contraception?</p> <p>If yes, type:</p>			If NO reasons why:		
10	<p>Gastrostomy?</p> <p>Feeding regimen:</p> <p>Any problems?</p> <p>Pancreatic sufficient?</p> <p>Pancreatic insufficient?</p>			<p>If YES: Date inserted:                      Type:</p> <p>If YES reasons why:</p> <p>Enzyme treatment?</p>		
11	<b>Previously tried airway clearance techniques</b>	<b>Current technique / Sessions per day / Adherence issues / Other</b>				
12	<b>Exercise</b>	<b>Comments</b>		<b>Current regimen</b>		
13	<b>MSK</b>	<b>Pain?</b>		<b>Problems / Comments</b>		
14	Are there any incontinence issues?			If YES please comment:		
15	Has transplantation been discussed?			Details of discussion:		



	ORGANISMS	Ever grown (YES/NO)?	Where grown (RBH, local?)	Date of first growth	Current
	<b>Please include eradication attempts - successful or not</b>				
16	Staphylococcus aureus Haemophilus influenzae Pseudomonas aeruginosa Stenotrophomonas maltophilia Achromobacter xylosoxidans Burkholderia cepacia complex, type: MRSA Atypical Mycobacteria, type: Other bacteria Aspergillus fumigatus Other fungus				
17	<b>HOSPITALISATION</b> How many times in the last 12 months?  Reasons for admission:  No. of courses IV antibiotics:  At home:  In hospital:				
18	<b>Medication list</b> (please include whether patient has tried DNase or HTS previously but stopped, with reasons why)	<b>Dose</b>	<b>Frequency</b>	<b>Route</b>	
19	Any allergies?			If YES describe the reaction:	
20	<b>COMPLICATIONS</b> Oxygen therapy Haemoptysis Pneumothorax ABPA DIOS	<b>Details</b>			

	Liver disease Oesophageal varices CF Related Diabetes Arthropathy Severe small airways disease Other associated conditions			
21	Does the patient receive any form of outreach support?			If YES please provide further details:
22	Has the patient had involvement/support from social services?			If YES please provide further details:
23	Has there been a psychological assessment and handover?			If NO reasons why:
24	Is the patient taking part in any research trials?			If YES, which ones?  Can the patient transition while taking part?  Have alternative plans been made?
	<b>Transition clinic</b>	<b>YES</b>	<b>NO</b>	<b>Variance and action taken</b>
1	At the transition clinic, has the patient been given transition information?			If NO reasons why:
2	Have the patient and family met all the members of the adult team today?			If NO, who do they need to meet?  Has this been arranged?
3	Have both teams met to discuss any problems and issues prior to clinic?			If NO reasons why:
4	Were treatment plans discussed?			Please give details.
5	Has the patient been asked if they would like to attend a second transition clinic?			If NO reasons why:
6	If they wish to, has a date been given?			Date:

7	Have family & patient visited Foulis ward?			If NO reasons why:
8	Have they received an appointment for an adult CF clinic?			Date of clinic: A, B or C clinic?
<b>Follow up at adult clinic</b>		<b>YES</b>	<b>NO</b>	<b>Variance and action taken</b>
1	Has the CF Registry co-ordinator been informed of the move?			Date:
2	Was the patient seen in the appropriate A, B, or C clinic?			If NO reasons why:
3	Were current medical notes available for the consultation?			If NO reasons why:
4	Has the Annual Review co-ordinator been informed?			Date:

Paediatric Clinic - Form completed by:

Date:

Adult Clinic - Form completed by:

Date:

**Please send a copy to (attaching a referral letter if outside the Royal Brompton Hospital):**

Adult Cystic Fibrosis Clinical Nurse Specialists ([cffhomecare@rbht.nhs.uk](mailto:cffhomecare@rbht.nhs.uk))

And one of the Adult CF physicians.

Department of Cystic Fibrosis  
Royal Brompton Hospital  
Sydney Street  
London SW3 6NP

**FAMILY & SOCIAL INFORMATION**

**We would be grateful if you could please complete this form as it helps the Adult CF Team get to know you before transition. Thank you.**

**YOUR FAMILY BACKGROUND**

Parents names:

Siblings names and ages:

CF-Siblings names and ages:

Who do you live with?

CF in extended family –relationship names and ages:

Ethnic origin:

**SOCIAL SUPPORT**

Disability Living Allowance: yes ☐ no ☐ Rate:

Mobility: yes ☐ no ☐

PIP: yes ☐ no ☐

**EDUCATION**

Sixth Form (GCSEs, A Levels, GVNQ)

College/University:

Career interest:

Special educational needs:

**EMPLOYMENT** (Saturday /part-time/ weekend/full-time)**OTHER COMMENTS****CONTACT DETAILS**

Your mobile phone number:

Your email address:

Your next of kin's mobile phone number:

Your next of kin's email address:

**This is for you to complete and will be sent to the adult CF team**

**ALL ABOUT ME – please introduce yourself to the adult team**

## Appendix 2 – Treatment of Non-tuberculous Mycobacteria (NTM)

### 1. Background

Nontuberculous mycobacteria (NTM) are environmental organisms with relatively low virulence, found in soil and water that are potential pulmonary pathogens increasingly affecting patients with cystic fibrosis (CF). The prevalence of NTM among CF patients, based on a recent large multicentre trial undertaken in the US, where NTM was defined as at least one positive NTM culture, is 13%. The UK CF Registry suggests a prevalence of ~8% (2015). There is some evidence for an association between NTM in CF and older age, poor nutrition, increased frequency of intravenous antibiotic administration, diabetes, treatment with corticosteroids or non-steroidal anti-inflammatory drugs, allergic bronchopulmonary aspergillosis (ABPA), *Pseudomonas*, *Staphylococcus* or *Aspergillus* chronic infection, and deteriorating lung function, but these have not been found consistently. The commonest NTM species affecting CF patients are *Mycobacterium abscessus* complex (MABSC) and *Mycobacterium avium* complex (MAC); the former is the more prevalent among European Centres. The natural history of NTM disease may vary between species; a recent epidemiological study and several case reports suggest that *M. abscessus* complex follows a more fulminant course and is associated with a less good outcome.

### 2. Indication for treatment of NTM

The presence of NTM in the sputum of patients with CF poses a significant diagnostic dilemma, as it may represent transient contamination, colonisation or infection known as NTM pulmonary disease (NTM-PD). Not all patients will benefit from treatment for NTM. In 2016 the European CF Society and the US CF Foundation published consensus recommendations on the management of NTM in CF [see Floto et al, Thorax 2016;71 Suppl 1:i1-22. Available on [http://thorax.bmj.com/content/71/Suppl\\_1/i1.full.pdf+html](http://thorax.bmj.com/content/71/Suppl_1/i1.full.pdf+html)].

Patients are defined as having NTM-PD if they meet clinical and radiological criteria with positive cultures from **two or more** separate expectorated sputum samples, or from a single BAL or from a biopsy with a positive culture. However, there is considerable overlap between the clinical and radiological presentation of NTM and CF per se, as well as between NTM and infection by other CF pathogens. The presence of HRCT changes attributable only to NTM is very hard to confirm in the presence of similar radiological findings occurring in CF and ABPA. While some patients with persistent NTM in sputum have declining clinical and radiographic parameters, this is not true of all patients. In identifying which patients require NTM treatment, it is essential that initially all non-mycobacterial organisms are maximally treated. Patients should be under close surveillance; starting treatment is often a consultant consensus decision and based on the risks and benefits of treatment for each individual.

Treatment should be tailored according to the specific species of NTM, which will be considered separately.

### 3. Treatment of *M. abscessus* complex

*M. abscessus* complex is universally resistant to standard anti-tuberculous agents and no antibiotic regimen based on *in vitro* susceptibilities has been shown to produce long-term

sputum conversion in patients with this organism. However if possible, initial antibiotics can be chosen according to sensitivities.

### **3.1) Dosage and Administration**

The regimen in Table 1, based on a 3 week intensive phase followed by a prolonged continuation phase (maintenance) is recommended as first line therapy. If patients do not tolerate or have side effects to any of the continuation drugs, alternative agents are suggested in Table 2. Patients on first line maintenance therapy will be regarded as ‘failing’ treatment or relapsing if they have the following:

- Increasing sputum and breathlessness
- Fevers
- Sweats
- Rising CRP
- No response to treatment with non-mycobacterial antibiotics
- Persistent positivity on sputum AAFB smear

In this case they will be given second line intensive and maintenance treatment, as charted in Table 3.

Maintenance treatment should include four drugs in total (either nebulised or oral preparation).

If a patient is admitted with an exacerbation during their maintenance phase, then all the maintenance drugs should be continued whilst being treated with the intensive phase drugs (except minocycline/doxycycline which should be stopped if tigecycline is used; and nebulised amikacin stopped if IV amikacin is used).

A favourable response to treatment will be defined as when a patient is rendered sputum culture negative on serial samples collected over a period of one year. At this point the organism will be regarded as eradicated and maintenance therapy may be stopped. A patient is considered NTM free if still clear at 12 months after completion of eradication therapy.

**Table 1. First line intensive & continuation therapy for *M abscessus* complex.**

<b>Intensive phase therapy (duration 3 weeks)</b>	
<b>Amikacin</b>	IV 30mg/kg od (max 1.5 g)
<b>Meropenem</b>	IV 40mg/kg (max 2grams) tds
<b>Cefoxitin</b>	IV 50mg/kg tds (max 12 g/day)
<b>Azithromycin</b>	Oral 10 mg/kg (max 500mg) od
<b>Continuation therapy (duration &gt;= 18/12 depending on response)</b>	
<b>Amikacin</b> Over 12 yrs 6-12 yrs	Nebulised 500mg bd Nebulised 250mg bd
<b>Moxifloxacin</b>	Oral 7.5 – 10mg/kg (max 400mg) od
<b>Minocycline</b> Over 12 years	Oral 100mg bd
<b>Co-trimoxazole</b> 6-12 years Over 12 years	Oral 480mg bd Oral 960 mg bd
<b>Azithromycin</b>	Oral 10mg/kg (max 500mg) od

- If the patient has allergies to any of first line IV drugs, add tigecycline. Tigecycline should be prescribed with regular anti-emetics such as ondansetron.
- Both cefoxitin and tigecycline can cause nausea. All patients should be adequately hydrated prior to starting intensive IV treatment, a dose of IV ondansetron should be given prior to the first dose of tigecycline; this may later be swapped to oral and may also be needed with cefoxitin.
- Some patients find that the continuation treatment also causes nausea and may need to continue on oral ondansetron long term. Adjustment of drug dosing schedules may help this. Second line anti-emetics are sometimes used.
- Avoid minocycline, doxycycline and tigecycline in patients less than 12 years of age, unless a dental assessment has been done and tetracycline drugs are considered safe because secondary dentition is complete.



**Table 2. Alternative drugs if patient is unable to tolerate or has side effects to any of the first line oral continuation drugs for *M abscessus* complex.**

Unable to tolerate	Drug to consider	
Moxifloxacin	<b>Ciprofloxacin</b>	Oral 20 mg/kg (max 750mg) bd
Minocycline	<b>Doxycycline</b> Over 12 years  <b>Co-trimoxazole</b> Over 12 years 6-12 years	Oral 100mg bd   Oral 960mg bd Oral 480mg bd
Azithromycin	<b>Clarithromycin</b>	Oral 7.5mg/kg (max 500mg) bd

- Avoid minocycline, doxycycline and tigecycline in patients less than 12 years of age, unless a dental assessment has been done and tetracycline drugs are considered safe because secondary dentition is complete.
- Further alternatives are linezolid and clofazamine.

**Table 3. Second line intensive and continuation therapy for *M. abscessus* complex.**

<b>Intensive phase therapy (duration 3 weeks)</b>	
<b>Amikacin</b>	IV 30mg/kg (max 1.5g) od
<b>Meropenem</b>	IV 40mg/kg (max 2g) tds
<b>Tigecycline</b> 8-11 yrs (see below re dentition)	1.2mg/kg (max 50 mg) bd
12 years or over	IV 100 mg loading dose, then 50mg bd Reduce to 50 mg od if not tolerated
<b>Azithromycin</b>	Oral 10mg/kg (max 500mg) od
<b>Continuation therapy (duration &gt;= 18/12 depending on response)</b>	
<b>Amikacin</b> Over 12 yrs 6-12 years  and/or  <b>Meropenem</b> Over 12 yrs 6 -12 years	Nebulised 500mg bd Nebulised 250mg bd    Nebulised 250mg bd Nebulised 125mg bd
<b>Minocycline</b> Over 12 years	Oral 100mg bd
<b>Azithromycin</b>	Oral 10mg/kg (max 500mg) od

- If the patient is unable to tolerate or has side effects to the oral drugs in the second line continuation therapy regimen, consider the alternative oral agents listed in Table 2.
- Avoid minocycline, doxycycline and tigecycline in patients less than 12 years of age, unless a dental assessment has been done and tetracycline drugs are considered safe because secondary dentition is complete

- Begin tigecycline at a dose of 50mg bd; or 1.2mg/kg bd (max 50mg) for children aged 8-11 assuming dentition has been checked. If unable to tolerate this due to vomiting the dose can be reduced to daily or alternate day dosing or 2 days out of 3. Tigecycline can cause nausea so should be prescribed with regular IV anti-emetics such as ondansetron (which can be switched to oral dose later). All patients should be adequately hydrated prior to starting intensive IV treatment.

### **3.2) Counselling - general**

- Patients will be counselled on the treatment regimen for *MABSC*, and its potential benefits and adverse effects. In particular they will be advised that treatment will be a minimum of 18 months and this may not ultimately result in their becoming culture negative for this organism.
- Patients will be advised that they will receive regular monitoring throughout the duration of treatment – see individual drug monographs for details.
- Hearing impairment may result from accumulative effects of nebulised amikacin, patients are advised to report any hearing problems or development of tinnitus.
- Amikacin must be stopped immediately if there are any balance problems.
- Patients will be advised to report side effects of treatment as soon as possible.

### **3.3) Monitoring - general**

- Full blood count and the patient's renal and hepatic function must be checked prior to initiating treatment.
- Renal and liver function should be checked at 12 weekly intervals unless stated otherwise in drug monographs.
- A baseline hearing test should be performed in children at the start of intensive therapy with IV amikacin.

## 4. Treatment of *Mycobacterium avium* complex (MAC)

It is recommended that the following treatment regimen is used for a minimum of 12 months after NTM culture conversion.

### 4.1) Dosage and Administration

Initial therapy should be triple oral therapy as listed in Table 4. Patients who are unwell should begin by having 2 weeks intravenous therapy with amikacin and meropenem. As with MABSC treatment we would consider the NTM to be eradicated when sputum samples are free of NTM for a 1 year period.

**Table 4. Drug treatment for MAC.**

Drug	Dose
<b>Rifampicin</b>	Oral 10-20mg/kg (max 600mg) od
<b>Azithromycin</b>	Oral 10mg/kg (max 500mg) od
<b>Ethambutol</b>	Oral 15mg/kg (max 1.5gms) od

### 4.2) Counselling - general

- Patients will be counselled on the treatment regimen for MAC, and its potential benefits and adverse effects. In particular they will be advised that treatment will be a minimum of 18 months or until they have been culture negative for a period of 12 months.
- Patients will be advised that they will receive regular monitoring throughout the duration of treatment.
- Patients will be advised to report any potential side effects of treatment such as jaundice, itching, visual disturbance as soon as possible.

### 4.3) Monitoring - general

- Full blood count and the patient's renal and hepatic function must be checked prior to initiating treatment.
- Visual acuity should be measured before starting Ethambutol
- Renal and liver function should be checked at 2 weeks. If LFTs are raised to five times the upper limit of normal at any stage, all drugs should be stopped and drugs restarted one at a time when bloods are back to normal with regular LFT and renal blood monitoring on re-introduction. If raised below 5x upper limit consideration should be given to stopping the rifampicin and ethambutol in the first instance, again with re-introduction slowly.

## 5. Treatment of other NTM

Treatment of other NTM should be guided by the sensitivities of the organism, and should include a combination of 3 drugs. Treatment is given for a minimum of 12-18 months as for MAC.

### **Appendix 3 - Risks of getting *P. aeruginosa* from the environment**

We understand that many parents are very concerned about their child ‘catching’ or acquiring *Pseudomonas aeruginosa* (PsA) from the environment. We realise this is a personal issue and that different families view things differently, especially in terms of balancing risk vs benefit. Parent’s views may also change with time *e.g.* as their child gets older, or depending on how well their child has been.

In order to ensure a consistent message, we have written this guide, which is a consensus view from the Brompton paediatric team and follows a comprehensive literature search. In some cases there is strong research evidence and we can be firm in our views. However for many situations, the evidence is lacking or itself inconsistent. In those instances, parents will need to decide for themselves what to let their child do and decisions are often best made using common sense.

The UK CF Trust state ‘It’s important to remember that life can be risky – we all have to weigh up risk against quality of life.’ We agree with this and would like children to lead as normal a life as possible, and not miss out on fun activities at home or school.

It is impossible to avoid contact with PsA, it is everywhere, and water is its natural environment. The risk of PsA acquisition is greater if PsA is present in water that is aerosolised (converted into a fine spray or mist), so it can be inhaled directly into the lungs. There is a small risk, but it is still possible, for a child to have PsA on their hands and put their fingers in the nose or mouth and hence inhale it. There is a dose effect, so the longer the exposure or the higher the bacterial content, the more likely the bacteria will be acquired and stay in the lungs. It is difficult to know whether drinking PsA-contaminated water affects the lungs as PsA can be found in stool samples in many healthy people. Always remember that other people with PsA infection are a potential source, and close contact with them puts children with CF at risk of infection.

We have focussed this guide on PsA, but obviously there are other organisms acquired from the environment that can be a problem, these are mentioned within the main guidelines where appropriate. These guidelines still apply to children who have already isolated PsA; it is possible to acquire more than one strain.

#### **Things to definitely avoid**

- **Hot tubs, Whirlpools, Spa pools, Jacuzzis®, Hydrotherapy pools**

There is strong evidence of the presence of PsA in warm water that is aerosolised and easily inhaled with the person’s head just above the water; and reported cases of acquired infection in adults with CF. PsA has been isolated from culture plates held 15 cms (6 inches) above the water surface when the tub was turned on.

- **Tropical greenhouses, butterfly houses**

Misting systems to water plants in tropical greenhouses and butterfly houses have been shown to contain PsA so are a risk as the fine water droplets are easily inhaled.

- **Outdoor misting systems**  
Some restaurants or other public areas have an outdoor misting system that sends a spray of mist downwards to keep people cool. We can find no evidence but there is a theoretical risk that the mist may contain PsA from the local water supply.
- **Squirting bath toys**  
Bath toys that have a valve on the base (*e.g.* plastic ducks) or that can squirt out water can be a problem if the water sits inside the toy for a long time, as they cannot be fully emptied and dried. There is evidence of a PsA outbreak on a children's cancer ward that originated in the toy box containing water-retaining bath toys. The same would apply to any hollow bath toy that retains water.
- **Swimming in stagnant ponds & canals** (see below).
- **Fish tanks (especially warm tanks for tropical fish)**  
Organisms have been isolated from fish tanks and cases reported of infection in people with CF. We believe they should be avoided. However the US guidelines [1] simply suggest that gloves should be worn when cleaning out a fish tank.
- **Compost** (heaps and bags)  
Compost is essentially decayed vegetation, and is like enriched soil, but it can contain *Aspergillus* spores, and also bacteria such as *Pseudomonas* species. It should definitely be avoided due to the particularly high risk of *Aspergillus*.

### **Things to take precautions with but allow**

- **Digging in the garden soil, playing in the park, playing outdoor sport**  
PsA is known to reside in soil, although interestingly despite this fact being frequently quoted, publications suggest PsA is infrequently cultured. A 1974 study in 58 agricultural sites in California found that a quarter of soil samples grew PsA (especially in soils where tomatoes were grown). However many studies since have found it to be rarely detected (*e.g.* a 2014 study of 380 samples from France & Burkina Faso). Soil that is contaminated by organic fertiliser or animal manure is best avoided. Any PsA present in someone's garden is only a potential source of infection if the child puts the soil on their face and specifically up their noses or in their mouths (from contaminated fingers). We therefore suggest playing in the garden or park should not be stopped, as long as the children's hands and face are cleaned properly afterwards. The same applies to older children playing outdoor team sport (football, rugby etc.) which we encourage as exercise is so beneficial. We believe running through piles of damp leaves (or collecting leaves) would also seem to be safe. The US guidelines suggest that people with CF should limit prolonged exposures to activity that generates dust from the soil or organic matter *e.g.* lawn mowing to decrease exposure to *Aspergillus* and *B cepacia*. If a child wants to 'garden' they could always wear gardening gloves.

Proper hand washing is imperative. That is not always possible when outside the home, so parents (and older children) may wish to carry small bottles/tubes of antibacterial gel (hand sanitisers) that can be bought in chemists and supermarkets.

- **Mud kitchens**

These are toy kitchen units made of wood, plastic and metal, where mud is used as the ingredient for all the food being made so gets all over the children's hands and probably faces! The same applies as digging in the garden, any PsA in the mud will not be aerosolised, so as long as the children's hands and face are cleaned properly afterwards, we believe the risk is minimal. There is no published evidence to further guide us.

- **Muddy puddles**

Mud is a mixture of compressed soil and water; a puddle that has dirty stagnant water in it may contain PsA (although there is no evidence). However if a child steps in it or even splashes in it, the water is not aerosolised sufficiently to be inhaled so we believe this is not a risk and need not be avoided. Pavement puddles dry so fast that the water does not stagnate and is also not in contact with soil/mud, so is perfectly safe to splash through.

- **Sandpits**

Sand can be contaminated with PsA and it has been occasionally isolated from some beaches (probably due to human contamination in the sea). In a sandpit with clean dry sand the risk is minimal, although the sand is often damp; nevertheless we believe the risk is only significant in a sandpit with free standing stagnant water. So we suggest sandpits are fine as long as there is no visible standing water; this will be easier to control in someone's own garden. It is worth keeping a lid on the sandpit to reduce the amount of rainwater that might collect. The CF Trust advises schools that the sand should be regularly changed although do not say how often. A sandpit in a park is less likely to be clean, but by far the most frequent contaminant is *Toxocara* from cat and dog faeces.

- **Swimming**

It is important children learn to swim for safety reasons. PsA is an aquatic organism preferentially living in water habitats and colonising moist environments. The water will not be aerosolised (apart from waterfalls), so it is unlikely to be an issue as long as it is not inhaled. Washing afterwards is obviously a good idea. **Inflatable toys** should be dried out after use, and not be left to hold stagnating water.

- **Sea** – PsA has been grown out in the open ocean. However sea water by a beach is most likely contaminated from human faeces. It is worth checking the cleanliness of beaches which can be done online for UK beaches (<https://www.gov.uk/quality-of-local-bathing-water>). We suggest swimming in the sea is fine.
- **Lakes** can also be contaminated in a similar way to the sea but again we do not believe this is a problem.
- **Rivers** – even rivers have isolated PsA but again we would not discourage swimming in a river (as long as it is deemed safe for bathers).
- **Ponds** – this is more likely to be a problem in a small stagnant pond due to rotting vegetation *e.g.*, leaves. In that case it should be avoided, although is likely to be safe in a large pond that looks clean.
- **Canals** – similarly to the ponds, the water is often stagnant and usually looks dirty. We would suggest avoiding this.
- **Swimming pools** – as long as the pool is disinfected (usually with chlorine) to recommended levels then this should not be a problem, although PsA has been isolated occasionally from both indoor and outdoor public pools. Caution though with hotels and renting holiday villas with private pools in case the pool is not treated properly.

- **Paddling pools**  
These will be fine as long as they are emptied after each use & dried out, then filled up again with fresh water when they are to be reused.
- **Water amusement parks**  
The water will be aerosolised and on some rides spray can be inhaled. However as long as the facility uses treated disinfected (usually chlorinated) water to industry standards this should be safe and can be checked in advance.
- **Pond-dipping**  
This is collecting pond life in a jar attached to a net that is dragged through the water. It is likely that the pond water (that may be stagnant) will get on the children's hands and of course may end up being flicked around when an adult is not looking, especially when there are a lot of children taking part. It is likely to be safe as long as it is supervised properly and the child cleans their hands properly afterwards. There is no evidence to guide us, and it is difficult to know what is best, so parents will have to decide whether they believe it to be a sufficient risk to stop the child joining in.
- **Touch pools in a public aquarium**  
It is most likely that there will be bacteria in the water, including non-tuberculous mycobacteria. However the water will not be aerosolised, and there are good hand-washing facilities on the spot, so we believe the children can take part as long as they definitely clean their hands well and are supervised carefully.
- **Petting zoos and farm visits**  
Clearly stagnant water or small ponds should be avoided. Caution also in chicken coops, stables and contact with mouldy hay for *Aspergillus*. Hand hygiene is important after stroking the animals and most places will have hand washing facilities for all the children anyway. There have been no reports of transmission of pathogens from farm animals or pet therapy animals to people with CF, although animals are a potential source of several types of infection (*e.g.* PsA from horses, MRSA from pigs).
- **Caves**  
These are often damp environments with water dripping down the sides of the walls. The water is not aerosolised and the child will not be in direct contact with the water. There is no evidence to guide us, but we believe a visit to a cave need not be avoided.
- **Showers**  
The shower heads can be a source of PsA with colonised biofilms, and the shower spray contains aerosolised droplets that can be inhaled. It is best to run the shower for 1-2 minutes before the child gets in.
- **Sink and bath taps**  
These can also contain PsA (in the form of biofilms) but the risk is reduced compared to showers as the water spray is not being inhaled. If the tap is in frequent usage the risk is also lessened, but taps that are rarely used should have the water run through them for 1 minute every day. This is unlikely to be an issue in someone's home. PsA is most often detected from kitchen and bathroom drains in homes of people without CF; and from shower and bathroom drains in homes of people with CF.



- **Water pistols and ‘super-soakers’**

Similarly to squirting bath toys, this could be a problem if the water is kept inside the toys for a long time. A forceful super-soaker could aerosolise the water and can be squirted in the face. However we suggest as long as they are emptied fully after use, and dried out they can still be played with. **Water play** should be safe as long as the water is fresh and has not sat stagnating in containers; toys should be dried out at the end.

- **Flower vases**

Water should be changed before it smells, and trim the leaves off stems so that they do not sit in the water.

- **Humidifiers & vaporisers**

Water sits in a reservoir which is evaporated and blown into the air. As long as the reservoir is kept clean, and fresh water put into it before use, it should be safe, but do not use it if the water has been stagnating in the reservoir for a while. Also never add disinfectant to the water – some have caused harmful interstitial lung disease.

- **Flushing toilets**

Aerosols containing bacteria, including PsA, can be created when flushing toilets, so the lids should be lowered before flushing.

### **Things that must not be avoided**

- **Dentist**

There has been concern expressed in the past about aerosolisation of PsA-contaminated water from dental chair units. PsA may get there from municipal water or the suck back of a patient’s saliva into the line due to lack of anti-retraction valves. It is critical that children with CF attend the dentist regularly, especially given the effect of some of the antibiotics and the potential high sugar diet. Furthermore, rotten teeth can promote PsA in the mouth which can infect the airways.

- **Drinking water**

PsA has been isolated in tap water, well water, drinking water dispensers (coolers), water from vending machines, bottled water, and even distilled water. There is no evidence that drinking water with the low levels of PsA found will cause lung infections, and high levels are required to colonise the gut. Drinking water need not be avoided, nor need the water be boiled first. The US guidelines suggest that tap water or well water that meets local public health standards may be used for drinking.

Many people use refillable water bottles. Mostly the filters are not antibacterial, but are carbon filters to remove chlorine and improve the taste. Certain designs mean that the filters remain wet, possibly even holding water, so these should be avoided. Similar advice is given for water jugs with filters. Bottles with antibacterial filters do exist (for camping etc.) but again it is important to know if the filter remains wet and possibly holds on to the bacteria, in which case they should be avoided.

[1] Saiman *et al.* *Infection prevention & control guidelines for cystic fibrosis: 2013 update.* *Infect Control & Hosp Epidemiol* 2014;35:S1-S67.

## Appendix 4 – Paediatric cystic fibrosis intravenous aminoglycoside consent form

The following information explains the aims, benefits, and risks of aminoglycoside antibiotics.

### What are intravenous (IV) aminoglycosides?

Aminoglycosides are antibiotics (given into a vein), used in children with cystic fibrosis (CF), to treat serious lung infections caused by bacteria such as *Pseudomonas aeruginosa* and *Mycobacterium abscessus* complex. The aminoglycoside antibiotics we use are tobramycin and amikacin.

### Reasons for starting aminoglycoside therapy

Both *Pseudomonas* and *Mycobacterium abscessus* complex infections are hard to eradicate and require treatment with more than one antibiotic. There is strong evidence that aminoglycosides are one of the most effective types of antibiotics for children with CF, so it is our standard practice to use them. This is in line with recommendations from both the UK CF Trust and the European Cystic Fibrosis Society. We use these antibiotics when we believe the potential benefits of this treatment outweigh the risks, which are outlined below.

### Side effects

Like many important medicines, aminoglycosides have side effects and can affect your child's kidneys and hearing, and therefore we always monitor drug levels in your child's blood to minimise the possibility of these occurring.

Although theoretically this is possible with a single aminoglycoside course, it is usually the accumulation of many courses (usually over several years), that increases the risk of hearing problems, even if every blood test for the drug concentration was within the normal range.

It should be emphasised that the possibility of significant hearing problems is small, even with many aminoglycoside courses. Some children may be more sensitive to these antibiotics than others but this is still a new area of research.

### Monitoring

Regular blood tests (weekly) will be done to ensure that the correct dose of antibiotic is given to help minimise the risk of side effects.

We will also arrange for children to have a baseline hearing test at their local hospital if they need amikacin for *Mycobacterium abscessus* complex infections; or are starting regular 3-monthly courses of IV antibiotics, and this will be repeated every year or sooner if concerns arise.

If symptoms such as hearing difficulties, tinnitus (ringing sound in the ears), dizziness or problems with balance are noticed, please tell your doctor as soon as possible. We will be monitoring for kidney problems but it is most important to stay well hydrated (drink plenty) especially in hot weather. If there are concerns, we will stop the aminoglycosides and use an alternative antibiotic, although the alternative antibiotics may not be quite as effective in treating the infection.

**Child or Parent/Carer name****Child or Parent/Carer signature**

.....

.....

Date.....

I agree to the treatment outlined above and have read and understood the information given to me and my questions have been answered.

**Interpreter name****Interpreter signature**

.....

.....

Date.....

I have explained the information above to the patient/parent/carer to the best of my ability and in a way in which I believe he / she can understand.

**Doctor name****Doctor signature**

.. .....

.....

Date .....

I have discussed the side effects with the patient and answered his / her questions.

Patient / parent / carer has given consent to treatment with IV aminoglycosides ☐

Patient / parent / carer has declined treatment with IV aminoglycosides ☐

Copy into patient notes

Copy given to patient/parent/carer

Copy into Audit Folder

October 2016

## Appendix 5 - Home visit report for 'Challenging CF' Protocol

<b>Name:</b>	<b>Address:</b>
<b>Dob:</b>	
<b>Hospital no:</b>	
<b>Date of visit:</b>	<b>Telephone no:</b>
<b>Name of Nurse performing visit:</b>	
<b>Name of Physiotherapist performing visit:</b>	

### Those at home at time of visit:

**The Home:** Flat/House/Garden  
 If flat: what floor?      Lift: yes / no      Stairs: yes / no  
 Immediate surroundings (i.e. busy road, trees, fields):  
 No of bedrooms:  
 Shared bedroom:      yes/no

**People living at home:** 1.      4.  
    2.      5.  
    3.      6.

### Pets:

Pets in the home: 1.      Pets living outside: 1.  
                                  2.      2.  
                                  3.      3.

### Other information

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### Overall impression of home organisation:

Very organised      Average      Below average      Very disorganised

Comments: \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

**Allergen Exposure****Moulds**

Evidence of damp	yes / no	details:
Evidence of mould on walls	yes / no	details:
Evidence of mould on windows	yes / no	details:

Other allergens/irritants:

*i.e. air fresheners, poor ventilation, mouldy food, rodent infestations etc*


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**Smoke**

Does Child smoke?	yes/no	
Do Parents smoke	yes / no	If yes; inside / outside
Other household members?	yes / no	
Do close friends smoke?	yes/no	
Evidence of smoke in home	yes / no	details:
Evidence of active smoking	yes / no	

<b>Any known Allergies?</b>	yes / no	Details:
-----------------------------	----------	----------

**Action required?**

## Medication

Current medication:

<b>Antibiotics</b>	Name	Dose	Frequency	Route	Available	In date
					Yes / no	Yes / no
					Yes / no	Yes / no
					Yes / no	Yes / no
<b>Antifungal</b>					Yes / no	Yes / no
					Yes / no	Yes / no
					Yes / no	Yes / no
					Yes / no	Yes / no
<b>Vitamins</b>					Yes / no	Yes / no
					Yes / no	Yes / no
					Yes / no	Yes / no
<b>Anti-reflux</b>					Yes / no	Yes / no
<b>Other</b>					Yes / no	Yes / no

Current Inhaled /nebulised Medication:

Name	Dose/Frequency	Route	Available	In date
			Yes / no	Yes / no
			Yes / no	Yes / no
			Yes / no	Yes / no
			Yes / no	Yes / no
			Yes / no	Yes / no
			Yes / no	Yes / no
			Yes / no	Yes / no

Nebuliser make:

Date of last nebuliser service:

Cleanliness of machine:

Correct cleaning/sterilization technique      yes/no

Correct administration of nebulised medication      yes/no

I-neb use:      yes/no      if yes assess computer data: result

Inhaler technique reviewed: yes/no                      comment:

Other medication previously used:

Medication location:

Spares available:    yes / no / some

Appropriate devices:                                      yes / no / some                      details:

Do parents supervise                                      yes / no / sometimes

Inappropriate amount of un-used med (stockpiling)    yes / no comment:

Prescription pick up rate:                                      <50% / 50 -80% / >80%

Details of medications issues discussed:

*(ie understanding of medication regime, knowledge of drug types, management of exacerbations etc)*

Advice given:

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### **Physiotherapy.**

Airway clearance technique:

ACBT ☐ Positioning ☐ Manual Techniques ☐ AD ☐ PEP MASK ☐ Pari PEP ☐ Flutter

☐ Acapella ☐ None ☐ Other ☐ Please specify...

**Frequency :**

**Duration:**

**Other techniques tried:**

**Exercise:**

**Posture Assessment:**

**Assessment of stress urinary incontinence:**

Other comments:

### **Nutritional Issues**

Enzyme replacement therapy                      yes/no

Type:    Dose:

Daily Routine of use (including at school):

Gastrostomy:                                      yes/no

Feeding regimen:

Previously identified issues yes / no  
If yes give details:

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- 1.
- 2.
- 3.
- 4.

**Signed:**



**Appendix 6 – Ivacafor proforma****IVACAFOR: COMMENCING TREATMENT**

NAME..... DOB.....  
 HOSP NO..... GENDER M/F

**Genotype** (circle as relevant):

G551D/ G178R/ S549N/ S549R/ G551S/ G1244E/ S1251N/ S1255P/ G1349D

2<sup>nd</sup> mutation .....

**PRE-DOSING DATA COLLECTION**

Date.....

FEV1 ..... (L) ..... (%)

FVC ..... (L) ..... (%)

Weight .....(kg)

Height ..... (cm)

**Sweat test** Date (within last 6 months) vol chloride  
 ...../..... ...../.....

**Liver function** Date (within last 6 months) .....  
 ALT..... AST ..... [normal range for each]

**Faecal pancreatic elastase-1:**..... Date (within last 6 months).....

**Ophthalmological exam?** Y/N

**Renal function normal?** Y/N

**Receiving interacting drugs?** Y/N If Y - which:

**PRESCRIBED DOSE:** Y/ other (reason):

[<14kg: 50mg granules bd; ≥14kg - <25kg: 75mg granules bd; ≥25kg: 150mg tablet bd]

**CHECK WHEN DISCUSSED WITH PATIENT:**

1. Potential drug interactions ☐
2. Take with fatty food ☐
3. Swallow whole/ do not chew ☐
4. Monitoring/ stopping criteria ☐

**RESEARCH: OPTIONAL**

1. Serum saved ☐
2. Urine saved ☐
3. Sputum obtained ☐
4. Lung clearance index performed ☐
5. Nasal brushing performed ☐
6. Nasal NO ☐

**Interacting drug list**

Azoles (itra/ vor/ posa)  
 Clarithromycin (not azithro)  
 Rifampicin  
 High dose steroids

**Consultant: NAME** ..... **SIGNATURE** .....

**Please send a copy to Prof Jane Davies – j.davies@rbht.nhs.uk**

**IVACAFTOR: MONITORING TREATMENT**

DATE.....

NAME.....

DOB.....

HOSP NO.....

GENDER M/F

Month/ year started treatment.....

**CURRENT DATA**

FEV1 ..... (L) ..... (%)

FVC ..... (L) ..... (%)

Weight .....(kg)

Height ..... (cm)

**Sweat test** [to be repeated at 1<sup>st</sup> follow up, then 6 months post initiation, then annually]

Date ..... vol ...../..... chloride...../.....

**Liver function** [to be repeated every 3 months for 1<sup>st</sup> year, then annually]

Date ..... ALT..... AST..... [normal range for each]

**Faecal pancreatic elastase-1** [to be repeated once 6 months post initiation]

Date ..... Result.....

**Ophthalmological exam** [to be repeated annually if <12 years old]

Date..... Normal? Y/N

**RE-CHECK:****Receiving interacting drugs?** Y/N If Y - which:**Prescribed dose:** Y/ other (reason):

[&lt;14kg: 50mg granules bd; ≥14kg - &lt;25kg: 75mg granules bd; ≥25kg: 150mg tablet bd]

**Check when discuss with patient**

1. Potential drug interactions
2. Take with fatty food
3. Swallow whole/ do not chew

☐  
☐  
☐
**Interacting drug list**

Azoles (itra/ vori/ posa)  
 Clarithromycin (not azithro)  
 Rifampicin  
 High dose steroids

**Doctor: NAME** .....**SIGNATURE** .....**Please send a copy to Prof Jane Davies – j.davies@rbht.nhs.uk**

## Appendix 7 - Drug Response Assessment testing

### DRUG RESPONSE ASSESSMENT TESTING PROFORMA

**\*\*\*THE TEST WILL NOT BE UNDERTAKEN WITHOUT ALL SHADED AREAS COMPLETED\*\*\***

APPROPRIATE PRESCRIPTION ATTACHED? ☐

PATIENT NAME: HOSPITAL NO:	DOB: PATIENT WEIGHT:	Inpatient/ Outpatient
DATE OF REFERRAL:                      REASON FOR REFERRAL: PRESCRIBER: <i>PRINT</i> : ..... <i>SIGN</i> ..... PRESCRIBER BLEEP/ EXT no. # CONSULTANT:		ALLERGIES

Terminal clean required post-test? (i.e. MRSA/ M. abscessus/B. cepacia): **YES / NO**

	Medicine	DOSE	Administered?	Initials for check
MEDICATION FOR TEST DOSE			YES    NO	
Diluent (e.g. 0.9% saline for Colistin/Amikacin etc)				
PRE TEST BRONCHODILATOR (if part of patient usual regime)			YES    NO	
POST TEST BRONCHODILATOR (please circle/indicate dose)	Salbutamol NEB INHALER	.....mg puffs	YES    NO	

**TO BE COMPLETED BY PHYSIOTHERAPIST:**

DATE OF TRIAL.....

SPIROMETRY APPROPRIATE?:    YES    NO

DEVICE USED? .....

TRIAL NOT COMPLETED? Why.....

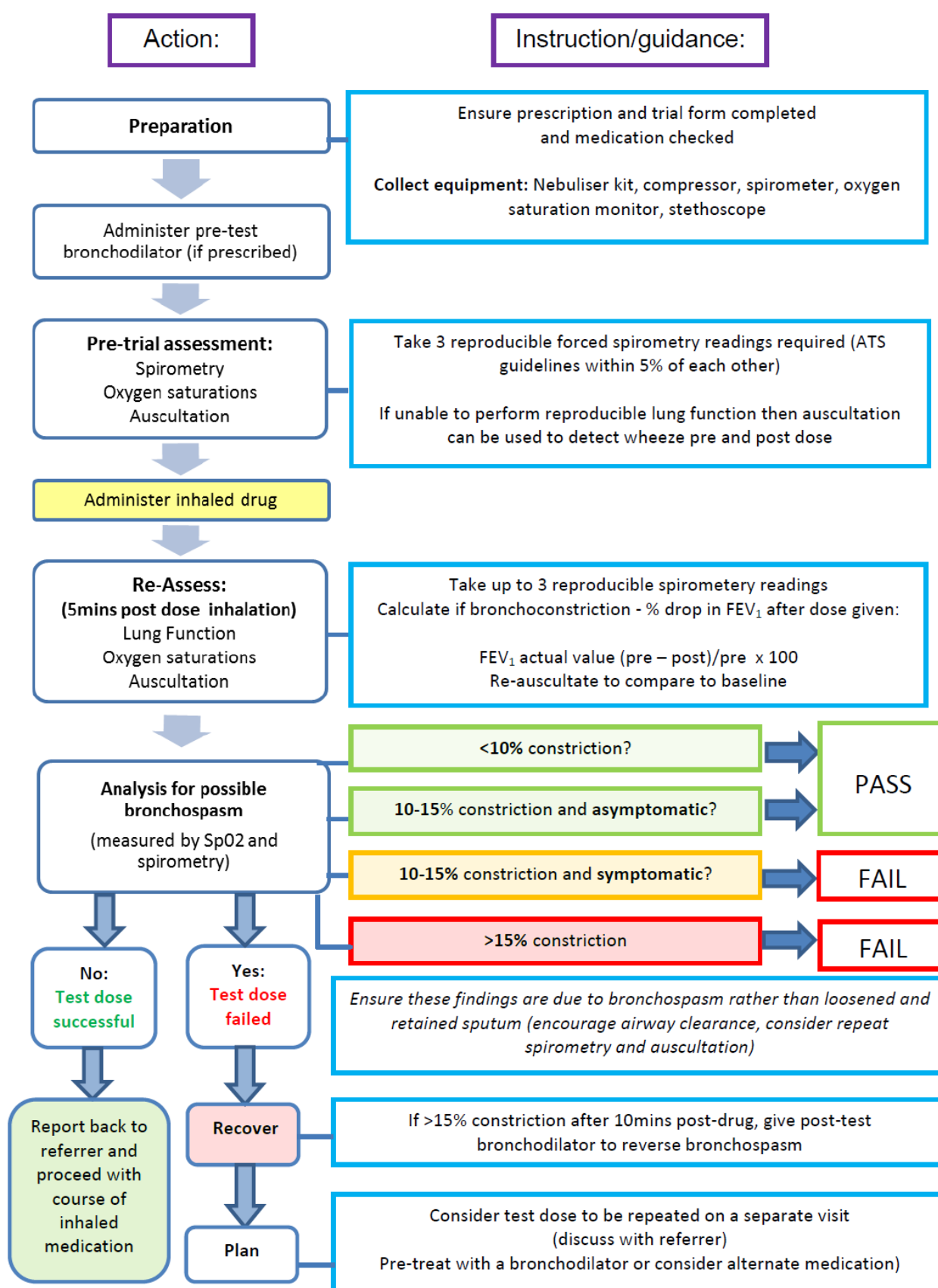
	FEV <sub>1</sub>	SpO <sub>2</sub>	Other (e.g. ausc/HR)
PRE test	L/min                      % pred.		
POST test	L/min                      % pred.		
% change	(see guidance attached)		
Symptoms/ comments			
10 mins post (if needed)	L/min                      % pred.		
% change			
Symptoms/ comments			

Inhalation technique discussed (i.e. DPI)

Explained potential adverse events ☐

Equipment explained/issued ☐

**Safe for Use:** Yes / No    Therapist signature \_\_\_\_\_ Date \_\_\_\_\_



**Appendix 8 - Guide for parents starting a child on a nebulised therapy**

## **Pseudomonas, Antibiotics and Nebulisers.....a guide for parents and carers**

This guide is designed for parents and carers whose child is starting nebulised antibiotics for the first time. It is intended to be read before your child starts antibiotic nebulisers. It is likely that these antibiotics will be required twice a day for at least a month so introducing them carefully is essential. We hope that this guide will help you and your child over the next few weeks.

At the back of this guide is a notes page for you to record useful information or any questions you may have for the team.

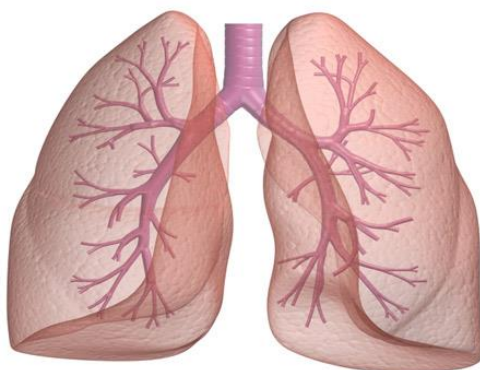
### **Pseudomonas...**

What is it? *Pseudomonas aeruginosa* to give it its full name (or *P aeruginosa* or *PsA*) is a bacterium that is often found in damp soil and stagnant water. As it is found in so many places it would be virtually impossible to prevent a child coming into contact with it at some point in their lives.

If your child's cough swab or sputum sample grows *Pseudomonas* the first treatment might be a course of oral antibiotics (Ciprofloxacin) as well as nebulised antibiotics i.e. antibiotics in a mist that your child breathes in.



### **Nebulised Antibiotics...**



Breathing in a mist of antibiotic medicine allows it to get directly to the lungs. The fine mist allows the smaller particles of medicine to get to the hard to reach parts of the lungs. A nebuliser also allows a higher dose of medicine to be given safely.

Nebulisers work best when your child is relaxed and breathing normally. We will give you some tips and ideas to get your child used to the nebuliser and the mask further on in this leaflet.

## Taking the nebuliser for the first time

In order to make sure that your child doesn't get wheezy when he/she has the nebulised antibiotics for the first time, we give the first dose at the Brompton or locally if your local hospital has this facility.

On the day of the first dose (the trial) your child will be seen as an Outpatient and they will be monitored whilst they have their first dose of nebulised antibiotic. For older children they will have a lung function test before and afterwards. Younger children will have their oxygen levels monitored with a pulse oximeter (as they would in clinic) and the physio will listen to their chest. Consider bringing treats for younger children as well as a favourite toy and DVD.



## Getting used to the nebuliser ....a staged approach

Once the Outpatient department has been notified that your child is starting nebulisers they will post a mask, filter and mouthpiece to you depending on the age of your child and if there is enough time. You will receive the nebuliser itself when you visit the Physiotherapy department.

### When you have received your mask, mouthpiece or other equipment try the following.....

**Stage 1** Play with the mask on a doll / toy, parents / carers. Once happy playing you can then put the mask to your child's face. Don't forget you can play with the mask at bath time as well



### After the trial and you have the nebuliser at home.....

**Stage 2** Look at the nebuliser together and play with the parts. Play with it for no more than five minutes. (Don't put any antibiotic medicine in at this stage)

**Stage 3** Choose a DVD to watch and 'nebulise' a doll, teddy or favourite toy

**Stage 4** Using the same DVD fully assemble the nebuliser and play with the mask on your child's face. Start with 10 seconds and build up. Give lots of encouragement and rewards such as stickers or sweets if appropriate.

**Stage 5** As above but use some of the **0.9% saline** in the nebuliser. Use a timer and see if your child can manage 30 seconds 3-4 times in a row. If so move onto the next stage.

**Stage 6** Your child should be ready to take the nebulised antibiotic. Keep giving lots of encouragement and praise. Your child might find it helpful to have a 5 minute warning before you start. Use the same DVD and then switch it off afterwards ready for the next time.



Remember, we want you and your child to be as comfortable and relaxed as possible so that the antibiotics can work really well. If your child is under 5 the homecare physiotherapists will ring you during this time but please contact the team if you feel you need extra support.

## Top Tips from other parents

**Best time** Think about when you can best fit the nebuliser into your everyday routine. Remember the antibiotic should be after physiotherapy. Try and pick a time when you will not be interrupted and are generally relaxed without time pressure

**Discussion** Is your child old enough to be prepared verbally e.g. "The doctors have asked you to take a new medicine to help with your cough. It is a special mist which you have to breathe in. You do it twice a day like cleaning your teeth."

**Consistency** Have a consistent approach. Same time, same place, same DVD etc.

**Rewards** With younger children (pre-school to 7 year olds) it can be really helpful to have prepared small immediate treats such as a sticker or sweet. What other younger (and older) patients seem to love is having a special jar/pot/bag used only to reward co-operation with the nebuliser. This can either be full of small treats (chocolate buttons/stickers/other items such as Moshi Monsters or Match Attack cards.) Alternatively it could be a lucky dip of instant privileges - for example watching Peppa Pig or reading a book with Mum/Dad. Older children may like the lucky dip approach or can be offered more planned rewards if preferred, such as staying up later or having a friend to play.

**Keep Calm** Keeping calm yourself will help your child to learn quickly to get used to using the nebuliser. Even if underneath you do not feel calm (we do understand that your child being prescribed nebulised antibiotics may be difficult for you for a number of reasons) try to 'act' calm. Think about your movements, tone of voice and what you are saying.

**Get ready** Take time to get used to the equipment. Make sure you have everything ready before you start. At the beginning your child may be worried that you are using a needle to mix up the medicine so this is best done out of sight. Give a 5 minute warning.

**Distraction** Have other means of distraction handy as well as a DVD e.g. books and toys. You will need to bring these with you to the trial appointment as well.

**When things go wrong** If at any time during the 'stages' your child becomes distressed, remove the nebuliser without comment. It is important not to 'reward' the child



by giving them a cuddle, or getting cross with them. Just walk calmly away and say 'that's ok, we will try again next time'. You may find it helpful to go back a stage. Please contact one of the people on the Useful Contacts list below to discuss further.

## FAQs...

### ***Can I give the nebuliser to my child when they are asleep?***

There needs to be exceptional circumstances when this may work best but there are reasons why it may not be the most helpful thing to do. Please do not do it because your child becomes distressed when they have the nebuliser while awake - their fears are likely to be heightened by being woken by the nebuliser. If this is the only way you are able to ensure that your child co-operates with the nebuliser, please do contact one of the people on the Useful Contacts list below for some suggestions about how to help with this.

### ***How do I wash the equipment?***

Keeping your nebuliser clean is vitally important. Full details will be given by your physiotherapist at the trial.

**If despite following all these guidelines your child is finding the nebuliser difficult please let your homecare team know and we will work with you to make it successful.**

## Useful Contacts...

Homecare Physiotherapists	Emma Dixon	07970 269452
	Nicky Murray	07791 584749
Homecare nursing team	Katie Dick	07971 224068
	Jackie Francis	0207 351 8755
	Laura Hayers	07973 173969
	Karen Henney	07971 224068
	Jo Gregory	0207 351 8755
Sn Ward Physiotherapist	Nic Collins	0207 352 8121 Bleep 7304
Paediatric Clinical Psychology	Michele Puckey	020 7351 8251



## This image shows a single sheet of white paper with horizontal blue ruling lines. The lines are evenly spaced and run across the width of the page. There are no margins, text, or other markings on the paper.

the

240

## Appendix 9 – Gastrostomy care

*Adapted from Chelsea & Westminster Dept. of Paediatric Gastroenterology advice sheets*

### IMPORTANT

- With newly inserted gastrostomies if there are leaks of fluid around the tube, or pain on feeding, or new bleeding, **stop feed immediately** and telephone 020 3315 8000 Bleep 4441 or 4448 for urgent advice.
- Always wash hands with soap and water or alcohol gel before and after handling the tube or feeds (please be aware that extra hygiene care must be taken with jejunal feeding).

### Corflo 12 Fr Gastrostomy - PEG (percutaneous endoscopic gastrostomy)



### Daily care

- 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.
- 7 days after the surgery - gently rotate the tube 360° daily.
- Tape the tube to the abdomen.
- 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.

### Emergency care

- If the tube is pulled out a tube will need to be put in the stoma as it will close over in 1–2 hours.
- You have been supplied with a nasogastric tube - insert an inch length of this tube into the stoma and tape it down, then come to the hospital where a new tube can be inserted (there may be bleeding—if so place light pressure with a cloth at the exit site).

### Tube blockage

1. Warm water (meaning room temperature but not cold or hot water) in a large syringe flushing and aspirating back and forth.

2. Consider that the tube may be kinked so reposition and wait 30 minutes to allow for peristalsis in the small bowel and try step 1 again—it is worth during any of the unblocking stages to consider repositioning.
3. Warm water in a 2 or 5ml syringe applying gentle pressure while flushing then convert to a 20–50ml syringe and try flushing with the larger volume of water.
4. Try flushing with sparkling water 10–15mls in a 20–50ml syringe.
5. Use clog zapper as directed if works then flush with 30mls water.
6. Try clog zapper a second time and if successful flush with 30mls of water.
7. If any of the above fails please contact your local hospital or visit A&E.

### **Stomach swollen and/or feels hard (venting or decompression)**

Some children suffer from trapped wind. This gas can be released by decompressing the stomach via the gastrostomy tube.

- Take a 50ml syringe, remove plunger and connect the syringe to the end of the extension set.
- Unclamp the tube to start the venting (removing air out of stomach) process—this can be done for up to 3 minutes.

### **Leakage from gastrostomy site**

- Try venting the stomach to relieve pressure.
- Clean and dry around the stoma site thoroughly.
- Cover with alleyvn or lyofoam dressing.
- If leakage persists and is starting to irritate the skin, try to apply orabase paste/cavilon sticks around the gastrostomy stoma to protect the skin and continue to cover with alleyvn or lyofoam dressing.
- If leakage persists, please contact your community team for assistance.

### **MINI Gastrostomy (Button)**



### **Daily care**

- Clean daily around the exit site of the stoma using water and a soft cloth.
- It is important that the area is dried gently but thoroughly.
- Gently rotate the tube 360° daily.
- 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.
- Flush the tube before and after all feeds and medications with at least 5–10mls of water (please use less if your child is fluid restricted).
- Ensure all medications are in liquid form.
- Change the water in the balloon once a week with 2.5mls of water.

- Maintain oral hygiene with regular teeth brushing.
- The extension sets will need to be changed every 2 weeks, please clean once every 24 hours.
- The mini button needs to be changed every 4 months—it is your responsibility as a parent to inform the community nurse when this is due to be done.

### **Emergency care**

If the tube is pulled out a tube will need to be put in the stoma as it will close over in 1–2 hours. You have been supplied with a 10FR NG tube or 12Fr G-tube.

Please insert 1 inch or 3cm length of this tube into the stoma (gastrostomy hole) and tape it down—then come to the hospital where a new tube can be inserted. There may be bleeding—if so place light pressure with a cloth at the exit site.

### **Tube blockage**

1. Warm water in a large syringe flushing and aspirating back and forth.
2. Consider that the tube may be kinked so reposition and wait 30 minutes to allow for peristalsis in the small bowel and try step 1 again—it is worth doing any of the unblocking stages to consider repositioning.
3. Warm water in a 2 or 5ml syringe applying gentle pressure while flushing, then convert to a 20–50ml syringe and try flushing with the larger volume of water.
4. Try flushing with sparkling water 10–15mls in a 20–50ml syringe.

If any of the above fails please contact your local hospital or visit A&E.

### **Stomach swollen and/or feels hard (venting or decompression)**

Some children suffer from trapped wind. This gas can be released by decompressing the stomach via the gastrostomy tube.

- Connect the feeding extension set to the stomach port.
- Take a 50ml syringe, remove plunger and connect the syringe to the end of the extension set.
- Unclamp the tube to start the venting (removing air out of stomach) process—This can be done for up to 3 mins.

### **Leakage from gastrostomy site**

- Try venting the stomach to relieve pressure.
- Clean and dry around the stoma site thoroughly.
- Cover with alleyvn or foam dressing—preferably non-adhesive foam dressings please.
- If leakage persists and is starting to irritate the skin, try to apply orabase paste/cavilon sticks around the gastrostomy stoma to protect the skin and continue to cover with alleyvn foam dressing.
- If leakage persists, then please contact your community team for assistance.

### **Discharge stock**

- X10—2.5ml clear syringes for the balloon.
- X2–3 mini extension sets.
- 12fr gastrostomy G-tube or 10fr and 12fr nasogastric tube.
- Roll of tape—micropore or mepore and gauze.
- Please ask the community team to give parents a spare mini gastrostomy tube of the child's size—for example 12fr x 2cm.

## Dressing Instructions

Post Insertion of surgically placed low-profile MINI gastrostomy button or MICKEY PEG-J tube with T-fasteners.



Primary Mini Gastrostomy Button



Primary Mickey PEG-J tube with T fasteners

## Routine Care

- Initial dressing to be done 3–4 days post insertion.
- Thereafter, dressing needs to be carried out once a week for another 4 weeks
- Please instruct community team according.
- Child to be discharged with appropriate dressings and 2 feeding extension sets.

## Dressing instructions

- Change the water in the balloon every 2 weeks only when the T-fasteners are still in situ.
- Remove the old dressing, including disconnecting the feeding extension from the button.
- Clean the site using saline and gauze—please note to clean underneath the T-fasteners by sliding a wet gauze underneath the T-fasteners and moving the gauze sideways.
- Dry the site well including underneath the T-fasteners.
- Place jelonet or mepitel underneath each T-fastener only.
- Cut a medium size square amount of the alleyvn/foam dressing and attach this underneath the button. The foam dressing should be underneath the button and covering all the T-fasteners.
- Attach a new feeding extension and cover the whole dressing with IV 3000 (please note that part of the feeding extension is also covered with the IV 3000)—Up to 2 or 3 IV 3000 may be needed to secure the dressing.
- The T-fasteners usually fall off by themselves in the first 4 weeks—if the TT fasteners have not come off after 4 weeks they will need to be cut off (this is the same as removing sutures—community nurses are able to do this).
- The above dressing will still need to continue for up to 4 weeks even if all T-fasteners come off.
- After 4 weeks the water can now be changed in the balloon weekly—please refer to normal gastrostomy or PEG-J care after this.
- Please teach parent how to change the water in the balloon as they would not have done this - if you have any questions please contact the specialist nurse or the surgical team on 020 3315 8000 bleep 4988/4441 or 020 3315 8627.

## Appendix 10 - Consensus statements for management of CFSPID

Table 1

The 31 statements that achieved consensus. These recommendations guide management of infants in Group A (normal sweat chloride value ( $<30 \text{ mmol L}^{-1}$ ) and two *CFTR* gene mutations, at least one of which has unclear phenotypic consequence) and Group B (intermediate sweat chloride value ( $30\text{--}59 \text{ mmol L}^{-1}$ ) and one or no *CFTR* mutations). One statement (A12) did not achieve satisfactory agreement.

Group A, normal sweat chloride value ( $<30 \text{ mmol L}^{-1}$ ) and two *CFTR* mutations, at least one of which has unclear phenotypic consequences

- A1 Infants should be followed up in specialist CF clinic. If they are seen in a non-CF clinic they should be reviewed by a CF physician (or a physician with an interest in CF).
- A2 For infants attending a specialist CF clinic, policies should ensure that the infant is not exposed to any increased risk of cross infection.
- A3 Infants should undergo a repeat sweat test aged 6-12 months. Depending on genotype, a further sweat test may be considered in the second year of life.
- A4 Infants should be reviewed in clinic between 6 and 12 months of age, and thereafter annually (or more frequently, as indicated by clinical concerns or family anxieties).
- A5 Annual review should clinically assess growth, weight gain and respiratory condition. Biochemical or radiological investigations should only be undertaken if clinically indicated.
- A6 Families should be fully informed regarding their child's genetic and biochemical results. They should understand that their child does not have a definitive diagnosis of cystic fibrosis and that this will be reviewed annually.
- A7 Reflecting the absence of a clear diagnosis, the term "Cystic Fibrosis Screen Positive, Inconclusive Diagnosis (CFSPID)" should be used to describe these infants.
- A8 Clinicians should review the CFTR-2 website at the annual review for new information regarding the infant's genotype and discuss these findings with the family.
- A9 Families and the primary care physician should be given clear information as to how to contact the CF team in the following situations; failure to gain weight adequately, persistent loose stools or persistent respiratory symptoms (more than 2 weeks).
- A10 Children should receive routine childhood immunizations.
- A11 Children should not be exposed to cigarette smoke.
- A13 Children and their families should be encouraged to adopt a healthy lifestyle consistent with national guidance on exercise, nutrition and other aspects of public health policy.
- A14 Families should be offered a referral for genetic counselling.
- A15 Details of infants in this group should be kept on an appropriate national database.
- A12 Did not reach consensus (79% agreement). Respiratory cultures should be taken routinely at annual review and when clinically indicated.

Group B, intermediate sweat chloride value ( $30\text{--}59 \text{ mmol L}^{-1}$ ) and one or no *CFTR* mutations

- B1 Infants should be followed up in a specialist CF clinic. If they are seen in a non-CF clinic they should be reviewed by a CF physician (or a physician with an interest in CF).
- B2 For infants attending a specialist CF clinic, policies should ensure that the infant is not exposed to any increased risk of cross infection.
- B3 Infants should undergo a repeat sweat test aged 6-12 months.
- B4 Clinic follow-up may be 3-monthly, or less frequently depending on clinical assessment. The frequency of follow-up appointments may lessen with time, but children should be followed up annually as a minimum standard.
- B5 Annual review should clinically assess growth, weight gain and respiratory condition. Biochemical or radiological investigations should only be undertaken if clinically indicated.
- B6 Families should be fully informed regarding their child's genetic and biochemical results. They should understand that their child does not have a definitive diagnosis of cystic fibrosis and that this will be reviewed annually.

Table 1 (continued)

Group B, intermediate sweat chloride value ( $30\text{--}59 \text{ mmol L}^{-1}$ ) and one or no *CFTR* mutations

- B7 Reflecting the absence of a clear diagnosis, the term "Cystic Fibrosis Screen Positive, Inconclusive Diagnosis (CFSPID)" should be used to describe these infants.
- B8 Clinicians should review the CFTR-2 website at the annual review for new information regarding the infant's genotype and discuss these findings with the family.
- B9 Families and the primary care physician should be given clear information as to how to contact the CF team in the following situations; failure to gain weight adequately, persistent loose stools or persistent respiratory symptoms (more than 2 weeks).
- B10 Oral antibiotics should be provided when the infant has a cough (lower threshold than for the general population). The Primary care physician should be provided with clear guidance to this effect. If the cough persists for more than 2 weeks, the infant should be reviewed by the CF team, respiratory cultures taken and further investigation considered.
- B11 Children should receive annual influenza vaccine in addition to all routine childhood immunisations.
- B12 Children should not be exposed to cigarette smoke.
- B13 Respiratory cultures should be taken routinely at annual review and when clinically indicated.
- B14 Children and their families should be encouraged to adopt a healthy lifestyle consistent with national guidance on exercise, nutrition and other aspects of public health policy.
- B15 Parents should be informed of the sweat test result and advised that during periods of high sweat loss\*, dietary salt intake should not be restricted. (\* hot weather, increased physical activity, fever etc.).
- B16 Families should be offered a referral for genetic counselling.
- B17 Details of all children in this group should be kept on an appropriate database.

## Appendix 11 – Gene mutation nomenclature

Berwouts S et al. Mutation nomenclature in practice: findings and recommendations from the cystic fibrosis external quality assessment scheme. Hum Mutat 2011;32:1197-203.

Traditional nomenclature	HGVS nomenclature	
	cDNA name	Protein name
G85E <sup>a</sup>	c.254G>A	p.Gly85Glu
R117H <sup>a</sup>	c.350G>A	p.Arg117His
621+1G>T <sup>a</sup>	c.489+1G>T	
711+1G>T <sup>a</sup>	c.579+1G>T	
R334W <sup>a</sup>	c.1000C>T	p.Arg334Trp
R347P <sup>a</sup>	c.1040G>C	p.Arg347Pro
A455E <sup>a</sup>	c.1364C>A	p.Ala455Glu
I507del <sup>a</sup>	c.1519_1521del (c.1519_1521delATC)	p.Ile507del
F508del <sup>a</sup>	c.1521_1523del (c.1521_1523delCTT)	p.Phe508del
1717-1G>A <sup>a</sup>	c.1585-1G>A	
G542X <sup>a</sup>	c.1624G>T	p.Gly542X
G551D <sup>a</sup>	c.1652G>A	p.Gly551Asp
R553X <sup>a</sup>	c.1657C>T	p.Arg553X
R560T <sup>a</sup>	c.1679G>C	p.Arg560Thr
1898+1G>A <sup>a</sup>	c.1766+1G>A	
2184delA <sup>a</sup>	c.2052del (c.2052delA)	p.Lys684AsnfsX38
2789+5G>A <sup>a</sup>	c.2657+5G>A	
3120+1G>A <sup>a</sup>	c.2988+1G>A	
3659delC <sup>a</sup>	c.3528del (c.3528delC)	p.Lys1177SerfsX15
3849+10kbC>T <sup>a</sup>	c.3718-2477C>T	
N1303K <sup>a</sup>	c.3909C>G	p.Asn1303Lys
R1162X <sup>a</sup>	c.3484C>T	p.Arg1162X
W1282X <sup>a</sup>	c.3846G>A	p.Trp1282X
CFTRdel2,3	c.54-5940_273+10250del (c.54-5940_273+10250del21080)	p.?
E60X	c.178G>T	p.Glu60X
P67L	c.200C>T	p.Pro67Leu
R75X	c.223C>T	p.Arg75X
394delTT	c.262_263del (c.262_263delTT)	p.Leu88IlefsX22
405+3A>C	c.273+3A>C	
406-1G>A	c.274-1G>A	
444delA	c.313del (c.313delA)	p.Ile105SerfsX2
R117C	c.349C>T	p.Arg117Cys
Y122X	c.366T>A	p.Tyr122X
621+3A>G	c.489+3A>G	
G178R	c.532G>A	p.Gly178Arg
711+5G>A	c.579+5G>A	
L206W	c.617T>G	p.Leu206Trp
E217G	c.650A>G	p.Glu217Gly
852del22	c.720_741delAGGGAGAATGATGATGAAGTAC	p.Gly241GlufsX13
935delA	c.803del (c.803delA)	p.Asn268IlefsX17
991del5	c.859_863del (c.859_863delAACTT)	p.Asn287LysfsX19
F311del	c.933_935del (c.933_935delCTT)	p.Phe312del
1078delT	c.948del (c.948delT)	p.Phe316LeufsX12
G330X	c.988G>T	p.Gly330X
R334Q	c.1001G>A	p.Arg334Gln
T338I	c.1013C>T	p.Thr338Ile
1154insTC	c.1021_1022dup (c.1021_1022dupTC)	p.Phe342HisfsX28
R347H	c.1040G>A	p.Arg347His
R352Q	c.1055G>A	p.Arg352Gln
S364P	c.1090T>C	p.Ser364Pro
1259insA	c.1130dup (c.1130dupA)	p.Gln378AlafsX4
T5	c.1210-12T[5]	
G480C	c.1438G>T	p.Gly480Cys
Q493X	c.1477C>T	p.Gln493X
I502T	c.1505T>C	p.Ile502Thr
1677delTA	c.1545_1546del (c.1545_1546delTA)	p.Tyr515X
V520F	c.1558G>T	p.Val520Phe
S549R(A>C)	c.1645A>C	p.Ser549Arg
S549N	c.1646G>A	p.Ser549Asn
S549R(T>G)	c.1647T>G	p.Ser549Arg
Q552X	c.1654C>T	p.Gln552X
A559T	c.1675G>A	p.Ala559Thr
1811+1.6kbA>G	c.1680-886A>G	
1812-1G>A	c.1680-1G>A	
D579G	c.1736A>G	p.Asp579Gly
1898+3A>G	c.1766+3A>G	
1898+5G>T	c.1766+5G>T	
G622D	c.1865G>A	p.Gly622Asp

2055del9>A	c.1923_1931delinsA (c.1923_1931delCTCAAAACTinsA)	p.Ser641ArgfsX5
2143delT	c.2012del (c.2012delT)	p.Leu671X
2141insA	c.2010dup (c.2010dupA)	p.Leu671IlefsX18
2183AA>G	c.2051_2052delinsG (c.2051_2052delAAinsG)	p.Lys684SerfsX38
K710X	c.2128A>T	p.Lys710X
2307insA	c.2175dup (c.2175dupA)	p.Glu726ArgfsX4
2347delG	c.2215del (c.2215delG)	p.Val739TyrfsX16
W846X	c.2538G>A	p.Trp846X
Q890X	c.2668C>T	p.Gln890X
2869insG	c.2737_2738insG	p.Tyr913X
3120G>A	c.2988G>A	
3199del6	c.3067_3072del (c.3067_3072delATAGTG)	p.Ile1023_Val1024del
3272-26A>G	c.3140-26A>G	
L1065P	c.3194T>C	p.Leu1065Pro
R1066C	c.3196C>T	p.Arg1066Cys
R1066H	c.3197G>A	p.Arg1066His
R1070Q	c.3209G>A	p.Arg1070Gln
W1089X	c.3266G>A	p.Trp1089X
Y1092X(C>A)	c.3276C>A	p.Tyr1092X
M1101K	c.3302T>A	p.Met1101Lys
D1152H	c.3454G>C	p.Asp1152His
R1158X	c.3472C>T	p.Arg1158X
S1196X	c.3587C>G	p.Ser1196X
3791delC	c.3659del (c.3659delC)	p.Thr1220LysfsX8
G1244E	c.3731G>A	p.Gly1244Glu
3876delA	c.3744del (c.3744delA)	p.Lys1250ArgfsX9
S1251N	c.3752G>A	p.Ser1251Asn
S1255X	c.3764C>A	p.Ser1255X
3905insT	c.3773dup (c.3773dupT)	p.Leu1258PhefsX7
4016insT	c.3889dup (c.3889dupT)	p.Ser1297PhefsX5
G1349D	c.4046G>A	p.Gly1349Asp
4382delA	c.4251del (c.4251delA)	p.Glu1418ArgfsX14
I148T <sup>b</sup>	c.443T>C	p.Ile148Thr
T7 <sup>b</sup>	c.1210-12T[7]	
T9 <sup>b</sup>	c.1210-12T[9]	
I506V <sup>b</sup>	c.1516A>G	p.Ile506Val
I507V <sup>b</sup>	c.1519A>G	p.Ile507Val
F508C <sup>b</sup>	c.1523T>G	p.Phe508Cys

More details about relevance of different CF gene mutations are available from CFTR2 database. [www.cftr2.org](http://www.cftr2.org).



## Appendix 12 – Hot weather advice

The movement of salt and fluid through the cells in the body is altered in cystic fibrosis. This means high levels of salt can be lost through sweating. This is especially important to consider in hot weather and even more so if a child is running around a lot or exercising. Your child will sweat more, meaning the sodium level in the body can drop quite quickly, and this also increases the risk of dehydration.

### Symptoms of salt depletion

- Feeling tired
- Lethargic (floppy in infancy)
- Thirsty
- Finding it difficult to concentrate
- Headaches
- Irritable
- Loss of appetite
- Feeling sick or vomiting
- Cramps in limbs
- Sunken eyes

If your child vomits, has sunken eyes (dark circles) or is lethargic or floppy it is very important that you seek medical advice straight away as these are signs of DEHYDRATION or even HEATSTROKE.

### Prevention of salt depletion

When travelling to very hot dry countries, or when the weather in the UK is particularly hot and dry it is vital to give additional salt and fluids to ensure the sodium levels remain normal.

These are some of the ways you can help:

- Keep out of the sun between the hours of 11am and 3pm.
- Provide opportunities for rest during the hottest time of the day.
- Infants: Dioralyte (or equivalent) sachets are ideal. Dioralyte is for oral rehydration and can be bought over the counter in chemists and supermarkets.
- Children: Ensure your child drinks plenty of fluid. Water, dioralyte and isotonic sports drinks are all good options. If choosing sports drinks, opt for the 'light' versions for smaller children as these have lower sugar content.
- Encourage your child to wear a hat and use usual precautions to avoid sunburn, including high factor sun cream.
- Add extra salt to your child's food and give them salty snacks like crisps, marmite and cheese.

### Supplements

Salt supplements are available as a way of giving extra salt to children with CF. These are very effective when children are feeling tired or getting cramps due to hot weather.

- **Infants 0-12months:** Up to 2 sachets of Dioralyte per day. Each sachet is mixed with 200mls of water (use cooled boiled water if under 6 months). Once made up, Dioralyte can be kept in the fridge for 24 hours. This can be easier to achieve by giving 100ml twice a day to younger babies.

- **Children 1-7 years old:** 2 salt tablets per day during hot weather. For those who will not take tablets, Dioralyte can be used, 2–4 sachets per day.
- **Children over 7 years old:** 2–4 slow release salt tablets per day during hot weather.

### **Drugs & the sun**

By the way, don't forget some drugs sensitise the skin to sun burn e.g. ciprofloxacin and voriconazole, so very high factor sun cream **MUST** be used.

If you have any concerns or questions about salt loss or managing in hot weather please contact the CF Team. If you are travelling to a hot country it is important to let the team know as soon as possible to plan supplements if needed.

## Appendix 13 – Travel letters



A lifetime of specialist care

Royal Brompton & Harefield **NHS**  
NHS Foundation Trust

**Royal Brompton Hospital**

Sydney Street

London

SW3 6NP

T: +44 (0)20 7352 8121

F: +44 (0)20 7351 8473

Date:

### TO WHOM IT MAY CONCERN

Dear Sir/Madam,

**Re:**

This child has cystic fibrosis and is currently under our care at the Royal Brompton Hospital. It is therefore necessary that the family carries with them on holiday the child's medications and these may include needles, syringes and a nebuliser device.

If any further information is required, please do not hesitate to contact the department at the Royal Brompton Hospital on 0207-351 8755; or after 5pm phone 0207-352 8121 and ask for bleep 1237 (on call paediatric respiratory SpR).

Yours faithfully,

PRINT NAME:

**Signed:**



A lifetime of specialist care

Royal Brompton & Harefield **NHS**  
NHS Foundation Trust

**Royal Brompton Hospital**

Sydney Street  
London  
SW3 6NP

T: +44 (0)20 7352 8121

F: +44 (0)20 7351 8473

Date:

**TO WHOM IT MAY CONCERN**

Dear Sir/Madam,

**Re:**

This child has cystic fibrosis and is currently under our care at the Royal Brompton Hospital. It is therefore necessary that the family carries with them on holiday the child's medications and these may include needles, syringes and a nebuliser device.

The child also has diabetes. It is essential that the family carry diabetic equipment for blood glucose monitoring (including a small lancet) and medication (insulin pens with needles) in their hand luggage.

If any further information is required, please do not hesitate to contact the department at the Royal Brompton Hospital on 0207-351 8755; or after 5pm phone 0207-352 8121 and ask for bleep 1237 (on call paediatric respiratory SpR).

Yours faithfully,

PRINT NAME:

**Signed:**



A lifetime of specialist care

Royal Brompton & Harefield **NHS**  
NHS Foundation Trust

**Royal Brompton Hospital**

Sydney Street  
London  
SW3 6NP

T: +44 (0)20 7352 8121

F: +44 (0)20 7351 8473

Date:

**TO WHOM IT MAY CONCERN**

Dear Sir/Madam,

**Re:**

This child has cystic fibrosis.

When the patient named above was examined, he/she was fit to travel and I do not foresee any problems with his/her health whilst abroad.

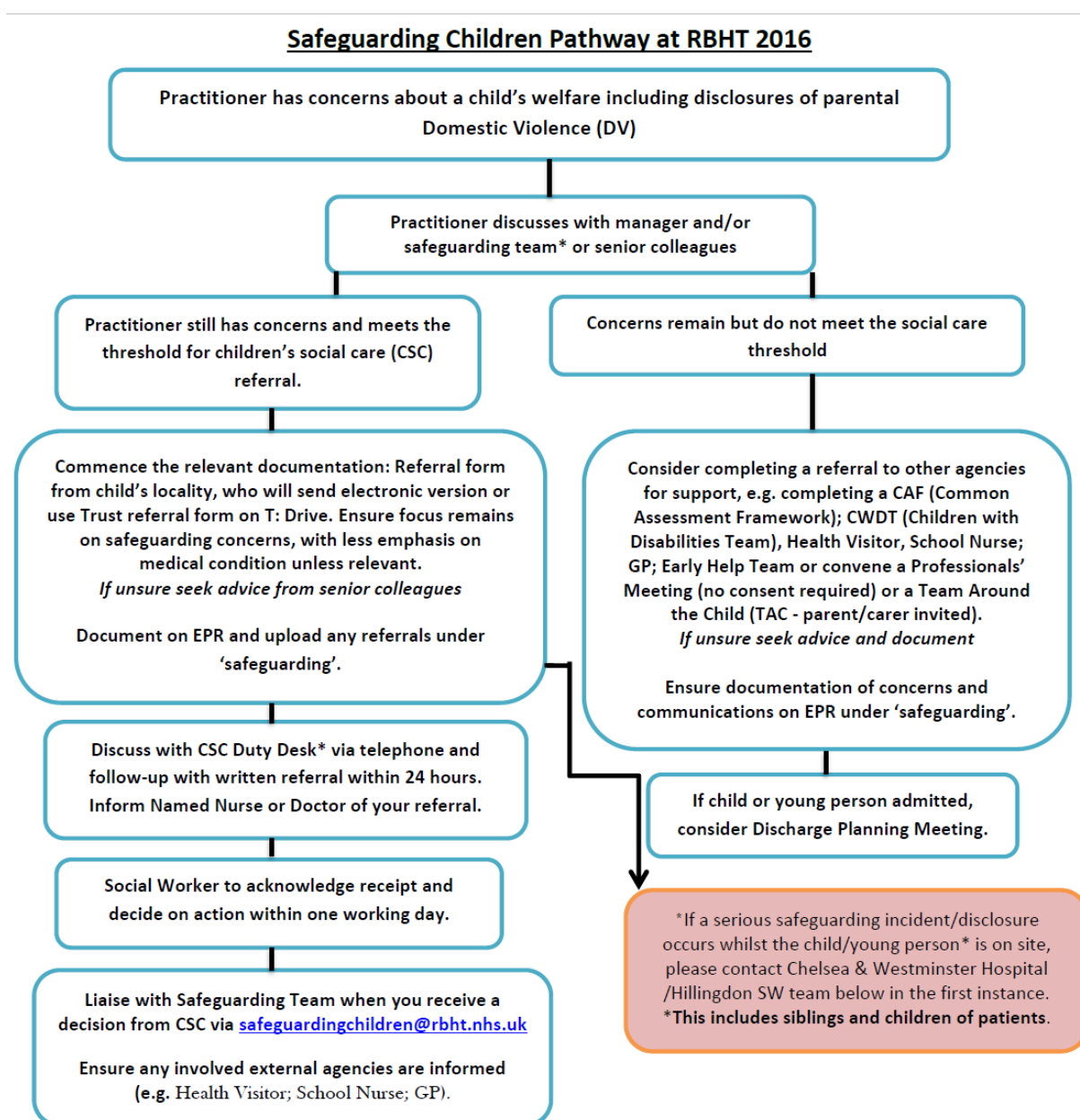
If any further information is required, please do not hesitate to contact the department at the Royal Brompton Hospital on 0207-351 8755; or after 5pm phone 0207-352 8121 and ask for bleep 1237 (on call paediatric respiratory SpR).

Yours faithfully,

PRINT NAME:

**Signed:**

## Appendix 14 – Safeguarding children pathway



### SAFEGUARDING ADVICE CONTACTS (as at January 2016)

[Safeguardingchildren@rbht.nhs.uk](mailto:Safeguardingchildren@rbht.nhs.uk)

• Michelle Nightingale: Trust Named Nurse for Safeguarding Children	0780 584 5693 Bleep: 1223
• Lorna Waite: Safeguarding Advisor	0789 622 0697 Bleep: 1278
• Ana Paz: Adult Safeguarding Lead Harefield Hospital	01895 823 737 ext. 5819
• Mark Rosenthal: Trust Named Doctor	0777 055 2881
• Jackie Lebidi: Rehabilitation & Therapies Social Worker Harefield Hospital	01895 823 737 ext. 6582
• <b>Chelsea and Westminster Hospital Social Work Team*</b> Mon to Fri 9-5pm ☎ 0203 315 1316 fax 0207 368 0215 Out of Hours EDT ☎ 0207 373 2227	
• <b>Hillingdon Social Work Team*</b> ☎ 01895 556644 Out of hours ☎ 01895 250 111	

Updated: January 2016

## Appendix 15 - Social security benefits

### 1. Disability Living Allowance for children

DLA provides help with the extra costs of bringing up a child with disability. It is paid on top of any other income and also gives access to other kinds of help. It is not means tested, so your income or savings will not be taken into account.

To make a new claim for DLA please Tel: 0345 712 3456 {press option 1}.  
For more information on DLA for children please go to [www.gov.uk](http://www.gov.uk).

There are two parts to DLA

- **Care component** - for children needing a lot of extra personal care, supervision or watching over because of their condition. This is paid at 3 different rates. It can be paid from the age of 3 months, or from birth for a terminally ill baby.
- **Mobility component** - for children aged 3 or over who cannot walk or have walking difficulties or aged 5 or over who need extra guidance or supervision walking outdoors.

#### 1) The care component

Your child can only qualify if they need more care or supervision than other children of the same age who are not disabled. The care component can be paid at one of three rates. The highest rate is paid if your child needs help throughout the day and throughout the night. The middle rate is paid if they need help throughout the day or throughout the night. The lowest rate is for a child if they need extra care for at least one hour per day.

#### 2) The mobility component

The mobility component can be paid at two different rates, each of which has very different qualifying conditions.

The higher rate

1. that a child is unable to walk
2. that a child is virtually unable to walk
3. 'the exertion required to walk would constitute a danger to life or would be likely to lead to a serious deterioration in health'

The lower rate

This rate can only be paid for children who are at least 5 years old. It is for children who can walk but need extra guidance or supervision outdoors. The difficulties can be due to physical or mental health problems.

### TIPS TO GIVE TO PARENTS

1. Don't lose benefit: the claim form will take some time to complete. Once you have lodged your DLA claim, if you have any further queries please contact the DLA Helpline on Tel: 0345 712 3456 {press option 3}.

2. Once at home, keep a diary of all the care given and time taken in connection with managing the child's condition. Include indirect and ancillary attention e.g. measuring doses, washing and drying and putting away of equipment.
3. Assume the person assessing the claim knows absolutely nothing about cystic fibrosis or children and is not a doctor.
4. Check out proposed answers with a professional familiar with daily care needs of a child with cystic fibrosis and if possible, with a local Citizen's Advice Bureau (CAB) or Welfare Rights Advisor.
5. Ask Cystic Fibrosis Trust for supporting letter.
6. You may want to send in the form by recorded delivery.
7. Keep a photocopy of completed form.

At 16 years of age when a child is in receipt of DLA they are usually contacted to complete the adult form. However now they will have to claim a PIP (Personal Independence Payment).

### **Carer's Allowance**

If a child receives either middle or higher rate of DLA care component either parent may claim Carers Allowance if he/she

- spends at least 35 hours per week caring for the child.
- passes U.K residence and presence tests.
- is not in full time education, is attending a course and/or having supervised study for 21 hours per week, not including meal breaks.
- if in work does not earn more than £110 per week once allowable expenses are deducted (these include tax, N.I, half of contribution to a pension scheme, some payments for child care to a person other than a close relative).

N.B Applying for benefits and appeals against decisions is complex and we recommend that families access appropriate specialist advice, from your local CAB or the Cystic Fibrosis Trust.

### **3. The Family Fund**

The Family Fund is funded by the Government to help families with severely disabled or seriously ill children. The Family Fund works within guidelines agreed by the trustees. These are concerned with the child's disability or illness, the family's financial circumstances and the kind of help given. The Family Fund cannot usually help if a family's income is more than £25,000 gross p.a. (figure June 2010). Disability Living Allowance and Child Benefit are not counted as income.



## Appendix 16 – NHSE National Service Specification

(accessed 12.7.16 - <https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/01/a01-spec-cystic-fibrosis-child.pdf>)



### SCHEDULE 2 – THE SERVICES

#### A. Service Specifications

<b>Service Specification No.</b>	A01/S/b
<b>Service</b>	Cystic Fibrosis (Children)
<b>Commissioner Lead</b>	
<b>Provider Lead</b>	
<b>Period</b>	12 Months
<b>Date of Review</b>	

#### 1. Population Needs

##### 1.1 National/local context and evidence base

Cystic fibrosis (CF) is the most common, life-limiting, recessively inherited disease in the UK, affecting about 7,700 people in England (1 in 2,500 live births). It results from mutations affecting a gene that encodes for a chloride channel called the cystic fibrosis transmembrane conductance regulator (CFTR), which is essential for the regulation of salt and water movements across cell membranes. Absent or reduced function of CFTR results in thickened secretions in organs with epithelial cell lining hence it is multi-system, although mainly affects the lungs, digestive system and vas deferens.

The airways become clogged with thick sticky mucus, which impairs the clearance of microorganisms. This leads to recurrent infection, inflammation, bronchial damage, bronchiectasis and eventually death from respiratory failure. Patients are often infected with *Staphylococcus aureus* and *Pseudomonas aeruginosa* but also by a number of other organisms, some of which are resistant to many antibiotics.

In about 85% of cases the pancreatic exocrine ducts become sufficiently blocked to cause maldigestion and intestinal malabsorption (pancreatic insufficiency). Infants may fail to thrive and older children and adults may become under-nourished.

About 15% of CF babies are born with a bowel blockage (meconium ileus) and some older patients develop recurrent blockages due to distal intestinal obstruction syndrome. Appetite is often adversely affected which is a problem as there is an

underlying increase in metabolic demands leading to a need for an increased energy intake.

There are a number of other complications: most males are infertile; a high proportion of older patients will develop CF-related diabetes requiring multiple daily insulin injections; chronic liver disease and portal hypertension may develop; joints can be affected (CF-arthropathy) and with age bones can be affected by reduced bone mineral density; nasal polyps and sinusitis are not uncommon. Behavioural and psychological problems that are often associated with any severe long-term medical condition may also be present.

Cystic fibrosis mainly affects Caucasian populations. It is uncommon in people of Afro-Caribbean origin and other ethnic groups. The carrier rate of a CF gene mutation in the UK is 1 in 25 with an incidence of 1 in 2,500 live births. Median population survival is 41.4 years (CF Registry 2012) and has been predicted to be at least 50 years for children born in 2000. However, the median age at death is currently 29 years and most people with CF who die each year are young adults, and occasionally some are children (3 in 2009).

## 2. Outcomes

### 2.1 NHS Outcomes Framework Domains & Indicators

<b>Domain 1</b>	<b>Preventing people from dying prematurely</b>
Forced Expiratory Volume in 1 second (FEV1)	Number of patients and % with FEV1 >85% by age group and sex
BMI centiles	Median BMI centile of centre cohort
Median Survival of National population	UK CF registry data
<b>Domain 2</b>	<b>Enhancing quality of life for people with long-term conditions</b>
Annual review and feedback	Number and % of patients who have had a post-annual review management plan with discussion
Accessibility of psychological support	Number and % of patients who have seen a psychologist within the past 12 months
<b>Domain 3</b>	<b>Helping people to recover from episodes of ill-health or following injury</b>
Timely initiation of treatment for exacerbation	% patients breaching standards of care for timing of admission.
Mucociliary clearance therapies	Number and % of children receiving mucociliary clearance therapies

<b>Domain 4</b>	<b>Ensuring people have a positive experience of care</b>
Admission to specialist unit/ward	% of patients admitted to a ward with specialist CF staff
Systematically measure patient and carer experience and satisfaction at a frequency driven by patient need	Systematic engagement and feedback on actions taken
<b>Domain 5</b>	<b>Treating and caring for people in safe environment and protecting them from avoidable harm</b>
Chronic Pseudomonas Aeruginosa infection (3+ isolates between two annual data sets)	% children with chronic pseudomonas infection
Pseudomonas (PA) Chronic PA is 3+ isolates between two annual data sets	Number and % of patients with Chronic PA infection on inhaled antibiotics by age group
Data Input	Number of complete annual data sets taken from verified data set expressed as a % of actual patient numbers

<p><b>3. Scope</b></p>
<p><b>3.1 Aims and objectives of service</b></p> <p><b>Aim</b></p> <p>The service aims to improve both life expectancy and quality of life for children with Cystic Fibrosis</p> <p><b>Objectives</b></p> <p>The service will deliver the aims of improving life expectancy and quality of life for children with CF by:</p> <ul style="list-style-type: none"> <li>• Making timely diagnosis (including in response to newborn screening) with appropriate counselling and psychological support to the child and their family.</li> <li>• Providing high quality proactive and preventative treatment and care to optimise lung function and nutritional status.</li> <li>• Ensuring a safe, cost effective, high quality service for the recipients of the services commissioned.</li> </ul>

- Ensuring equity of access to services for the CF population.
- Facilitating autonomy and transition from children's care to adult care and encouraging independent care.
- Supporting parents and families of children with CF, as well as the child.
- Supporting the child in helping them to manage their CF independently in order that they can aspire to a life less hindered by their condition and providing support to their families where appropriate.
- Ensuring effective communication between patients, families and the service providers.
- Providing a personal service, sensitive to the physical, psychological and emotional needs of the patients and their families.

This specification sets out the core elements of the service and standards by which CF services will be provided. Its purpose is not to define who the providers are. It defines the service to be provided and is supported by payment by results (PbR) currencies and funding streams. The specification will be used to define the models of care, agree the providers and establish robust shared care/network care arrangements where appropriate.

This service specification does not include generic healthcare services such as dental service, general practice services, ophthalmology services etc. required by individuals with CF which will be accessed in the same way as by the non-CF population. However, close liaison is vital between CF services and generic services and the CF service will have processes in place to ensure that communication takes place.

The providers of the service will demonstrate that they are meeting, or with the support of commissioners, are working towards meeting, the requirements of this service specification. Specialist CF Centres not currently meeting the specification will have a plan to do so by April 2014 which has been agreed with commissioners. Network care providers not currently meeting this specification will have a plan to do so by April 2016 which has been agreed with commissioners.

### 3.2 Service description/care pathway

The guiding principle within the service requirements is that all services will be provided in accordance with the CF Trust document "Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK" (2011). Care is directed by a specialist centre.

#### All Services

As a minimum:

- Every CF specialist centre will have a Director who is responsible for the service
- Every individual will have a named CF consultant in accordance with section 3.1 of the CF Trust document "Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK" (2011)
- The model of care must be governed by assurances of standards of care, access with care at home or close to home (where appropriate), and consistency and equity of access including the provision of home antibiotic services.
- Inpatient, day care, outpatient, diagnostic and homecare services will be co-ordinated to ensure continuity of care for the patient.



- Patients and their families will be seen in an age appropriate, comfortable environment, ensuring privacy, dignity and protection from cross infection.
- Patients and their families will be afforded the right to be fully informed of their condition, and to ensure that information is communicated in an understandable, sympathetic and age appropriate manner.
- Patients and their families will be encouraged to participate in the planning of their care.
- Patients and their families will be made aware how to contact their clinical teams and cystic fibrosis support groups.
- Within the required timescales, complete and accurate data is submitted to the UK CF Registry subject to patient consent.

### **Specialist Care Responsibilities**

Specialist centres will be responsible for providing the care plan for all patients. This includes the responsibility for determining when high cost drug (such as Domase, Tobramycin, Colistimethate sodium and Aztreonam lysine) will be prescribed, in accordance with the national commissioning policy.

All specialist centres need to be fully operational and in a position to take referrals. Clearly defined links must be in place with community services and hospitals. Centres serving more rural areas must be able to demonstrate an ability to provide either network care or outreach care for children where appropriate.

All main centres will need a Service Manager with dedicated time and responsibility for the CF service.

Specialist centres must be able to provide cover for annual leave, study leave and long term absence (e.g. long term sickness or maternity leave) of centre staff.

The service must be able to provide for urgent care needs and advice 24 hours a day, 7 days a week. This will include management of emergencies such as haemoptysis, pneumothorax and bowel obstruction (including Distal Intestinal Obstruction Syndrome).

Telephone advice must be available. Clear contact numbers will be given to patients to enable them to obtain advice from the specialist team at any time. During out of hours contact, a process must be in place to ensure a clear line of communication with a CF specialist. The specialist centre will agree arrangements for 24 hour services with network clinics to ensure equity of access across a network service.

### **Network Care**

Network care providers will typically have fewer numbers of patients than a specialist centre and so may have fewer staff. Care is therefore provided in partnership with the specialist CF centre that co-ordinates the network. Providers of network care for children will meet the requirements detailed in section 2.3 of the CF Trust document "Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK" (2011).

As a minimum the network service will have:

- A local CF multi-disciplinary team meeting the standards detailed in section 2.3 of the CF Trust document "Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK" (2011).
- Regular locally run CF multi-disciplinary team out patient clinics some of which will be joint clinics with the specialist CF centre that co-ordinates the network. Each patient will be seen by the full specialist multi-disciplinary team at least twice /year, either in a joint clinic at the network centre or at the specialist centre.
- Inpatient facilities suitable for routine CF admissions.
- Ward nurses with sufficient CF experience.

Annual reviews will take place at the specialist CF centre (unless the Network CF Clinic can provide all recommended clinical reviews and investigations, in which case it may be done jointly by both teams in the local centre).

Network care providers must be able to comply with the standards specified below for CF inpatient care.

Network care providers must be able to provide cover for annual leave, study leave and long term absence (e.g. long term sickness or maternity leave).

#### **Outreach Care**

Outreach care differs from Shared/Network Care. Outreach care is provided by the specialist centre using the facilities of a local provider. Outreach care does not require the local provider to have any CF specialist staffing.

Outreach care can be provided for children where geographical constraint makes attendance at the specialist centre difficult. The full multi-disciplinary team will be present at outreach clinics.

#### **Multi Disciplinary Approach to Specialist Paediatric CF Care**

Care will be delivered by a multi-disciplinary team of trained, experienced, specialist healthcare professionals who routinely care for a critical mass of CF patients at a specialist centre. The levels of staffing within multi-disciplinary teams must be in line with the recommendations set out in section 3 of the Cystic Fibrosis Trust document "Standards for Clinical Care of Children and Adults with Cystic Fibrosis in the UK" (2011).

#### **General**

All staff working within the CF service have an obligation to undertake continuing education and training to ensure updating of knowledge and skills. Core members of the CF multi-disciplinary team will be members of, and regularly contribute to, their relevant specialist interest group. Attendance at National/International specialist conferences will be demonstrable. It is recognised that not all staff will be able to attend every meeting every year; therefore the service will be able to demonstrate that there are internal mechanisms for feedback to the multi-disciplinary team.

Each member of each professional group must demonstrate continuing professional

development (CPD) in CF.

The service will have processes in place to ensure adequate workforce planning.  
The service will be able to demonstrate that an appraisal process is in place for all staff.

Study days and network meetings will be run by the service for core and wider workforce teams.

Regular audit of services must be performed. Specific audits may be requested by the commissioner. Participation in research studies is encouraged.

There will be clear succession planning for staffing to ensure continuity of care into the future.

Each professional group will be required to meet the minimum competencies defined within section 3 of the Cystic Fibrosis Trust "Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK" (2011) and the defined care pathway. In particular the following will be achieved:

#### **Composition of multi-disciplinary team**

##### **Service Clinical Director/Lead CF Consultant**

The consultant in charge of the paediatric service must have a certificate of training (CCT) in paediatrics with accreditation in paediatric respiratory medicine or equivalent in cumulative experience. He/she must also have at least three years experience working as a consultant in an accredited paediatric CF centre. He/she must be able to demonstrate active participation and attendance at national/international meetings and have a track record in teaching, audit and research. He/she must engage in the management of the service as a whole ensuring leadership of the multidisciplinary team and clinical governance of the service.

##### **Cystic Fibrosis Nurse Specialists**

CF Nurse Specialists must meet the standards identified in the CF Trust document "National Consensus Standards for the Nursing Management of Cystic Fibrosis" May, 2001.

Nurse Specialists will be members of the UK Cystic Fibrosis Nursing Association and must work within a CF multidisciplinary team.

All nurse specialists must be registered with the Nurses and Midwives Council and those working with children must have undergone specific paediatric training.

##### **Physiotherapists**

Specialist CF Physiotherapists must meet the standards identified in the Association of Chartered Physiotherapists in Cystic Fibrosis (ACPCF) document "Physiotherapy National Standards of Care for people with Cystic Fibrosis 2011". They will be members of the ACPCF special interest group.

##### **Dieticians**



Specialist CF Dieticians meet the standards defined in Nutritional Management of Cystic Fibrosis (April 2002) and will be members of the UK Cystic Fibrosis Nutrition Group.

### **Medical Staffing**

Specialist Consultants must have had training in a recognised CF Centre. They must be able to demonstrate active participation and attendance at national/international meetings and have a track record in teaching, audit and research. Specialist Consultants will also have CCT in paediatrics with accreditation in paediatric respiratory medicine.

Middle grade medical support will in most instances comprise a Trainee in paediatric respiratory medicine but may include a non- career grade with appropriate experience.

### **Pharmacists**

Pharmacists must be registered with the General Pharmaceutical Council and be a member of the Cystic Fibrosis Pharmacists Group. Pharmacists' practice will reflect Pharmacist Standards in Cystic Fibrosis Care 2011.

### **Clinical Psychologists**

Clinical Psychologists must be registered with the Health and Care Professions Council and be a member of the UK Psychosocial Professions in CF Group (UKPPCF).

### **Social Workers**

Social Workers must be registered with the Health and Care Professions Council and be a member of the UK Psychosocial Professions in CF Group (UKPPCF).

### **Provision of Care**

#### **Annual Review**

A full review must be undertaken by the specialist centre once a year, in line with the standards defined in The CF Trust document "Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK" (2011)

A personal care plan must be produced by a consultant and agreed with the patient as a result of every annual review undertaken.

#### **Outpatient Care**

Routine appointments should be every 2 to 3 months when stable and more often if not. The outpatient clinics are multidisciplinary with all patients being reviewed by the doctor and a CF nurse specialist, a physiotherapist and dietician at all routine reviews. There should be access to psycho-social support.

#### **Inpatient Care**

Beds in a ward suitable for cystic fibrosis care must be available within 24 hours for an emergency admission, as well as capacity to ensure elective and urgent admissions can be



managed appropriately. There must not be a delay of more than one week of the proposed admission date for a routine/planned/elective course of treatment.

Inpatient facilities will meet the standards defined in the Cystic Fibrosis Trust "Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK" (2011).

In particular, inpatients will:

- be entitled to and receive physiotherapy treatment 7 days a week if appropriate,
- have access to a specialist CF dietetic input at least twice a week, and more frequently if clinically appropriate,
- be seen by a CF consultant at least twice a week, and have access to consultant advice,
- be seen every day by a member of the medical team and have access to a Middle Grade doctor who is formally linked to the CF service,
- have access to a CF nurse specialist,
- have access to education facilities and support for school/college and examinations as appropriate,
- have access to appropriate play and recreational facilities 7 days a week,
- have provision for appropriate vascular access available at all times,
- have facilities for sedation for procedures (e.g. line insertion) available at all times,
- have access to facilities for exercise.

Every CF patient will be in their own room, with en-suite facilities to minimise the risk of cross infection and to enable them to continue life as normally as possible.

Patients must be admitted to wards that are familiar with the care and management of children with this condition and have developed the required expertise.

Nurses on the inpatient wards require specific expertise, and be committed to the CF service, with regular input and training from the specialist CF nurses. Patients will be admitted to a ward staffed by CF specialists or to wards that are familiar with the care and management of individuals with this condition and have developed the required expertise.

Provision will be made for inpatients to have a choice of food including high energy options and access to high energy mid meal snacks and drinks. This must include evenings and weekends.

#### **IV Antibiotics**

The service must have the ability to commence IV antibiotics on any day of the week.

An urgent course of treatment will be implemented within a maximum of 24 hours of the clinical decision being made.

There must not be a delay of longer than one week of the proposed admission date for a routine/elective/planned course of treatment.

Where appropriate, IV antibiotics may be provided at home, following receipt of the initial dose at the specialist CF centre or network care hospital.

**Homecare**

The life long multi-system nature of cystic fibrosis means that a complex regimen of home treatment is often recommended. Many patients and families require regular and consistent outreach from community services to support them in this care. This will include:

- Support in the community by the specialist CF multi- disciplinary team.
- Open access to nursing care in the community. This may be a CF nurse specialist from the CF service, or local Community nurses including children's nurses who have specific training, experience and supervision in CF.
- Patients undertaking home IV antibiotic therapy will have a formal assessment of suitability. This will include formal training and an assessment of competency of the patient and their carers in administering the IVs as well as the suitability of the home environment. There must also be planned review and assessment by the prescribing physician to ensure efficacy of each course of home IV antibiotics.
- Support for patients receiving overnight enteral feeding.
- Care of indwelling vascular access devices, gastrostomies and other stoma.
- Physiotherapy input where appropriate.
- Liaison with nurseries, school or college for patients still in education.
- Support through times of change in an individual's health including introduction of treatment for diabetes or home oxygen therapy and end of life care.

Where clinically appropriate home treatment is encouraged.

**Outpatient and Day Case Facilities**

The service will ensure that the facilities are available to support the best quality CF service allowing seamless care between the home and hospital. Thus patients can be seen routinely in an outpatient facility but there must be provision for urgent review and providing the first dose of an antibiotic course either in the outpatients or a day case facility or ward.

The facilities must take the need for infection control into consideration and demonstrate compliance with section 4.1 of the Cystic Fibrosis Trust "Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK" (2011) when providing facilities for annual reviews, treatment, day case etc. This will include ensuring that CF patients are not kept waiting in communal waiting areas and that they remain segregated from each other at all times so as to minimise the risk of cross infection.

**Equipment**

The service will ensure that all relevant equipment is available, maintained and kept up to date in order that patients can receive and make use of appropriate equipment as well as treatment. In particular, the service will ensure that the following equipment is available as required:

The service will ensure that there is access to the provision of high quality spirometry (i.e. meeting UK/EU standards) for all appropriate patients. Access will be available to the home care team to enable the monitoring of selected patients in the home with oxygen saturation monitors and home spirometry.

Patients who need home oxygen therapy will receive timely assessment and prescription of oxygen according to the National Home Oxygen service.

Individual patients will have access to a range of clinically appropriate airway clearance devices.

There will be a comprehensive nebuliser service, which aims to provide devices that deliver drugs in a fast and efficient manner. The service will also be able to provide a range of mechanical devices required to provide intermittent positive pressure breathing and non-invasive ventilation where needed.

Individual patients will have access to blood sugar monitors and continuous glucose monitoring systems (CGMS). Inpatient access to enteral feeds, feeding pumps, nasogastric (NG) tubes, percutaneous endoscopic gastrostomy (PEG) tubes and gastrostomy buttons.

GPs will provide NG tubes, feeds and feeding pumps and giving sets for enteral feeding through an approved/agreed contractor or local community nursing service.

### **Diagnostics**

The service will have access to all appropriate specialist CF diagnostic services, including:

- A microbiology laboratory that meets the 'Laboratory Standards for Processing Microbiological Samples from People with Cystic Fibrosis. First edition. September 2010.' and that routinely cultures for recognised CF pathogens such as *Burkholderia cepacia* complex and also performs tobramycin levels.
- Specialist radiology services, including contrast GI studies for bowel obstruction, ventilation perfusion scans, CT thorax, angiography, specialist liver scans, dual energy X-ray absorptiometry (DXA) bone scans and interventional services.
- A laboratory that performs specialist biochemical analysis such as faecal elastase and complies with the Association for Clinical Biochemists guidelines on performance 2003 of sweat tests.
- Specialist lung function laboratory that will test patients as well as provide support and training for those staff performing spirometry in the clinic setting.
- Epithelial ion transport testing (where required this facility will be available by collaborative arrangements with an appropriately equipped specialist CF Centre).
- Facilities to undertake bronchoscopy.

### **Other aspects of Paediatric CF Specialist Care**

#### **Diabetes Care**

Management of CF related diabetes will be in accordance with the document 'Management of Cystic Fibrosis-related Diabetes Mellitus (2004)'. In particular:

- There will be joint management between the CF multi-disciplinary team and a diabetes specialist experienced in the management of CF related diabetes (CFRD).

The provider must have a documented protocol which describes how CFRD will be identified.



The provider will undertake an annual audit which demonstrates compliance with the protocol.

### **Transitional Care**

Transition from paediatric to adult care is the norm for all patients. Transition will be planned with the patient and their parent(s)/carer(s) with due regard to patient choice. There should be an underlying assumption that transition is natural and expected. All parents/carers will be made aware as early as possible that transition into adult services will take place.

Arrangements for transition to adult services will commence from the age of 12 years and will be completed by the age of 18, when responsibility for care transfers to the specialist adult cystic fibrosis centre. The specialist paediatric cystic fibrosis centre responsible for the care of the child will be responsible for ensuring that transition arrangements are put in place for each child. It is particularly important that these arrangements are carefully co-ordinated where the patient has had the majority of their care provided at a paediatric network clinic.

Every specialist paediatric CF service will have a formal policy for transition that is agreed with all specialist adult CF services to which their patients transfer.

The specialist paediatric CF centre will ensure the following:

- Early discussion with the patient and carers about the process of transition. Options for adult care will be detailed. The age for transition will be flexible but agreed 2-4 years in advance, with the intention to complete before 18th birthday.
- Notification to the adult centre of intention to proceed with transition.
- Copies of letters and the annual review report are provided to the adult centre at least in the year prior to the anticipated transition clinic.
- There is documented paediatric and adult multi-disciplinary team member liaison, involving all multi-disciplinary team groups.
- There is the opportunity to visit the adult centre, to meet key multi-disciplinary team members and view both IP and OP facility. Such a visit could be repeated if requested.
- There is a joint clinic with detailed clinical handover.

Specialist adult CF centres will demonstrate that they are actively engaging in the transition process for each child via an annual audit report to commissioners of the experience of patients who transitioned during the year.

### **Surgery**

The decision to undertake surgery for patients with CF must be made jointly between the relevant surgeon, the CF clinicians and the child and their parents or carers. Acute admissions for acute abdominal pain will be managed by the CF team, in collaboration with other relevant clinicians. Where possible, surgical procedures should be undertaken at a hospital which also provides a CF service. If this is not possible, full access to CF specialists must be available to ensure that the child's CF needs are fully taken into account, including during any post operative period of inpatient care. A clear care plan must be developed, with regular contact and review between the relevant parties.

The surgical units must have a protocol or guideline relating to children with CF which has been developed in collaboration with the CF service. This protocol will specify required

standards of cross infection control and dietary/physiotherapy support.

General anaesthetic must be undertaken by a paediatric anaesthetist with experience of CF, and conducted within appropriate facilities in accordance with the Royal College of Surgeons' publication regarding quality standards for paediatric surgery; Surgery for Children; Delivering a First Class Service (2008).

The surgical service must have access to a CF clinician, to ensure communication regarding any surgical procedure, before during and after the procedure.

### **Transplantation**

When the possibility of transplantation is appropriate, it will be discussed with the child and family as early as possible. Access to information will be readily available to patients and their families.

Referral to the transplant centre for further assessment, if appropriate, will be made as soon as potential candidacy has been assessed.

Work up for transplantation will be undertaken in line with the guidance, processes and pathways defined by the transplant centre.

### **Palliative Care**

Centres will demonstrate:

- Good working relationships with and access to the general palliative care team attached to the hospital/local hospice/local community team and their involvement in all such patients.
- Clear documentation of End of Life discussions.
- Access to bereavement support for families.
- Clinical review and debrief following a patient death.

### **Infection Control**

Policy and procedures must be in place to protect patients from the risk of cross-infection, both as in- and out-patients (Cystic Fibrosis Trust standards of care and subsequent updates to infection control standards). All children will be admitted to a facility which provides specialist CF care in single rooms with en-suite facilities.

### **Clinical Governance**

Clinical Governance will be demonstrated via:

- Microbiological surveillance to identify infection control issues and use of particular antibiotics.
- Proportion of patients with chronic *Pseudomonas* infection.
- Monitoring of lung function (FEV1) and rate of decline.
- Body Mass Index (as a percentile for children).
- Reviews of all deaths.

- Benchmarking with other similar centres, including use of the UK CF Registry data when available.
- Number and resolution times of complaints.
- Departmental risk register.

### General Paediatric Care

*When treating children, the service will additionally follow the standards and criteria outlined in the Specification for Children's Services (attached as Annex 1 to this Specification).*

### 3.3 Population covered

The service outlined in this specification is for patients ordinarily resident in England\*; or otherwise the commissioning responsibility of the NHS in England (as defined in *Who Pays?: Establishing the responsible commissioner* and other Department of Health guidance relating to patients entitled to NHS care or exempt from charges).

\* - Note: for the purposes of commissioning health services this EXCLUDES patients who, whilst resident in England are registered with a GP Practice in Wales, but INCLUDES patients resident in Wales who are registered with a GP Practice in England.

The Provider shall provide paediatric services for patients with cystic fibrosis. Paediatric services shall be provided for patients up to the age of 18.

### 3.4 Any acceptance and exclusion criteria and thresholds

Referrals can come from a number of sources, following the identification of a patient with suspected CF. These will include:

- Antenatal diagnosis of CF.
- A newborn screening result that suggests a high likelihood of CF.
- Clinical suspicion by a general paediatrician, GP or other hospital specialist.
- Neonatal diagnosis of meconium ileus.

Diagnostic services will be provided for patients suspected of having cystic fibrosis. Following referral with suspected CF, the service will be responsible for:

- Investigations leading to a rapid and clear diagnosis, where possible.
- Appropriate counselling of patients/parents.
- Early introduction of required treatment.

For the purposes of this specification, a cystic fibrosis patient is defined as:

- Having a confirmed or strongly suspected diagnosis of cystic fibrosis, which includes:
  - A compatible clinical history, supported by one or more of the following:
    - A positive sweat test
    - Two known disease forming CF gene mutations
    - Evidence of functional epithelial ion transport abnormality

### 3.5 Interdependencies with other services/providers

There is no requirement for co-location with other services

The service will provide access or referral to specialists within:

- Endocrinology, including diabetes (with an interest in CF related diabetes), with joint clinics available on a regular basis,
- Hepatology,
- Gastroenterology,
- Rheumatology,
- ENT,
- Vascular services,
- Thoracic surgery,
- Palliative care,
- Clinical genetics,
- Transplantation services,
- Psychiatry,
- Paediatric Surgery,
- Gynaecology,
- Renal services,
- Anaesthetic services,
- Gastro-intestinal surgery,
- Pre-natal and new-born screening services.

If not available at a network care centre, processes must be in place to demonstrate clear pathways including Out of Hours/Emergency Care.

#### 4. Applicable Service Standards

##### 4.1 Applicable national standards e.g. NICE

###### Core Standards

The following standards are regarded as core standards and need to be achieved in order for a contract to be awarded for CF services. Where the remaining standards in this specification are currently met, they must continue to be met. Where the remaining standards in this specification are not met they will need to be met over time. In such cases the provider will agree with the commissioner a detailed development plan for achieving them (see section 2.1.5).

Every specialist centre must have a Director responsible for the service.

The CF multidisciplinary team (minimum of doctor, nurse specialist, physiotherapist and dietician) must be available for care of in- and out-patients. All children will be seen by a specialist physiotherapist and dietitian at each routine clinic visit.

Policy and procedures must be in place to protect patients from the risk of cross-infection, both as in- and out-patients. All children will be admitted to a facility which provides specialist CF care in single rooms with en-suite facilities

Microbiological analysis of respiratory samples and age appropriate lung function must be carried out at all out-patients visits.



Within the required timescales, the service will meet the minimum dataset requirements of the UK CF Registry (subject to patient consent).

**Network clinics** - There will be regular locally run CF multi-disciplinary team outpatient clinics some of which will be joint clinics with the specialist CF centre that co-ordinates the network. Each patient will be seen by the full specialist multi-disciplinary team at least twice /year, either in a joint clinic at the network centre or at the specialist centre.

#### **4.2 Applicable standards set out in Guidance and/or issued by a competent body (e.g. Royal Colleges)**

The services within this specification will be provided with reference to the following publications:

- The CF Trust document "Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK" (2011)
- National Consensus Standards for the Nursing Management of Cystic Fibrosis. May 2001.
- Nutritional Management of Cystic Fibrosis. April 2002.
- Association of Chartered Physiotherapists in Cystic Fibrosis document "Physiotherapy National Standards of Care for people with Cystic Fibrosis 2011"
- Clinical Care Pathway
- Management of Cystic Fibrosis-related Diabetes Mellitus (2004)
- Department of Health National Definition Set for Cystic Fibrosis (2009)
- Standards of care for patients with cystic fibrosis: A European consensus
- Pharmacist Standards in Cystic Fibrosis Care 2011
- Medicines Optimisation: Helping patients to make the most of medicines - Good practice guidance for healthcare professionals in England.  
<http://www.rpharms.com/promoting-pharmacy-pdfs/helping-patients-make-the-most-of-their-medicines.pdf>

These standards may change over time and as required, the service specification and service level agreements will be updated to reflect such changes.

The service will meet and maintain national quality standards and any other national quality requirements that may from time to time be specified including multi-disciplinary Peer Review.

The service will meet the minimum dataset requirements of the UK CF Registry so as to enable all patients in the service to annually be assigned a banding. The bandings are linked to the appropriate national tariff will be used by commissioners for funding purposes. Detailed information on what is and is not included in the national tariff can be found in the Department of Health document "Payment by Results Guidance for 2011-12" This information may be superseded by subsequent guidance:  
[http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/documents/digitalasset/dh\\_126157.pdf](http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_126157.pdf)

### **5. Applicable quality requirements and CQUIN goals**

**5.1 Applicable quality requirements (See Schedule 4 Parts A-D)**

**5.2 Applicable CQUIN goals (See Schedule 4 Part E)**

### **6. Location of Provider Premises**



<b>The Provider's Premises are located at:</b>
<b>7. Individual Service User Placement</b>

ADOPTED

## **ANNEX 1 TO SERVICE SPECIFICATION:**

### **PROVISION OF SERVICES TO CHILDREN**

#### **Aims and objectives of service**

**This specification annex applies to all children's services and outlines generic standards and outcomes that would be fundamental to all services.**

The generic aspects of care:

The Care of Children in Hospital (Health Service Circular 1998/238) requires that:

- Children are admitted to hospital only if the care they require cannot be as well provided at home, in a day clinic or on a day basis in hospital.
- Children requiring admission to hospital are provided with a high standard of medical, nursing and therapeutic care to facilitate speedy recovery and minimize complications and mortality.
- Families with children have easy access to hospital facilities for children without needing to travel significantly further than to other similar amenities.
- Children are discharged from hospital as soon as socially and clinically appropriate and full support provided for subsequent home or day care.
- Good child health care is shared with parents/carers and they are closely involved in the care of their children at all times unless, exceptionally, this is not in the best interest of the child. Accommodation is provided for them to remain with their children overnight if they so wish.

#### **Service description/care pathway**

All paediatric specialised services have a component of primary, secondary, tertiary and even quaternary elements.

The efficient and effective delivery of services requires children to receive their care as close to home as possible dependent on the phase of their disease.

Services should therefore be organised and delivered through "integrated pathways of care" (National Service Framework for children, young people and maternity services (Department of Health & Department for Education and Skills, London 2004))

#### **Interdependencies with other services**

All services will comply with *Commissioning Safe and Sustainable Specialised Paediatric Services: A Framework of Critical Inter-Dependencies* – Department of Health (DH)

#### **Imaging**

All services will be supported by a 3 tier imaging network ('Delivering quality imaging services for children' DH 13732 March 2010). Within the network:

- It will be clearly defined which imaging test or interventional procedure can be performed and reported at each site
- Robust procedures will be in place for image transfer for review by a specialist radiologist, these will be supported by appropriate contractual and information governance arrangements
- Robust arrangements will be in place for patient transfer if more complex imaging or intervention is required
- Common standards, protocols and governance procedures will exist throughout the network.
- All radiologists, and radiographers will have appropriate training, supervision and access to continuing professional development
- All equipment will be optimised for paediatric use and use specific paediatric software.

### Specialist Paediatric Anaesthesia

Wherever and whenever children undergo anaesthesia and surgery, their particular needs must be recognised and they should be managed in separate facilities, and looked after by staff with appropriate experience and training.<sup>1</sup> All UK anaesthetists undergo training which provides them with the competencies to care for older babies and children with relatively straightforward surgical conditions and without major co-morbidity. However those working in specialist centres must have undergone additional (specialist) training<sup>2</sup> and should maintain the competencies so acquired<sup>3</sup> \*. These competencies include the care of very young/premature babies, the care of babies and children undergoing complex surgery and/or those with major/complex co-morbidity (including those already requiring intensive care support).

As well as providing essential co-dependent service for surgery specialist anaesthesia and sedation services may be required to facilitate radiological procedures and interventions (for example MRI scans and percutaneous nephrostomy) and medical interventions (for example joint injection and intrathecal chemotherapy), and for assistance with vascular access in babies and children with complex needs such as intravenous feeding.

Specialist acute pain services for babies and children are organised within existing departments of paediatric anaesthesia and include the provision of agreed (hospital wide) guidance for acute pain, the safe administration of complex analgesia regimes including epidural analgesia, and the daily input of specialist anaesthetists and acute pain nurses with expertise in paediatrics.

\*The Safe and Sustainable reviews of paediatric cardiac and neuro- sciences in England have noted the need for additional training and maintenance of competencies by specialist anaesthetists in both fields of practice.

### References

1. Guidelines for the Provision of Anaesthetic Services (GPAS) Paediatric anaesthetic services. RCoA 2010 [www.rcoa.ac.uk](http://www.rcoa.ac.uk)
2. Certificates of Completion of Training (CCT) in Anaesthesia 2010
3. Continuing Professional Development (CPD) matrix level 3

### **Specialised Child and Adolescent Mental Health Services (CAMHS)**

The age profile of children and young people admitted to specialised CAMHS day/in-patient settings is different to the age profile for paediatric units in that it is predominantly adolescents who are admitted to specialised CAMHS in-patient settings, including over-16s. The average length of stay is longer for admissions to mental health units. Children and young people in specialised CAMHS day/in-patient settings generally participate in a structured programme of education and therapeutic activities during their admission.

Taking account of the differences in patient profiles the principles and standards set out in this specification apply with modifications to the recommendations regarding the following:

- Facilities and environment – essential Quality Network for In-patient CAMHS (QNIC) standards should apply (<http://www.rcpsych.ac.uk/quality/quality accreditation audit/qnic1.aspx>)
- Staffing profiles and training - essential QNIC standards should apply.
- The child/ young person's family are allowed to visit at any time of day taking account of the child / young persons need to participate in therapeutic activities and education as well as any safeguarding concerns.
- Children and young people are offered appropriate education from the point of admission.
- Parents/carers are involved in the child/young persons care except where this is not in the best interests of the child / young person and in the case of young people who have the capacity to make their own decisions is subject to their consent.
- Parents/carers who wish to stay overnight are provided with accessible accommodation unless there are safeguarding concerns or this is not in the best interests of the child/ young person.

### **Applicable national standards e.g. NICE, Royal College**

Children and young people must receive care, treatment and support by staff registered by the Nursing and Midwifery Council on the parts of their register that permit a nurse to work with children (Outcome 14h Essential Standards of Quality and Safety, Care Quality Commission, London 2010)

- There must be at least two Registered Children's Nurses (RCNs) on duty 24 hours a day in all hospital children's departments and wards.
- There must be an Registered Children's Nurse available 24 hours a day to advise on the nursing of children in other departments (this post is included in the staff establishment of 2RCNs in total).

Accommodation, facilities and staffing must be appropriate to the needs of children and separate from those provided for adults. All facilities for children and young people must comply with the Hospital Build Notes HBN 23 Hospital Accommodation for Children and Young People NHS Estates, The Stationary Office 2004.



All staff who work with children and young people must be appropriately trained to provide care, treatment and support for children, including Children's Workforce Development Council Induction standards (Outcome 14b Essential Standards of Quality and Safety, Care Quality Commission, London 2010).

Each hospital who admits inpatients must have appropriate medical cover at all times taking account of guidance from relevant expert or professional bodies (National Minimum Standards for Providers of Independent Healthcare, Department of Health, London 2002). "Facing the Future" Standards, Royal College of Paediatrics and Child Health.

Staff must carry out sufficient levels of activity to maintain their competence in caring for children and young people, including in relation to specific anaesthetic and surgical procedures for children, taking account of guidance from relevant expert or professional bodies (Outcome 14g Essential Standards of Quality and Safety, Care Quality Commission, London 2010).

Providers must have systems in place to gain and review consent from people who use services, and act on them (Outcome 2a Essential Standards of Quality and Safety, Care Quality Commission, London 2010). These must include specific arrangements for seeking valid consent from children while respecting their human rights and confidentiality and ensure that where the person using the service lacks capacity, best interest meetings are held with people who know and understand the person using the service. Staff should be able to show that they know how to take appropriate consent from children, young people and those with learning disabilities (Outcome 2b) (Seeking Consent: working with children Department of Health, London 2001).

Children and young people must only receive a service from a provider who takes steps to prevent abuse and does not tolerate any abusive practice should it occur (Outcome 7 Essential Standards of Quality and Safety, Care Quality Commission, London 2010 defines the standards and evidence required from providers in this regard). Providers minimise the risk and likelihood of abuse occurring by:

- Ensuring that staff and people who use services understand the aspects of the safeguarding processes that are relevant to them
- Ensuring that staff understand the signs of abuse and raise this with the right person when those signs are noticed.
- Ensuring that people who use services are aware of how to raise concerns of abuse.
- Having effective means to monitor and review incidents, concerns and complaints that have the potential to become an abuse or safeguarding concern.
- Having effective means of receiving and acting upon feedback from people who use services and any other person.
- Taking action immediately to ensure that any abuse identified is stopped
- and suspected abuse is addressed by:
  - having clear procedures followed in practice, monitored and reviewed that take account of relevant legislation and guidance for the management of alleged abuse

- separating the alleged abuser from the person who uses services and others who may be at risk or managing the risk by removing the opportunity for abuse to occur, where this is within the control of the provider
- reporting the alleged abuse to the appropriate authority
- reviewing the person's plan of care to ensure that they are properly supported following the alleged abuse incident.
- Using information from safeguarding concerns to identify non-compliance, or any risk of non-compliance, with the regulations and to decide what will be done to return to compliance.
- Working collaboratively with other services, teams, individuals and agencies in relation to all safeguarding matters and has safeguarding policies that link with local authority policies.
- Participates in local safeguarding children boards where required and understand their responsibilities and the responsibilities of others in line with the Children Act 2004.
- Having clear procedures followed in practice, monitored and reviewed in place about the use of restraint and safeguarding.
- Taking into account relevant guidance set out in the Care Quality Commission's Schedule of Applicable Publications
- Ensuring that those working with children must wait for a full CRB disclosure before starting work.
- Training and supervising staff in safeguarding to ensure they can demonstrate the competences listed in Outcome 7E of the Essential Standards of Quality and Safety, Care Quality Commission, London 2010

All children and young people who use services must be:

- Fully informed of their care, treatment and support.
- Able to take part in decision making to the fullest extent that is possible.
- Asked if they agree for their parents or guardians to be involved in decisions they need to make.

(Outcome 4I *Essential Standards of Quality and Safety*, Care Quality Commission, London 2010)

### **Key Service Outcomes**

Evidence is increasing that implementation of the national Quality Criteria for Young People Friendly Services (Department of Health, London 2011) have the potential to greatly improve patient experience, leading to better health outcomes for young people and increasing socially responsible life-long use of the NHS.

Implementation is also expected to contribute to improvements in health inequalities and public health outcomes e.g. reduced teenage pregnancy and STIs, and increased smoking cessation. All providers delivering services to young people should be implementing the good practice guidance which delivers compliance with the quality criteria.

Poorly planned transition from young people's to adult-oriented health services can be associated with increased risk of non adherence to treatment and loss to follow-up, which

can have serious consequences. There are measurable adverse consequences in terms of morbidity and mortality as well as in social and educational outcomes. When children and young people who use paediatric services are moving to access adult services (for example, during transition for those with long term conditions), these should be organised so that:

- All those involved in the care, treatment and support cooperate with the planning and provision to ensure that the services provided continue to be appropriate to the age and needs of the person who uses services.

The National Minimum Standards for Providers of Independent Healthcare, (Department of Health, London 2002) require the following standards:

- **A16.1** Children are seen in a separate out-patient area, or where the hospital does not have a separate outpatient area for children, they are seen promptly.
- **A16.3** Toys and/or books suitable to the child's age are provided.
- **A16.8** There are segregated areas for the reception of children and adolescents into theatre and for recovery, to screen the children and adolescents from adult patients; the segregated areas contain all necessary equipment for the care of children.
- **A16.9** A parent is to be actively encouraged to stay at all times, with accommodation made available for the adult in the child's room or close by.
- **A16.10** The child's family is allowed to visit him/her at any time of the day, except where safeguarding procedures do not allow this
- **A16.13** When a child is in hospital for more than five days, play is managed and supervised by a qualified Hospital Play Specialist.
- **A16.14** Children are required to receive education when in hospital for more than five days; the Local Education Authority has an obligation to meet this need and are contacted if necessary.
- **A18.10** There are written procedures for the assessment of pain in children and the provision of appropriate control.

All hospital settings should meet the Standards for the Care of Critically Ill Children (Paediatric Intensive Care Society, London 2010).

There should be age specific arrangements for meeting Regulation 14 of the Health and Social Care Act 2008 (Regulated Activities) Regulations 2010. These require:

- A choice of suitable and nutritious food and hydration, in sufficient quantities to meet service users' needs
- Food and hydration that met any reasonable requirements arising from a service user's religious or cultural background
- Support, where necessary, for the purposes of enabling service users to eat and drink sufficient amounts for their needs
- For the purposes of this regulation, "food and hydration" includes, where applicable, parenteral nutrition and the administration of dietary supplements where prescribed
- Providers must have access to facilities for infant feeding, including facilities to support breastfeeding (Outcome 5E, of the Essential Standards of Quality and Safety, Care Quality Commission, London 2010)



All paediatric patients should have access to appropriately trained paediatric trained dieticians, physiotherapists, occupational therapists, speech and language therapy, psychology, social work and CAMHS services within nationally defined access standards.

All children and young people should have access to a professional who can undertake an assessment using the Common Assessment Framework and access support from social care, housing, education and other agencies as appropriate.

All registered providers must ensure safe use and management of medicines, by means of the making of appropriate arrangements for the obtaining, recording, handling, using, safe keeping, dispensing, safe administration and disposal of medicines (Outcome 9 Essential Standards of Quality and Safety, Care Quality Commission, London 2010). For children, these should include specific arrangements that:

- They are supported to have a health action plan
- Facilities meet the appropriate requirements of the Disability Discrimination Act 1995

They meet the standards set out in Transition: getting it right for young people. Improving the transition of young people with long-term conditions from children's to adult health services. Department of Health, 2006, London.



## Appendix Two

Quality standards specific to the service using the following template:

Quality Requirement	Threshold (trigger for breach)	Method of Measurement	Consequence of breach
<b>Domain 1: Preventing people dying prematurely</b>			
Children (above 5 years) attending a specialist CF centre should have a FEV1 of >85%	< 55%	UK CF Registry data	Internal review with report to commissioners External review for outliers
Median BMI percentile of centres should be 50% or greater	Median BMI percentile less than 50	UK CF Registry data	Internal review with report to commissioners External review for outliers
<b>Domain 2: Enhancing the quality of life of people with long-term conditions</b>			
All children should have an annual review and management plan discussed with the family	<85%	Self report dashboard	Internal review and submission of improvement plan
All children should have access to psychological support at annual review	<85%	Self report dashboard	Internal review and submission of improvement plan
<b>Domain 3: Helping people to recover from episodes of ill-health or following injury</b>			
All children over the age of 6 years should be offered inhaled mucolytic therapy	< 70%	UK CF Registry data	Internal review
There should be no delay (as defined by national service specification) in initiating IV antibiotic therapy for pulmonary exacerbation	Breach percentage >10%	Self report /dashboard/CQIN	Commissioner review
<b>Domain 4: Ensuring that people have a positive experience of care</b>			
All children requiring inpatient care should be admitted to a ward staffed by CF specialist staff (as defined by national specialist service specification)	<95%	Quality dashboard	Commissioner review
All specialist CF units should systematically measure patient and	Yes/No	Self report demonstrating systematic	Commissioner review

Quality Requirement	Threshold (trigger for breach)	Method of Measurement	Consequence of breach
carer experience and satisfaction at a frequency driven by patient need		engagement and feedback on actions taken	
<b>Domain 5: Treating and caring for people in a safe environment and protecting them from avoidable harm</b>			
Adherence to standards of care to prevent cross infection. Centres should have a low prevalence of chronic pseudomonas infection	>14%	UK CF Registry	Internal review with report to commissioners  Commissioner review for outliers
All children chronically infected with Pseudomonas Aeruginosa should receive inhaled antibiotic therapy. Percentage of patients with chronic PA on inhaled antibiotics by age group	< 85%	UK CF Registry data	Internal review with report to commissioners  Commissioner review for outliers

## **Appendix 17 - Payment by Results guidance**

This is the most comprehensive (and original) explanation of PbR for CF. Taken from –

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/214902/PbR-Guidance-2013-14.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/214902/PbR-Guidance-2013-14.pdf).

### **Cystic fibrosis**

704. We are introducing a year-of-care tariff for patients with cystic fibrosis (CF) by transitioning from non-mandatory to mandatory prices.

#### *Currency*

705. The CF currency is a complexity-adjusted yearly banding system with seven bands of increasing complexity. There is no distinction between adults and children.

#### *Banding*

706. Bandings are derived from clinical information including cystic fibrosis complications and drug requirements. The bands range from band one, for the patients with the mildest care requirements (involving outpatient treatment two to three times a year and oral medication) to band five, for patients at the end stage of their illness (requiring intravenous antibiotics in excess of 113 days a year with optimum home or hospital support).

707. The CF tariff is designed to allow specialist CF multidisciplinary teams to direct care in a seamless, patient centred manner, removing any perverse incentives to hospitalise patients who can be well managed in the community and in their home. Furthermore, it will allow early intervention, as per international guidelines, to prevent disease

progression for example through the use of anti-pseudomonas, inhaled/nebulised antibiotics and mucolytic therapy.

708. Patients are allocated to a band by the Cystic Fibrosis Trust using data from its national database, the UK CF Registry, and feeding it into a template that produces the banding.
709. Banding will be issued each February using the data input to the UK CF Registry. This information is based on a calendar year's data and will be used both to fine tune the planning assumptions made for the next financial year and for initial planning purposes for the following year. Access to the banding data from the registry and information on the number of patients being cared for must be made by the lead clinician in each trust.
710. The bands issued in February 2013 by the CF Registry will be the final bands for all patients for 2013-14 and will be used for contracting purposes. There will be no movement of patients between bands during any one financial year as a full year of data is required for a patient to be appropriately banded.
711. Each provider will be responsible for ensuring that there is sufficient quality data for a patient to be banded through the CF Registry.

#### *Patient numbers*

712. Each year there are likely to be changes in the number of patients in each band in the cohort of CF patients at any one centre. This may be due to increases and decreases in patient numbers due to births, transition from children's to adult services, natural patient movement from one area to another, transplantation and deaths. Whilst the tariff is payment for a year of care, in reality payments are most likely to be made in twelfths as part of contract payments. Changes in patient numbers will be addressed as follows:
  - (a) New births.  
Payment is calculated from the beginning of the month in which the patient is born. New births will be banded as 2A, which recognises the additional costs associated with diagnosis, care and treatment of a new patient. These patients will move to the band derived from the matrix process described above when the bandings are revised for the following year.
  - (b) Transition to adult services or another specialist CF centre.  
Clinical transition or transfer to another centre may take place at any time during the year. **For the purposes of payment** the two centres must agree a date at which responsibility of care will transfer. The date on which responsibility ceases must always be the last day of a calendar month and the date on which the new centre assumes responsibility for care must always be the first day

of the new calendar month. These finalised dates will be used by commissioners to cease payment to the original centre and commence payment to the receiving centre.

In some circumstances, such as where young people are away at university or patients need care whilst on holiday, there may not be a formal transfer of care, as an individual may not wish or need to have their care transferred to a new centre. Should treatment be required when someone is away from the centre responsible for their care, the hospital should submit reasonable costs to the responsible centre for the cost of the treatment provided and the responsible centre will be expected to pay for that care. This will be a provider to provider transaction.

- (c) Deaths. Payments for patients who die will cease at the end of the month in which they die.
- (d) Transplants. Heart and heart/lung, lung and other transplants have a separate commissioning mechanism. Payment of the CF tariff for patients receiving a transplant will cease at the end of the month in which they receive their transplant. Commissioning of any continuing care from a CF specialist centre following a transplant will be part of the transplant commissioning arrangements.

#### *Information on patient number variations*

- 713. Each provider will be responsible for informing commissioners of changes in patient numbers due to new births, newly diagnosed patients, transition and transfers, deaths and transplants to enable commissioners to reconcile payments on a regular basis. The UK CF Registry will be used to verify the changes reported by providers and ongoing validation of patient numbers will be undertaken through the CF Trust.
- 714. It will be incumbent upon providers to agree upon payment for any patient who has not formally transferred responsibility for their care to another centre.
- 715. Some patients may express a desire not to be registered with the CF Trust. If this is the case the provider will need to work with the CF Trust to discuss how the appropriate band can be established.

#### *What is included in the tariffs?*

- 716. The tariffs cover all treatment **directly related to cystic fibrosis** for a patient during the financial year. This includes:
  - (a) Admitted patient care and outpatient attendances (whether delivered in a specialist centre or under shared network care arrangements)



- (b) Home care support, including home intravenous antibiotics supervised by the CF service, home visits by the multidisciplinary team to monitor a patient's condition, eg management of totally implantable venous access devices (TIVADs), collection of mid-course aminoglycoside blood levels and general support for patient and carers
  - (c) Intravenous antibiotics provided during in-patient spells
  - (d) Annual review investigations.
717. Any episode directly related to CF specific care (admitted patient care or outpatient activity) will not attract additional activity based payments as these are included in the annual banded tariff, eg admitted for treatment of exacerbation of chest infection, admitted for medical treatment of CF distal intestinal obstruction syndrome, admitted with a new diagnosis of CF-related diabetes to establish a new insulin regimen.
718. For any patient admission or outpatient contact that is for the purpose of cystic fibrosis, the HRG is included in the Year of Care tariff regardless of whether it is one of the CF specific diagnosis driven HRGs or not. We would expect all outpatient CF activity is recorded against TFC 264 and TFC 343.
719. Some elements of services, included in the CF tariffs, may be provided by community services and not the specialist CF centre, such as home care support, including home intravenous antibiotics supervised by the cystic fibrosis service, home visits by the multidisciplinary team to monitor a patient's condition (eg management of totally implantable venous access devices (TIVADs)) and collection of mid-course aminoglycoside blood levels. In such cases there will need to be agreement between the relevant parties on reimbursement from the tariffs paid to the specialist CF centre.

*What is excluded from the tariffs?*

720. The following are excluded from the mandatory CF tariff:
- (a) High cost CF specific **inhaled/nebulised** drugs: Colistimethate sodium, Tobramycin, Dornase alfa, Aztreonam Lysine, Ivacaftor and Mannitol.
  - (b) Insertion of gastrostomy devices (PEG) and insertion of totally implantable venous access devices (TIVADs) are not included in the annual banded tariff. These surgical procedures should be reimbursed via the relevant HRG tariff.
  - (c) Neonates admitted with meconium ileus who are subsequently identified to have cystic fibrosis should not be subject to the CF tariff until they have been discharged after their initial surgical procedure. This surgical procedure should be reimbursed via the relevant HRG tariff. Once discharged after their initial surgical procedure subsequent CF treatment will be covered by the CF

tariff. Annual banding should not include the period they spent as an admitted patient receiving their initial surgical management.

721. CF patients may require medical input from other specialties for non-CF specific care. The costs relating to non-CF specific care are not included in the annual banded tariff. These episodes of care will be covered by tariffs assigned to the relevant HRG or TFC, eg obstetric care for a female patient with CF, activity associated with CF related diabetes, ENT outpatient review for nasal polyps and ENT surgery for removal of nasal polyps.

### *Drugs*

722. Prescription of the high cost drugs Colistimethate sodium, Tobramycin, Dornase alfa, Ivacaftor and Aztreonam Lysine that are used in the treatment of CF patients will be initiated by the specialist CF centre. Continuation of the prescription, whether from the specialist CF centre or the GP, will be by local arrangement.
723. Funding of Colistimethate sodium, Tobramycin, Dornase alfa, Ivacaftor and Aztreonam Lysine will be governed by the national commissioning policy. Commissioners will need to ensure that the arrangements are clear with each specialist CF centre for the continuing prescription of these drugs to enable the appropriate funding flow.
724. Where continuation of prescribing is left with the specialist CF centre, the use of home delivery systems should be encouraged.
725. GPs will continue to prescribe and fund all other chronic specific medication, for example long-term oral antibiotics, pancreatic enzyme replacement therapy and vitamin supplements.
726. There is a number of high cost antifungal treatments excluded from PbR, which are therefore not included in the CF tariff.
727. Costs associated with long-term nutritional supplementation via gastrostomy or nasogastric tube feeding are not included in the CF tariff.
728. Commissioning of nutritional supplements will continue to be the responsibility of CCGs. However there must be close liaison between the specialist CF centre and Primary Care to ensure the continued prescription of the most appropriate supplement.

### *Tariff principles*

729. CF care is provided on the basis of the following principles:
- (a) All patients will be registered with a CF specialist centre which will be responsible for all care directly related to the patient's CF.

- (b) CF centres will be responsible for ensuring that the data for all the patients for whom they are responsible are entered on the national CF database, the UK CF Registry. If patients/carers do not wish to have their data to be entered on the UK CF Registry, they must express this wish in writing to their clinician at the specialist centre and the centre will need to work with the CF Trust to establish an appropriate band.
- (c) All CF treatment and care for both adults and children will be delivered by clearly designated providers.
- (d) For adults all the treatment and care will be the responsibility of the specialist centre with no shared care arrangements in place.
- (e) For children, the treatment centre will initiate all treatments with treatment and care being delivered in either a centre or designated district general hospitals within the framework of network care. Inter-trust service level agreements will be in place to support these arrangements.
- (f) The providers of CF services – centres and network units – will need to comply with the relevant service specification and meet the service standards.
- (g) Access to and eligibility for CF specialist drugs will be determined by national commissioning policy.
- (h) The relevant CF centre will be responsible for initiating all current CF specialist drugs.

730. Using these principles, payment of CF tariffs will only be made to specialised CF centres from whom the NHS Commissioning Board is commissioning CF services. The formal process of designating treatment centres will take some time and further guidance will be issued through the NHS Commissioning Board.

#### *Network/Outreach care*

731. Network care is a recognised model for paediatric care. Network care clinics take place in district general hospitals close to the homes of people with CF, where care is provided in partnership with the responsible specialist CF centre. This model must provide care that is of equal quality and access as full specialist centre care.
732. Discussions regarding network care arrangements have identified the need to clearly define the responsibilities of specialist centres and their relationship with shared care providers. A full description of responsibilities of the CF specialist centre in the paediatric network model of care is included in the national service specification.
733. Outreach care is defined as care provided by a specialist centre care team who travel to a local district general hospital. In all cases, CF tariffs will only be paid to designated specialist CF centres.



*Payment for Network care*

734. Payment of tariffs will only be made to specialist centres which may then elect to undertake network care with shared care providers. There will need to be an agreement of the appropriate reimbursement between the specialist provider and each appropriate network provider based on delivered inputs and compliance with the relevant service specification and service standards.

*Details of the tariffs*

735. The tariffs for 2013-14 are included in the *tariff information spreadsheet*. The tariffs for bands 1A and 2 remain the same, reflecting the similar costs of service provision. As cystic fibrosis is in itself a specialised service the tariffs are not eligible for any top-up.

**Below is the abbreviated information from the latest NHSE Monitor guidance 2016/17.**

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/509697/2016-17\\_National\\_Tariff\\_Payment\\_System.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/509697/2016-17_National_Tariff_Payment_System.pdf)

*Cystic fibrosis pathway payment*

115. The cystic fibrosis pathway currency is a complexity-adjusted yearly banding system with seven bands of increasing complexity of patient need. The tariff relates to a year of care. The pathway does not distinguish between adults and children.
116. The cystic fibrosis pathway currency was designed to support specialist cystic fibrosis multidisciplinary teams to provide care in a seamless, patient-centred manner, removing any incentives to hospitalise patients whose care can be well managed in the community and in their homes. Furthermore, it allows early intervention (following international guidelines) to prevent disease progression, for example, through the use of antipseudomonal inhaled/nebulised antibiotics and mucolytic therapy.



## Appendix 19 – CF Trust consensus documents, factsheets & leaflets

These are available on the CF Trust website – <https://www.cysticfibrosis.org.uk/life-with-cystic-fibrosis/publications>. Press ctrl+click on titles.

### Consensus Documents

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#### **Nutritional Management of Cystic Fibrosis. September 2016.**

Consensus document on nutritional management of cystic fibrosis. Published: September 2016

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#### **NTM interim guidelines. October 2013.**

Suggestions for infection prevention and control of *Mycobacterium abscessus*. Published: October 2013

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#### **Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK. Second edition. December 2011.**

Consensus document outlining standards of care. Published: December 2011

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#### **Pharmacy Standards of Care. November 2011.**

Consensus document outlining pharmacy standards in CF care. Published: November 2011

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#### **Standards of Care and Good Clinical Practice for the Physiotherapy Management of Cystic Fibrosis. Second edition. June 2011.**

Consensus document outlining standards of care and good practice for physiotherapy. Published: June 2011

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#### **Laboratory Standards for Processing Microbiological Samples from People with Cystic Fibrosis. First edition. September 2010.**

Consensus document outlining laboratory standards for processing microbiological samples. Published: September 2010

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#### **Antibiotic Treatment for Cystic Fibrosis. Third edition. May 2009.**

Consensus document on antibiotic treatment for cystic fibrosis. Published: May 2009

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#### **Methicillin-resistant *Staphylococcus aureus* (MRSA). April 2008.**

Consensus document on MRSA. Published: April 2008

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#### **European cystic fibrosis bone mineralisation guidelines. February 2011.**

Consensus document on bone mineralisation in cystic fibrosis. Published: February 2011

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#### ***Pseudomonas aeruginosa* infection in people with Cystic Fibrosis. Suggestions for Prevention and Infection Control. Second Edition. November 2004.**

Consensus document on prevention and infection control of *Pseudomonas aeruginosa*. Published: November 2004

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#### **The *Burkholderia cepacia* Complex - Suggestions for Prevention and Infection Control. Second edition. September 2004.**

Consensus document on suggestions for prevention and infection control of *Burkholderia cepacia* Complex. Published: September 2004

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**Management of Cystic Fibrosis-related Diabetes Mellitus. June 2004.**

Consensus document on managing CF-related diabetes mellitus. Published: June 2004

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**National Consensus Standards for the Nursing Management of Cystic Fibrosis. May 2001.**

Consensus document on standards for nursing management of CF. Published: May 2001

**Factsheets**

**The Cystic Fibrosis Trust Support Service**

**Home intravenous therapy**

**Steroid treatment in cystic fibrosis**

**Family genetic testing - 'cascade screening'.**

**Housing for people with cystic fibrosis**

**The sweat test in cystic fibrosis**

**Diagnosis in adulthood**

**School and cystic fibrosis**

**Transition from paediatric to adult care: Guide for young people**

**Nutrition: a guide for adults**

**Higher education**

**Transition from paediatric to adult care: Guide for commissioners and hospital / clinical teams**

**Nutrition: a guide for children and parents**

**Employment**

**Lung transplantation in cystic fibrosis**

**Nutrition: a guide for feeding infants**

**Financial help**

**Melioidosis and tropical travel**

**Cystic fibrosis-related diabetes**

**Prescription charges**

**Inhaled therapy**

**Urinary incontinence**

**Physiotherapy: airway clearance**

**Portacaths in cystic fibrosis**

**Cystic fibrosis and bone health**

**Physiotherapy: treatment for babies and toddlers**

## Appendix 20 – Useful telephone numbers

### Royal Brompton Hospital - 0207 352 8121

#### Extensions

Admissions paediatric coordinator	2118, 8556, 2371, bleep 1256
Bed Manager (Rose ward)	8588, bleep 7078
Biochemistry	8411
Bone densitometry	8666
CF Secretary	8674
Dietitian	8465, bleep 7101
Foulis ward (adults)	8069, 4070
Haematology	8406
LCI	8233
Lung function	8910
Microbiology	8451
Nuclear medicine	
-- Bone densitometry	8666
-- Ventilation Scans	8666
Pharmacist (paediatric)	4375, bleep 7403 or 7425
Pharmacy (drug information)	4589
Pharmacy (dispensary)	8038, 7777
Physiotherapy	8088, 8436 bleep 7300, 7304, 7311
Rose Ward	2411, 2412, 2413, 8543
Ventilation Scans	8666
X-ray (Sydney St – in patients)	2326
X-ray (Fulham Wing – clinic)	4668
X-ray PACS	8275

### External numbers

CF Trust	020 3795 1555 1, Aldgate, London EC3N 1RE <a href="http://www.cysticfibrosis.org.uk">www.cysticfibrosis.org.uk</a>
CF Foundation (USA)	<a href="http://www.cff.org">www.cff.org</a>
Great Ormond Street Hospital	0207 405 9200
Kennedy-Galton Centre (genetics)	0208 869 2795
Public Health England Colindale	0208 200 4400 61 Colindale Avenue, London NW9 5EQ

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