Physiotherapy for Cystic Fibrosis in Australia: A Consensus Statement

Foreword

This Consensus Statement has been written by physiotherapists who are experienced in the management of cystic fibrosis in Australia. The document was developed as a project of the Australian Chapter, International Physiotherapy Group for Cystic Fibrosis.

Chairperson: Dr Brenda Button
Senior Clinician Physiotherapist
Alfred Hospital, Melbourne

Editor: Dr Anne Holland
Associate Professor, Physiotherapy
La Trobe University / Bayside Health, Melbourne

Writing group:

Ianthe Astley-Bowden	Launceston General Hospital, Tasmania
Antonia Bedford	Alfred Hospital, Victoria
Jenny Bishop	Westmead Hospital, NSW
Margaret Bradshaw	Barwon Health Geelong Hospital, Victoria
Jenny Busch	Royal Hobart Hospital, Tasmania
Brenda Button	Alfred Hospital, Victoria
Robyn Cobb	The Prince Charles Hospital, Queensland
Rosie Day	John Hunter Children's Hospital, NSW
Ruth Dentice	Royal Prince Alfred Hospital, NSW
Julie Depiazzi	Princess Margaret Hospital, Western Australia
Michael Doumit	Sydney Children's Hospital, NSW
Jane Ethelston	North West Regional Hospital, Tasmania
Jenny Follett	The Children's Hospital at Westmead, NSW
Cameron Geddes	Monash Medical Centre, Victoria
Kathleen Hall	The Prince Charles Hospital, Queensland
Anne Holland	La Trobe University / Bayside Health, Victoria

Annemarie Lee	Alfred Hospital, Victoria
Rachael McAleer	Monash Medical Centre, Victoria
Prue Munro	Alfred Hospital, Victoria
Jenny Murphy	Mater Adult's Hospital, Queensland
Ranj Patra	Monash Medical Centre and Alfred Hospital, Victoria
Sarah Pike	Royal Children's Hospital, Queensland
Angela Potter	Women's and Children's Hospital, South Australia
Esta-Lee Tannenbaum	Royal Children's Hospital, Victoria
Nathan Ward	Royal Hobart Hospital, Tasmania
Dianne White	Royal Adelaide Hospital, South Australia
Kathryn Williamson	Sir Charles Gairdner Hospital, Western Australia
Christine Wilson	Royal Children's Hospital, Queensland
Michelle Wood	Mater Adults' Hospital, Queensland

Our thanks are extended to the following professionals for their valuable comments and review of this document:

Dr Mark Elkins, Dr Judy Morton, Dr Peter Middleton, Dr Kathy Stiller, Ms Kate McQueen, Ms Colleen Jackson.

We would also like to acknowledge the assistance of the Dietitian's Association of Australia Cystic Fibrosis Interest Group, whose input aided the process of development and layout of the document.

Review Date: This document is due for review in 2012

Table of Contents

List of Abbreviations

3MST	three minute step test
6MWT	six minute walk test
ABPA	allergic bronchopulmonary aspergillosis
ACBT	active cycle of breathing technique
ACT	airway clearance technique
AD	autogenic drainage
BC	breathing control
BGL	blood glucose level
BMD	bone mineral density
CF	cystic fibrosis
CFRD	cystic fibrosis related diabetes
CPAP	continuous positive airway pressure
FEV_1	forced expiratory volume in one second
FET	forced expiration technique
FVC	forced vital capacity
GOR	gastro-oesophageal reflux
HFCWO	high frequency chest wall oscillation
HPOA	hypertrophic pulmonary osteoarthropathy
IPG/CF	International Physiotherapy Group / Cystic Fibrosis
IPV	intrapulmonary percussive ventilation
MST	modified shuttle test
NHLBI	National Heart, Lung, and Blood Institute

NIV	non-invasive ventilation
$PaCO_2$	partial pressure of carbon dioxide
PEFR	peak expiratory flow rate
PD	postural drainage
QOL	quality of life
TEE	thoracic expansion exercises
WHO	World Health Organisation

Executive Summary

Physiotherapy management is a key element of care for people with cystic fibrosis (CF). Airway clearance therapy, exercise and inhalation therapy are cornerstones of treatment and are associated with improved long-term outcomes. As survival improves, complications of CF such as musculoskeletal pain, urinary incontinence and cystic fibrosis related diabetes are becoming more apparent and require physiotherapy management strategies. Physiotherapists are members of the multidisciplinary CF team throughout the lifespan, from initial diagnosis to the care of end-stage disease.

Although significant evidence exists to support physiotherapy management in CF, there is considerable variation in clinical practice across Australia. The need for a consensus statement which was applicable to the Australian healthcare context was identified by members of the writing group, in order to support clinicians in delivering best practice care. The objective of this document is therefore to optimise physiotherapy management of people with CF in Australia.

The statement provides recommendations for the key areas of physiotherapy management for patients with CF, including airway clearance therapy, inhalation therapy, exercise, musculoskeletal management, care of the complex patient, management of the newly diagnosed patient, transition from paediatric to adult care, end-of-life care and infection control.

Some of the key recommendations and associated levels of evidence are outlined below:

1. Airway clearance techniques are a cornerstone of CF care and should be performed across the lifespan (C).

2. The active cycle of breathing technique, positive expiratory pressure (PEP) therapy, oscillating PEP and autogenic drainage are effective forms of airway clearance therapy which may be performed independently (B).

3. Modified postural drainage is recommended in infants and young children where active participation in airway clearance therapy is not possible (B).

4. Positive expiratory pressure devices can be used whilst nebulising hypertonic saline, isotonic saline or bronchodilators but are not recommended whilst nebulising antibiotics or dornase alfa (D).

5. Where possible, nebulized medication should be taken via mouthpiece (C).

6. Dornase alfa may be administered before or after airway clearance techniques with the regimen adapted to each individual. A minimum of 30 minutes should be allowed between nebulization and commencing airway clearance (B).

7. Exercise is recommended for patients with CF throughout the lifespan (B).

8. Exercise prescription should be tailored to the individual and comply with established exercise prescription guidelines (B).

9. Prompt assessment and treatment of acute musculoskeletal pain should be provided (D).

10. Women with CF should be taught preventative / rehabilitative strength and endurance exercises for the pelvic floor (C).

11. Education by the physiotherapist should begin at diagnosis (D).

12. During the process of transition, paediatric and adult physiotherapists should communicate directly regarding the detailed aspects of each patient's physiotherapy care (D).

13. Non-invasive ventilation is a useful adjunct to airway clearance in patients with severe disease in whom dyspnoea and fatigue limit airway clearance (B).

14. Patients with CF should undertake an exercise program designed to optimise their physical function while on the transplant waiting list (D).

15. Physiotherapy treatment at the end of life should be tailored to each patient's wishes (D).

16. Patients with different organisms should not carry out airway clearance physiotherapy together (C).

17. Patients should not share airway clearance therapy or inhalational therapy equipment under any circumstances (C).

This document will be due for review in 2012. Responsibility for organising the review process will be taken by the incumbent chairperson of the Australian chapter of the IPG/CF and country contact person for Australia in the IPG/CF.

1 Introduction

1.1 Background to the consensus statement

Physiotherapy management is a key element of care for people with cystic fibrosis (CF). Airway clearance therapy, exercise and inhalation therapy are cornerstones of treatment and are associated with improved long-term outcomes [1-3]. Although significant evidence exists to support physiotherapy management in CF, there is considerable variation in clinical practice. A survey of CF centre physiotherapists from 19 centres across Australia in August 2006 identified practice variations in prescription of airway clearance therapy, exercise prescription, use of inhalation therapy, infection control practices and end-of-life care. At present there are no detailed recommendations to guide physiotherapy practice in the Australian context.

This consensus statement provides recommendations for the key areas of physiotherapy management for patients with CF, including airway clearance therapy, inhalation therapy, exercise, musculoskeletal management, care of the complex patient, management of the newly diagnosed patient, transition from paediatric to adult care, end-of-life care and infection control. The recommendations are based on evidence up to and including 2007. Where there is a lack of strong evidence on which to base recommendations, consensus of the CF physiotherapy writing group is provided. Areas where consensus could not be reached are highlighted and the different management approaches in Australia are presented.

1.2 Purpose and Scope

The objective of this document is to optimise physiotherapy management of people with CF in Australia.

The purpose of the consensus statement is:

1. To provide recommendations regarding best-practice physiotherapy management for physiotherapists caring for infants, children and adults with CF
2. To promote physiotherapy management of people with CF that is evidence-based where possible and reflects the best available knowledge
3. To standardise the physiotherapy care of people with CF across Australian centres
4. To provide a reference tool to support training of physiotherapists in best-practice

CF management and to support isolated practitioners who care for people with CF.

1.3 Consultation Process

August 2005

The need for an Australian consensus statement was identified at a meeting of the Australian Chapter of the International Physiotherapy Group for CF (IPG/CF Australia) which was held at the 5th Australian and New Zealand Cystic Fibrosis Conference in Adelaide. Dr Brenda Button, the IPF/CF country contact physiotherapist for Australia, was appointed as the Chairperson of the committee. Preliminary discussion of topics to be included was undertaken.

January to July 2006

All known physiotherapists working in CF care were invited via email to participate in the development of the consensus statement. Topics were selected and refined into seven groups. Topic areas were allocated to contributors and volunteers appointed as group leaders. Initial literature searches were performed.

September 2006

Members of the writing group attended a consensus workshop in Melbourne. Surveys were conducted in each topic area to identify areas where there is consensus in clinical practice and areas where clinical practice differs between centres.

September 2006 – February 2007

The first draft of each section was prepared by the writing groups and circulated to the whole group for comment and revision

February – May 2007

The second draft of each section completed by each writing group, incorporating comments from all members

June – July 2007

The document compiled into one editorially-consistent text by the editor. Draft of complete document was circulated to group for review prior to the next meeting

August 2007

All group members were invited to attend a workshop held in conjunction with the 7th Australian and New Zealand Cystic Fibrosis Conference, Sydney. Areas of disagreement and concern were highlighted and discussed. Feedback was sought from

group members on all sections of the document, particularly recommendations. Feedback was incorporated into draft.

November – December 2007
The draft document was offered to stakeholders for comment. These included CF physicians Australia-wide, CF consumers and advocates, and expert physiotherapists who were not part of the writing group.

January – March 2008
Comments and feedback from stakeholders were incorporated into the final version of the statement. Final consultation with writing group members was undertaken.

1.4 Methods

The literature search for this document was conducted using electronic databases including MEDLINE, CINAHL, EMBASE and PEDro. Manual search of reference lists and conference proceedings were undertaken. Searches were limited to articles in English. Literature up to and including 2007 was included. Given the limited evidence available for many areas of physiotherapy practice, both randomised controlled trials and research conducted with less robust designs were included.

The available evidence was categorised according to the National Heart, Lung, and Blood Institute (NHLBI) categories [4] and are listed in Table 1.

The recommendations were formulated by consensus amongst the writing group, made up of physiotherapists with clinical experience in the management of patients with cystic fibrosis. Areas where consensus was not achieved are stated and the alternative management practices are outlined.

The consensus statement will be disseminated amongst physiotherapists working in CF centres throughout Australia in hard copy and CD ROM. They will also be made available on the Cystic Fibrosis Australia website.

1.5 Review process

This document will be due for review and updating in 2012. The process will be coordinated by the incumbent chairperson of the Australian chapter of the IPG/CF and the contact physiotherapist for the IPG/CF in Australia. Prior to this update, an

evaluation of the document will be undertaken via a survey of physiotherapy practice across all centres in Australia. Update of the document will incorporate the findings of the evaluation as well as new evidence from the scientific literature.

Table 1: Levels of Evidence: National Heart, Lung, and Blood Institute (NHLBI) categories (reference)

NHLBI category	Sources of evidence	Definition
A	Randomised controlled trials (RCTs). Rich body of data.	Evidence is from endpoints of well-designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants
B	Randomised controlled trials (RCTs). Limited body of data.	Evidence is from endpoints of intervention studies that include only a limited number of patients, posthoc or sub-group analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomised trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C	Non randomised trials. Observational studies.	Evidence is from outcomes of uncontrolled or non randomised trials or from observational studies
D	Panel consensus judgment.	This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was deemed insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria

Reference: NHLBI/WHO Workshop Report. Global Initiative for Chronic Obstructive Lung Disease (GOLD): Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. National Institutes of Health / National Heart, Lung and Blood Institute April 2001

1.6 Disclosure statement

Development of the consensus statement was funded in part by unrestricted educational grants from Roche Pharmaceuticals and Solvay Pharmaceuticals. This funding was used to support travel to the consensus conference in Melbourne in September 2006 and to assist dissemination by hard copy and CD ROM. A grant from Cystic Fibrosis Australia supported the editorial role of Dr Holland. These funding bodies were not involved in formulation of the consensus statement or the recommendations.

Writing group conflict of interest and funding declarations are outlined in Appendix 12.

2 Airway Clearance Techniques

2.1 Rationale for Airway Clearance Techniques in Cystic Fibrosis

Cystic fibrosis is a genetic, life-limiting disorder. Obstruction of exocrine glands by viscous secretions causes pathological change in a range of body systems. In the lungs this is manifest as abnormal mucus secretion in the airways, which is responsible for persistent infection and inflammation. This process is the major contributing factor to severe airway damage and deteriorating lung function. The thickness and amount of airway secretions overwhelm the body's normal mucus transport mechanisms and therefore treatment methods that improve mucus clearance are considered essential in optimising respiratory status and slowing the progression of lung disease.

Chest physiotherapy has been defined as 'the external application of a combination of forces to increase mucus transport' [5]. Because the aim of these techniques is to clear sputum from the airway, and to encompass the range of modern techniques available, modern chest physiotherapy is usually referred to by the generic term of 'airway clearance techniques' [6].

Airway clearance techniques (ACTs) are usually commenced as soon as the diagnosis of CF is made, often soon after birth. In infants airway clearance techniques are performed by the parents, however as children grow older they are taught techniques that can be performed independently of an assistant [7]. Patients are required to undertake this treatment both during acute exacerbations and prophylactically between infections [8].

It has been stated that 'physiotherapy has a major influence in limiting the adult consequences of CF' [9] p240. This is based on the assumption that airway clearance techniques have both short-term beneficial effects, and are able to slow the rate of pulmonary deterioration over time. A Cochrane review has concluded that airway clearance techniques have short-term beneficial effects on mucus transport in CF however there was no evidence regarding long-term effects [10]. One uncontrolled study has evaluated the effects of withdrawing airway clearance for three weeks and found a detrimental effect on lung function [1]. Beyond this study there is little evidence regarding the long-term efficacy of ACT versus no treatment. Due to the ethical concerns regarding the withholding of such a well-established treatment it is

now considered unlikely that such a trial could be conducted, especially in adults with established lung disease [6].

A recent Consensus Conference Report on Cystic Fibrosis Adult Care describes airway clearance as a 'cornerstone' of treatment [11] p5S. As such it is the role of physiotherapists to ensure that the airway clearance techniques prescribed have a sound basis in physiology and can be effectively performed across the lifespan. This chapter discusses the various airway clearance techniques that a physiotherapist may perform or prescribe for a person with CF.

2.2 Active Cycle of Breathing Technique

The active cycle of breathing technique (ACBT) consists of breathing control (BC), thoracic expansion exercises (TEEs) and the forced expiration technique (FET) [12]. Studies using the ACBT have shown it to be an effective technique for the mobilisation and clearance of secretions [13]. It is not further improved by the adjuncts of positive expiratory pressure [14], oscillating positive expiratory pressure [15, 16] or mechanical percussion [17]. An improvement in lung function following the instigation of the ACBT has been shown [18].

Physiotherapy practice

During the ACBT, BC is followed by TEE. Breathing control is then repeated followed by the FET. The entire ACBT is repeated until the huff sounds dry and is non-productive, or it is time for a rest. A minimum of ten minutes in a productive position is recommended. If more than one position is needed, two positions are usually sufficient for one treatment session. The total treatment time is between ten and thirty minutes. A full description of the ACBT can be found in Appendix 1.

The ACBT regimen is flexible and adapted to suit the individual. The ACBT should never be uncomfortable or exhausting and the huff should never be violent. The sitting position alone is often effective and adherence to treatment is frequently better than with other positions. In some people other gravity assisted positions may be indicated. In non-CF bronchiectasis it has been shown that the horizontal, side lying position is as effective as the head down tipped position and preferred by patients, who report fewer side effects such as head ache and sinus pain [19]. The ACBT can be used independent of an assistant and in any position. If an assistant is present, chest percussion or vibration can be combined with TEE.

The ACBT is widely applicable in CF. It can be performed by all patients who can follow instructions and is useful in all stages of disease. The ACBT is a useful treatment option in patients where other techniques are contraindicated (eg haemoptysis). In patients with a small pneumothorax treated conservatively (no intercostal drain), breath holds (inspiratory pauses) are not recommended (D).

2.3 Autogenic Drainage

Autogenic drainage (AD) is a technique based on the principle of reaching the highest possible airflow in different generations of bronchi by controlled breathing [20]. It was introduced by Chevallier [21], as a result of the observation that children with difficult asthma frequently cleared more sputum during breathing exercises, playing, laughing or spirometry than they did during conventional chest physiotherapy. One of the aims of AD is to avoid airway closure that may be caused by coughing and forced expiratory manoeuvres [22].

Autogenic drainage has three phases. During the 'unstick' phase, breathing takes place at low lung volumes in order to unstick peripheral mucus. This is followed by the 'collect' phase, where the mucus is collected from the middle airways by breathing at tidal volume level. In the final 'evacuate' phase, breathing takes place at higher lung volumes in order to evacuate secretions from the central airways. A full description of AD can be found in Appendix 2.

Greater expiratory flow rates are generated in smaller airways with AD compared to forced expirations [23]. Short-term studies have shown that AD is as effective as postural drainage and percussion [24], oscillating PEP [25] and the ACBT [26].

Physiotherapy practice

Autogenic drainage is not an easy technique to learn for either patient or therapist. A physiotherapist wanting to use this technique should attend an AD course or spend time with a physiotherapist experienced in teaching AD. Autogenic drainage requires a patient that is 'in tune' with their body and can sense the location of the mucus. Considerable patience is required when learning and undertaking AD as it can be time consuming.

Autogenic drainage aims to prevent airway collapse and reduce limitation to expiratory flow [27]. As such it is likely to be useful in patients who have unstable airways or evidence of airway hyperreactivity [28]. Some patients become air-hungry

when breathing at low lung volumes. These patients may need to take a normal resting breath and then return to breathing close to residual volume.

This technique may be adapted for infants and young children, where it is known as assisted AD. The therapist places their hands on the child's chest to manually increase expiratory flow and prolong expiration towards residual volume [29]. These thoracic compressions are carried out gently, following the child's breathing pattern and stabilising the abdominal wall. Excessive force and discomfort must be avoided as the child will resist the manoeuvres if uncomfortable.

2.4 Positive Expiratory Pressure (PEP) Therapy

Positive expiratory pressure (PEP) therapy is defined as breathing with a positive expiratory pressure of 10 – 20 cmH_2O [30]. The theoretical rationale for the use of PEP therapy is that in the presence of small airway obstruction caused by secretion retention, the relative resistance to airflow in collateral channels will be reduced. The application of positive pressure to the airway will allow an increased volume of air to accumulate behind the obstruction, and the pressure gradient across the sputum plug will force secretions centrally toward the larger airways, from where they can be expectorated [31, 32]. It is proposed that PEP is also effective through increasing the volume in neighbouring lung units, which in turn provide an outward pull on the obstructed unit, allowing re-expansion and improved airflow [33]. Improvement in gas mixing and oxyhaemoglobin saturation following PEP support this rationale [34].

In an early study by Falk et al [32], PEP was shown to be superior to postural drainage in terms of sputum clearance. In comparison to conventional chest physiotherapy over a twelve month period, McIlwaine et al [35] found PEP to be superior to conventional chest physiotherapy in children. Over a twelve month period, McIlwaine [36] found a significantly greater rate of decline in lung function in children using oscillating PEP compared to PEP whereas Newbold [37] found no significant difference in decline of lung function between adults using the two therapies. A Recent Cochrane review concluded that PEP was no more or less effective than other forms of airway clearance and that there was some evidence of patient preference for PEP over other techniques [38].

Physiotherapy Practice

Positive expiratory pressure therapy can be delivered through a face mask or a mouthpiece. A noseclip may be necessary during the training phase for mouthpiece

PEP. In both systems, PEP is created by exhaling through a narrow opening, providing resistance to expiration. The resistor should provide a steady PEP of 10-20cmH_20 during the middle of expiration. The technique to be used with PEP is described in Appendix 3.

Contraindications: The use of PEP therapy is contraindicated where there is an undrained pneumothorax.

Precautions to PEP therapy include inability to tolerate an increased work of breathing, raised intracranial pressure, haemodynamic instability, recent facial, oral or oesophageal surgery, acute sinusitis, active haemoptysis, middle ear pathology, and drained pneumothorax [39].

2.5 High Pressure PEP

High pressure PEP therapy is a modification of PEP therapy which includes a full forced expiration against a fixed mechanical resistance [40]. This method uses the same PEP system as PEP therapy (Astra Tech, Denmark). The theoretical rationale for high pressure PEP is that the forced expiration against a marked resistive load will squeeze air from hyperinflated lung units into unobstructed and atelectatic lung units. The back pressure from the stenosis effects a homogenised slow expiratory evacuation of all lung units. The reduced airflow velocity is counterbalanced by the effects of dynamic airway bronchial compression.

The expiratory resistance is individually determined by connecting the PEP set-up to a pneumotachograph and performing a series of forced vital capacity manoeuvres with different resistors. The resistor that provides the greatest increase in forced vital capacity (FVC) over baseline values, along with a sustained plateau in expiratory flow, is chosen for use during treatment [40].

Studies on the use of high pressure PEP have been limited and only conducted at one centre. Existing evidence shows that high pressure PEP is of benefit in both the short and long term with improved sputum clearance, lung function and a reduction in hyperinflation [28, 41, 42].

Physiotherapy practice

High pressure PEP is effective in patients with collapsible airways, tracheomalacia,

bronchomalacia or respiratory muscle weakness. The technique for high pressure PEP is described in Appendix 4.

Contra-indications to high pressure PEP include pneumothorax, cardiac disease, frank haemoptysis, lung surgery and asthma. High pressure PEP is not recommended for patients who are exhausted and are unable to meet the demands of this energy-consuming technique.

2.6 Bottle PEP

Bottle PEP is a form of PEP therapy which is intended to promote collateral ventilation and increase functional residual capacity (FRC), recruit obstructed or collapsed airways, improve gas exchange and assist in the central mobilisation of pulmonary secretions [33, 43, 44].

Bottle PEP consists of plastic tubing surrounded by a column of water. During expiration through the tubing the water creates positive pressure which is transmitted through the tubing to the airways. The amount of PEP achieved is dependent on the depth of water, diameter of tubing and patient expiratory flow rate. An advantage of bottle PEP is that it can be assembled from equipment commonly available in a hospital setting and is therefore inexpensive. Instructions for assembling bottle PEP can be found in Appendix 5.

Physiotherapy Practice

To date there have been no studies specifically evaluating the efficacy of bottle PEP. The indications, dosage, contraindications and precautions for bottle PEP are assumed to be the same as those for PEP therapy. An additional precaution for bottle PEP is its use in patients who are at risk from drinking water and who cannot reliably follow instructions (commonly those on a fluid restriction or at risk of aspiration).

Given that bottle PEP provides a wet environment in which bacterial growth might readily occur, care must be taken with infection control. Water should be replaced after each session with the bottle and tubing rinsed and air-dried. The bottle and tubing should be replaced regularly (D).

2.7 Oscillating PEP

Oscillating PEP refers to a variety of devices that combine PEP and oscillation of

airflow. The addition of oscillation is thought to loosen secretions and thus facilitate airway clearance [45]. When the resonance frequency of the pulmonary system is achieved, the pressure variations are amplified, maximising the vibrations of the airway wall. The three most commonly used devices are the Flutter®, the Acapella® and the RC-Cornet®.

Contraindications to oscillating PEP are frank haemoptysis and undrained pneumothorax.

Precautions: Caution should be exercised in patients who are unable to tolerate an increased work of breathing, those with raised ICP, haemodynamic instability, recent facial, oral or oesophageal surgery, acute sinusitis or middle ear pathology [39].

2.7.1 The Flutter®

The Flutter® is a pipe-shaped device consisting of a mouthpiece and a small ball which occludes the opening of a plastic cone. When the patient exhales into the device, positive expiratory pressure is generated. When this pressures reaches 10 – 25 cmH_2O, the ball rises and expiratory pressure drops. The rise and fall of the ball and its movement along the surface of the cone creates an oscillatory vibration of the air within the airways many times a second throughout exhalation.

Of all the oscillating PEP devices available, the Flutter® has been the most thoroughly studied. Short term trials indicate that the Flutter® is at least as effective as other ACTs [25, 46-49] and that it significantly reduces sputum viscoelasticity [25]. Long-term data are less conclusive. In a one-year randomised controlled trial comparing the Flutter® with the PEP mask in children with CF, greater deterioration in lung function and increased rate of hospitalisation was seen in the Flutter® group [36]. However, a more recent study over 13 months showed no difference in lung function between groups randomly assigned to PEP or Flutter® [37].

Physiotherapy practice:

The Flutter® produces a range of oscillation frequencies between 2-32 Hz. Only frequencies between 8 – 16 Hz have been found to be useful for airway clearance [45]. The frequency can be modulated by changing the inclination of the device either slightly up (higher frequency) or slightly down (lower frequency). The performance of the Flutter® is gravity-dependent such that the device must be positioned upright in order to produce oscillation. It therefore requires practice and skill to use the Flutter® in positions other than sitting. Because of the complexity of the technique, children

may need supervision to use the Flutter® effectively. The technique for Flutter® is described in Appendix 6.

2.7.2 Acapella®

The Acapella® combines the principles of high frequency airflow oscillation and PEP by employing a counterweighted lever and magnet. During expiration, air passes through a cone, which is intermittently occluded by a plug attached to a lever. A dial at the distal end of the device adjusts the proximity of the magnet and counterweighted plug, thereby adjusting the frequency, amplitude and mean pressure of airflow through the device.

It is known that the *in vitro* pressure and frequency characteristics of the Acapella® are similar to those of the Flutter® [50]. However, there are limited data regarding its clinical efficacy. In a randomised cross-over trial of ACBT versus Acapella® in bronchiectasis, no differences were found between weight of sputum expectorated, although a greater proportion of patients preferred the Acapella® [51].

Physiotherapy practice

The Acapella® produces a PEP range of 7-35 cmH20, and a frequency of airflow oscillation of 0-30Hz. Adjusting the dial clockwise increases the resistance of the vibrating orifice, which will allow the patient to exhale at a lower flow rate and with increased PEP. The Acapella® is not gravity-dependent and can be used in any body position. The technique for Acapella® is described in Appendix 6.

2.7.3 RC-Cornet®

The RC Cornet® consists of a mouthpiece, a hose contained within a semicircular tube and a sound damper. During exhalation, a kink is produced in the hose which moves along the length of the tube, producing PEP and airflow oscillation. Twisting the mouthpiece alters the pressure and flow. By changing from positions one through four, the twist on the hose is increased, thereby creating a larger pressure oscillation.

There is currently very limited evidence available regarding use of the RC Cornet® in CF, with only abstracts available in the literature. At present expert clinical opinion suggests that the RC Cornet® may be used in a similar manner to other oscillating PEP devices.

Physiotherapy practice

The RC Cornet® can be held at any angle during treatment, so it may be used with the patient in sitting or in recumbent positions. The technique for RC Cornet is described in Appendix 6.

2.8 Postural Drainage

2.8.1 Postural Drainage in gravity-assisted positions

Postural drainage was first introduced for the treatment of CF in the 1950's and remained the cornerstone of therapy until the 1980's. Postural drainage consists of placing the patient in a position that allows gravity to assist in draining mucus from the periphery of the lungs. Usually 6-12 postural drainage positions are used depending upon which lobes or segments of the lung are to be drained. The recognised positions were published in 1950 [52].

Many studies use postural drainage as the comparison for the 'newer' techniques. Reisman et al [53] reported postural drainage to be superior to the forced expiration technique in terms of maintaining FEV_1. Beneficial effects of postural drainage on sputum clearance have been reported [54, 55]. However, Mortensen et al [56] demonstrated no advantage of postural drainage over PEP. Lannefors et al [57] reported maximal clearance from the dependent lung region during postural drainage using imaging and inhaled radiolabelled particles, indicating that gravity is not the only factor influencing mucus clearance during postural drainage.

A growing body of research has challenged the efficacy and safety of the traditional treatment of head-down postural drainage in infants. Gastro-oesophageal reflux (GOR) is common in infants, children and adults with CF [58-60]. A number of studies have demonstrated provocation of GOR during head-down tilted postural drainage in infants, children and adolescents with CF [58, 61, 62]. One study from the UK did not reproduce these results in infants; however the head-down position utilised was not as acute, older infants were studied and they avoided the prone head down tilted position [63]. A long-term study has shown that infants with CF who performed postural drainage had significantly worse lung function and more radiological changes at five years compared to those who did not use head-down tilt [64]. The association between GOR, postural drainage and reduced respiratory function has not yet been demonstrated in adults.

Other negative effects attributable to postural drainage have also been documented.

Increased dyspnoea related to positions using head-down tilt has been reported compared to when the same treatment is performed in horizontal positions [19]. Oxyhaemoglobin desaturation during postural drainage with FET has been demonstrated [65], although other authors stated that they were able to prevent desaturation in a group of CF subjects with similar disease severity by incorporating periods of relaxed breathing [66].

Physiotherapy practice

Postural drainage in gravity-assisted positions should not be used in infants with CF or in patients of any age with symptoms of GOR [58, 61, 62]. There is no consensus as to whether postural drainage has a role in management of other patients. The majority of Australian centres no longer use postural drainage incorporating head-down tilt in any patients with CF. It is generally accepted that other ACTs are at least as effective and have fewer risks.

If postural drainage is employed, careful individual assessment should be used to establish whether gravity assisted drainage positions are of clinical benefit. Some patients may not be able to tolerate the recognised positions and therefore a comfortable position in which effective breathing techniques can be carried out is likely to be most beneficial. It is inappropriate to use gravity assisted positions immediately following meals. Caution should be exercised in the presence of cardiac failure, severe hypertension, cerebral oedema, aortic and cerebral aneurysms, severe haemoptysis, abdominal distension or after recent surgery or trauma to the head or neck.

2.8.2 Modified postural drainage

Modified postural drainage involves positioning for airway clearance without use of head-down tilt. The recommended positions for infants include:

- supine 30^{o} head up
- prone horizontal
- left and right horizontal side lying
- upright chest position for apical segment of upper lobe, leaning against therapist/carer shoulder and avoiding slumped sitting which increases intra-abdominal pressure [58].

The available evidence suggests that modified postural drainage is at least as

efficacious as positions that use head-down tilt and is superior to traditional postural drainage in infants. In a five year follow up of infants randomized to either standard postural drainage or modified postural drainage, the modified group had fewer radiological changes and significantly better lung function at 6 years of age [64]. In an adult study comparing treatment in head down versus horizontal positions, there was no difference in amount of sputum expectorated, but patients reported fewer side effects in horizontal positions [19].

Physiotherapy practice

In infants and small children when active participation is not possible, modified PD is the optimal treatment choice [64]. The infant's head should be well supported, avoiding shaking movements during treatment which has been associated with adverse outcomes in premature infants [67]. Treatment should be commenced at least 1- 2 hours after a feed. A maximum of 20 minutes per treatment session is recommended.

2.9 Percussion and vibration

Percussion (or chest clapping) involves clapping of the chest wall at a frequency of approximately 3-6 Hz in order to produce an energy wave, which is transmitted through the chest wall to the airways [5]. Percussion is a useful technique to help mobilise mucus and may stimulate increased tidal volumes and coughing in infants and children. It is performed using a cupped hand with a rhythmical flexion and extension action of the wrist. In adults percussion can be done with one or two hands. In infants percussion is performed using two or three fingers of one hand.

Vibrations involve shaking of the chest wall. The hands are placed on the chest wall and during expiration, a vibratory action in the direction of the normal movement of the ribs is transmitted through the chest wall. Vibration produces a lower frequency of oscillation than percussion but produces higher expiratory flow rates than PEP or oscillating PEP [68]. These effects may increase mucus transport.

The clinical effects of percussion and vibration on airway clearance are unclear. Sutton and colleagues [69] did not find any increase in tracheobronchial clearance when manual percussion and vibration were added to postural drainage [69]. However, addition of percussion and vibration to a regimen that included postural drainage and the active cycle of breathing technique resulted in significant improvement in the FEV_1/FVC ratio on the day following treatment compared to

treatment which did not include these manual techniques [70]. Percussion may increase hypoxemia [32] but this may be prevented if combined with thoracic expansion exercises [66]. A literature review by Gallon [71] suggests that percussion is only indicated in patients with excessive sputum production.

Physiotherapy practice

Percussion and vibrations are used as an adjunct to postural drainage. Percussion should never be uncomfortable and should be done over a layer of clothing or other cushioning fabric to avoid sensory stimulation of the skin. Single-handed chest clapping is advocated if self treatment is advised. If the physiotherapist is concerned that percussion may cause hypoxemia, the patient should be monitored with a pulse oximeter. Vibrations should never be uncomfortable and should be adapted to suit the individual patient. Percussion and vibrations should be used when patients are unable to participate actively in airway clearance therapy and require passive treatment (D).

Contraindications: Patients with severe osteoporosis, frank haemoptysis, fractured ribs and chest injuries. Rib fractures were reported in a neonate with hyaline membrane disease following percussion [72].

Precautions: Caution should be used in patients with hyper-reactive airways, severe bronchospasm and osteopenia.

2.10 Other airway clearance techniques

High frequency chest wall oscillation and intrapulmonary percussive ventilation are alternative airway clearance techniques which are commonly used in the United States and Europe respectively. These techniques are not currently used in clinical practice in Australia. The evidence and indications for these techniques are presented in this section. Given the lack of clinical experience with, and access to, these techniques in Australia, no recommendations are made regarding their use.

2.10.1 High Frequency Chest Wall Oscillation (HFCWO)

High frequency chest wall oscillation (HFCWO) is a patient-delivered form of airway clearance therapy consisting of an inflatable vest and an air-pulse generator. It is also known as high frequency chest compression (HFCC). The vest inflates to a nearly constant background pressure with a superimposed frequency of air pressure oscillations throughout inspiration and expiration [73]. It has been proposed that

HFCWO assists sputum removal by increasing air flow at low lung volumes; increasing expiratory flow bias, resulting in an increased annular flow of mucus toward the mouth; and decreasing viscoelasticity of mucus by reducing cross-linking [74].

The majority of evidence suggests that HFCWO is at least as effective as conventional chest physiotherapy in terms of sputum clearance and lung function parameters [75-79]. Sputum clearance with HFCWO is reported to be similar to PEP therapy [78] however other authors report that it is less effective than ACBT [80].

Physiotherapy practice

High frequency chest wall oscillation is usually commenced at low pressures and frequencies and then increased to therapeutic optimum as the patient tolerates. Different devices allow a different range of oscillation and frequency settings. The HFCWO should be paused approximately every five minutes for huffing and coughing. In Australia, HFCWO has only recently become available but due to the high cost of this equipment in comparison to other airway clearance techniques it has not yet entered clinical practice.

Contraindications: Unstable neck injury, port being accessed under vest, pulmonary embolism, lung contusion, current haemoptysis, haemodynamic instability, rib fractures, large pleural effusion or empyema.

Precautions: End stage disease (end expiratory volume may fall below closing capacity), port under the vest (not currently accessed), recent oesophageal surgery, distended abdomen, bronchospasm, osteoporosis, coagulopathy [81].

2.10.2 Intrapulmonary Percussive Vibration (IPV)

Intrapulmonary Percussive Ventilation (IPV) consists of an open breathing circuit with a pressure-flow converter and a high output nebuliser. During IPV, high frequency minibursts of gas (at 100-300 cycles/min) are superimposed on the patient's own respiration at pressures of 5-35 cmH_20. The driving pressure and frequency are individually titrated to patient comfort and thoracic movement. Three forms of therapy are provided during IPV; percussive oscillatory vibrations to loosen retained secretions, high-density aerosol delivery to hydrate viscous mucus plugs, and positive expiratory pressure (PEP) to recruit alveolar lung units.

Current evidence suggests that IPV is at least as effective as postural drainage and

percussion in patients with CF [76, 82, 83]. It has similar short-term efficacy to the Flutter® [84]. More research is needed to evaluate the long-term efficacy of IPV in comparison to modern airway clearance techniques.

Physiotherapy practice

Intrapulmonary Percussive Ventilation is not currently in use in Australia, despite much experience with its use in Europe. The cost of the equipment required is likely to remain a barrier to its use in the short-term.

Contraindications: Non-drained pneumothorax

2.11 Physical Exercise as Airway Clearance

Physical exercise that increases minute ventilation leads to the mobilisation of pulmonary secretions and enhances airway clearance [57, 85-87]. Some people with mild lung disease and good lung function use exercise together with forced expiration (huffing), coughing and expectoration as stand-alone airway clearance therapy. Others with more extensive lung disease and larger volumes of sputum use exercise as an adjunct to a formal airway clearance therapy regimen.

A transient increase in FEV_1 and peak expiratory flow rate (PEFR) following exercise has been demonstrated in CF [88-90], suggesting that exercise may result in increased flow transients and bronchodilation. This may facilitate the clearance of secretions and improve ventilation. Coughing induced by exercise also contributes to its effectiveness as an airway clearance technique [91]. A meta-analysis including 53 subjects and three trials found that the addition of exercise to ACTs resulted in a significant increase in FEV_1 compared to ACT alone [92]. Whether exercise can be used as an alternative to ACTs is less clear. In hospitalised subjects with CF, treatment using conventional chest physiotherapy resulted in greater weight of expectorated sputum than exercise alone [86]. In contrast, Cerny and colleagues [91] found that there were no differences in expectorated sputum weight or lung function in hospitalised subjects who performed ACT alone or exercise alone. One crossover trial has compared the effects of exercise, gravity-assisted drainage and PEP on mucus clearance using inhaled radioactive tracer [57]. All treatments incorporated the FET. Although there were no statistically significant differences between the treatments, there was a trend to lower mucus clearance following the exercise treatment.

Physiotherapy Practice

Clinically, physical exercise is used as an ACT to achieve the following:

- mobilise mucus
- open up collapsed or plugged airways by increasing ventilation
- increase expiratory flow which loosens mucus from the airway wall via shear forces
- increase resting lung volumes
- increase regional ventilation via gravitational effects by exercising in different positions such as upright, sitting, supine, side lying or prone lying

Patients with milder lung disease often prefer to carry out physical exercise before airway clearance therapy as it mobilises secretions and makes airway clearance therapy more effective, where as those with advanced bronchiectasis and large volumes of daily sputum need to do airway clearance therapy before being able to enjoy exercise.

Suitable forms of exercise to promote mucociliary clearance include: walking, running, jogging, horse riding, swimming, bicycling, rowing, dancing, martial arts, step training, stair climbing, skipping, trampoline jumping, sailing, water and snow skiing, snow boarding, surfing and other whole-body, sustained forms of exercise. Team sports such as hockey, soccer, football, basketball, netball, polo etc combine all the physiological benefits of exercise while incorporating group and social activity which in turn promote regular participation in physical exercise.

Forced expirations and expectoration should always be interspersed with physical exercise in order to optimise airway clearance therapy. More detail regarding exercise assessment and prescription can be found in Chapter 4.

2.12 Clinical Decision Making regarding Airway Clearance Techniques

There are a number of evidence based airway clearance techniques available for use in cystic fibrosis. In order to maximise adherence and physiotherapist / patient co-operation, it is recommended that an appropriate individualised physiotherapy program is developed using sound clinical reasoning and input from the patient and their family. The individualised program should include airway clearance and emphasise the importance of physical activity. Clinical and social factors that will

influence the decision about the most appropriate airway clearance regimen for the individual include; age, independence, patient preference, cooperation, adherence, financial status, family or social support and clinical status.

Recommendations

1. **Airway clearance techniques are a cornerstone of CF care and should be performed across the lifespan (C).**

2. **The ACBT is an effective form of airway clearance and can be used by people with acute and chronic lung disease independently or in conjunction with other airway clearance techniques (B). It may be used in patients where other techniques are contraindicated, eg haemoptysis (D).**

3. **PEP therapy, oscillating PEP and autogenic drainage are effective forms of airway clearance which may be performed independently (B).**

4. **PEP therapy and oscillating PEP should be avoided if there is suspected untreated pneumothorax (D).**

5. **Bottle PEP can be used as an alternative to conventional PEP therapy in circumstances of lack of equipment or patient / physiotherapist preference in individual circumstances (D).**

6. **Autogenic drainage may be beneficial in patients with unstable airways as the technique avoids airway closure (C).**

7. **Postural drainage in head-down positions should not be used routinely in infants with CF (B) or in patients of any age with known or suspected GOR (C). There is no consensus as to whether postural drainage has a role in management of other patients.**

8. **Modified postural drainage is recommended in infants and young children where active participation in airway clearance therapy is not possible (B).**

9. **Percussion and vibrations should be used when patients are unable to participate actively in airway clearance therapy and require passive treatment (D). Caution should be exercised in patients with reduced bone density (D).**

10. **Physical exercise is an effective adjunct to airway clearance which enhances respiratory function (A) and may improve mucus expectoration (B). It should be accompanied by modulated forced expirations and coughing to optimize cephalad movement of secretions and evacuation from the bronchial tree (D).**

3 Inhalation Therapy as an Adjunct to Physiotherapy

Inhalation therapy is a significant component of the management of the respiratory sequelae associated with cystic fibrosis (CF). It is a multi-disciplinary area of practice, with the input from each discipline varying between CF centres. Airway clearance techniques may be enhanced with effective inhalation therapy and inhalation therapy may be enhanced by effective airway clearance techniques. Due to this co-dependent relationship, physiotherapists should be adequately skilled in the area of inhalation therapy in order to maximise the effectiveness of both treatments.

The main determinants of deposition pattern for nebulized medications are breathing pattern during inhalation, droplet size and age/condition of the lung [93]. Inhalation therapy techniques and equipment therefore have the potential to alter the amount of drug which is delivered to its desired destination.

3.1 Inhalation Therapy Technique (including Adjuncts to Inhalation Therapy)

It is widely accepted that a quicker breath results in greater central deposition [93]. A slower breath results in a more peripheral deposition pattern, improved homogeneity of the deposition pattern and increased overall drug deposition [94]. Slow steady breaths with occasional deep breaths should therefore be used to promote improved deposition [95].

Combining airway clearance techniques and inhalation therapy is one way the time-related burden of care may be reduced in CF. However the literature provides limited evidence on the impact of this practice. Combining positive expiratory pressure (PEP) with inhalation therapy in patients with CF results in significantly lower lung deposition, a reduction in the inner-outer ratio and no difference in the apical-basal ratio of deposition [96]. This indicates that although there was less aerosol deposited in the lungs, there was a redistribution of the aerosol towards the periphery. Whether this would impact on the effectiveness of the inhaled medication remains unclear.

Frischknecht-Christensen et al [97] explored the introduction of a PEP device (facemask PEP) with the use of inhaled β_2 agonists via an MDI. The study showed improved bronchodilation, dyspnoea, cough and mucus production when compared to administration of the β_2 agonist alone. Stites et al [98] reported that the use of high frequency chest wall oscillation in combination with inhalation therapy did not result

in increased deposition of an inhaled solution compared to inhalation following standard chest physiotherapy. However in patients with COPD, addition of the RC-Cornet®. oscillating PEP device during nebulisation of ipratropium bromide resulted in improved bronchodilation [99]. These conflicting results highlight the need for further research into the combination of airway clearance techniques and inhalation therapy.

Physiotherapy Practice

The combination of PEP with inhalation therapy (hypertonic or isotonic saline and occasionally salbutamol) is commonly prescribed by physiotherapists around Australia. Some physiotherapists also combine inhalation therapy with positioning, and breathing techniques such as the active cycle of breathing technique or autogenic drainage. There is insufficient research investigating the combination of inhalation therapy and airway clearance to make recommendations regarding this practice.

The combination of inhalation therapy with ACTs could be considered in those patients who do not regularly perform any other form of airway clearance, or where adherence to ACTs is low and or a large number of nebulized medications are prescribed.

3.2 Mode of Delivery

Given the varying physico-chemical behaviours of the drugs nebulized in CF, it is important to use a specific nebuliser/compressor combination that has been proven to be effective for that preparation. By changing from an inefficient nebuliser system to an efficient one, there can be up to a ten-fold increase in the dose delivered [93]. Aspects that need to be considered are: flow/pressure characteristics of the driving source, the tubing connecting the nebuliser and the driving source, the nebuliser itself and the user interface (mask versus mouthpiece) [93].

Lannefors [100] recommends that when a medication may be administered via either a dry powder inhaler, metered dose inhaler or a nebuliser, the dry powder inhaler should be the preferred option due to ease of use. The exception to this is for the administration of inhaled steroids, where a metered dose inhaler and a spacer should be utilised to reduce systemic bioavailability and reduce growth of *candida albicans* in the mouth. In those patients unable to use a dry powder inhaler (eg poor respiratory function leading to poor inspiratory flow rates, cognitive impairments or muscular dysfunction) a metered dose inhaler and spacer should be chosen.

For bronchodilators, the European Respiratory Society recommends any certified nebuliser system as being appropriate and that a facemask or mouthpiece may be used. A mouthpiece is preferred for administration of anticholinergics to avoid irritation of the eyes [93]. A mouthpiece may not be appropriate if the sinuses are a target of therapy [101].

Ultrasonic nebulisers should not be used for dornase alfa as they can alter its physico-chemical properties, rendering it ineffective [102]. A list of recommended nebulisers is provided in the dornase alfa consumer medicine information sheet.

It is often recommended that patients use an expiratory filter when nebulising antibiotics [95]. This is primarily due to the potential side effects for other people. In the hospital setting, it is recommended that a high efficiency expiratory filter be used to prevent contamination of the environment and allergic reactions from staff. In the community, people with CF should take their antibiotics in a well ventilated room by themselves. If they have a sibling with CF, an expiratory filter should be used [103].

Physiotherapy Practice

Where possible, nebulized medication should be taken via a mouthpiece to maximise delivery of the drug to the airways. The exception to this is young children who may be unable to coordinate the use of a mouthpiece effectively, or where sinuses are a target of therapy, or those acutely unwell with shortness of breath. Bronchodilators should be delivered by metered dose inhaler and spacer except in situations where this may be clinically ineffective eg paediatrics or acutely unwell patients with shortness of breath (nebulisers should be used in these circumstances). Metered dose inhalers with spacer should be used for the administration of inhaled corticosteroids. Patients should be encouraged to rinse their mouth with water and gargle afterwards to reduce the risk of thrush.

3.3 Mixing Inhaled Medications

The concept of mixing nebulized medications simultaneously is often raised in an attempt to decrease the time burden associated with use of multiple inhaled agents. The European Respiratory Society [93] advise against mixing medications due to concerns about both safety and effectiveness, unless the specific mixture (including preservatives if applicable) has been studied. Whilst some medications may be chemically stable once mixed, there is often a lack of research regarding the aerodynamic properties of these mixed solutions [104].

Dornase Alfa

It is recommended by the manufacturers that dornase alfa not be mixed due to fears of reactions between medications [104, 105].

Antibiotics

Tobramycin can be mixed with albuterol and ipratropium if refrigerated. Tobramycin should otherwise not be mixed. Colistin and preservative-free unit-dose salbutamol inhalation solution remains stable for over an hour. There are inconsistent reports regarding the mixing of colistin and acetylcysteine [104].

Hypertonic Saline

Delvaux et al [106] found that by mixing salbutamol with hypertonic saline during an induced sputum procedure in asthmatics, the quality of the sputum produced was not altered but the level of protection against bronchospasm was improved. This occurs despite pre-treatment with 400µg of salbutamol via a metered dose inhaler and a spacer. Hypertonic saline should not be mixed with any other medication eg dornase alfa, antibiotics.

Other Medications

Budesonide can be mixed with terbutaline, albuterol, cromolyn, acetylcysteine and ipratropium; ipratropium can be mixed with albuterol or N-acetylcysteine sodium [104]. Caution should be taken if mixing salbutamol and an anticholinergic (eg ipratropium bromide) due to a small number of reports of acute angle closure glaucoma associated with this combination [107].

Physiotherapy Practice

Inhalation therapy is time-consuming and patients may wish to mix inhaled medications in an effort to reduce the time-burden of CF health care. Given the lack of research regarding the effect of mixing nebulized medications on aerodynamic properties and chemical composition, it is recommended that medications are not routinely mixed. Physiotherapists should direct patients to their CF doctor or pharmacist for advice on the mixing of inhaled medications.

3.4 Timing and Order of Inhaled Medications

There is no consensus regarding the optimal timing of dornase alfa in relation to ACTs. A randomised crossover trial has shown significant improvements in small airway function if dornase alfa is administered before ACTs [108]. However, previous

authors showed equal efficacy when dornase alfa was administered before or after ACTs, except in the subgroup of patients colonised with *P aeruginosa* who had greater improvement in FEV_1 when dornase alfa was administered after ACTs [109]. These disparate results may indicate differences in clinical characteristics - there may be a subgroup of patients who produce copious secretions that may receive more benefit if dornase alfa is administered after ACTs, allowing the medication to remain in the airway for a longer period. It has also been demonstrated that a longer time interval between administration of dornase alfa and airway clearance (eg inhalation before bedtime) is more effective than inhalation immediately preceding treatment [110]. There appear to be no detrimental effects on sleep quality or nocturnal cough associated with administering dornase alfa before bedtime [111]. Given the long-term beneficial effects of dornase alfa on lung inflammation in CF [112], ensuring that patients are adherent to daily inhalation is of greater importance than the time of administration. It is therefore currently suggested that dornase alfa be administered before bedtime if that is acceptable to the patient, whilst acknowledging that this regimen may need to be altered for individuals in order to optimise adherence.

The British Thoracic Society Nebuliser Project Group [95] recommended that bronchodilators be administered prior to ACTs, however there is to date no objective evidence that this enhances the benefits. If patients have known bronchodilator responsiveness then bronchodilator therapy and airway clearance techniques should precede the delivery of other inhaled medications [113]. Nebulized antibiotics should be administered after airway clearance and bronchodilators, in order to maximise the drug deposition within the lungs and to protect against bronchoconstriction [103]. It does however need to be recognised that some patients with CF demonstrate increased airway obstruction post bronchodilator therapy due to a reduction in smooth muscle tone [114].

Physiotherapy Practice

Bronchodilators should be administered prior to airway clearance if patients have previously demonstrated a benefit from bronchodilator therapy. It also generally advised that saline (isotonic or hypertonic) be taken either before or during ACTs.

Dornase alfa can be administered prior to ACTs, however it is recognised that individual variations in response may govern when this preparation is administered. Efforts should be made to maximise the time interval between administration of dornase alfa and ACT; this may involve administration of dornase alfa at bedtime.

When providing advice to patients on order of inhaled medications, especially in relation to timing of ACT, any specific recommendations or instructions that are given by the prescribing physician or pharmacist should be followed.

3.5 Nebuliser Maintenance

Nebuliser devices are sources of bacterial contamination and can lead to an increased risk of patient infection. It has been suggested that the inhalation of aerosols contaminated with gram-negative bacteria generated from home-use nebulisers may be a primary route for bacterial colonisation of the lung in CF [115].

There is no one method which has been recommended for cleaning home nebulisers Rosenfeld et al [116] suggested that soaking and rinsing with tap water for at least one minute followed by air drying is an effective cleaning method. This finding was published in an editorial and the weight of the evidence is unclear. Reychler et al [117] found that cleaning via a dishwasher (temperature of 70^{o}C) or immersion for 20 minutes in a litre of Hexanios 0.5% hypochlorite solution or hot water (40^{o}C) combined with detergent were all effective against the common pathogens found in patients with CF. Acetic acid (vinegar) however was found to be ineffective against *Staphylococcus aureus* and *Stenotrophomonas maltophilia*.

Physiotherapy Practice

All physiotherapists should be aware of the possible contamination of inhalation therapy equipment and the implications this may have for the patient's health. Cleaning methods should be reinforced as part of routine assessment and treatment. A review of the patients' cleaning technique may be incorporated into annual inhalation therapy reviews, outpatient clinic appointments or during an inpatient admission and this may be performed by any member of the CF health care team with appropriate and relevant knowledge.

It is recommended that nebuliser equipment and inhalation devices be cleaned after every use according to the techniques recommended by the local CF centre's infection control department (D). Nebuliser bowls should be replaced frequently according to the manufacturer's guidelines and pumps should be serviced at regular intervals according to the manufacturer's instructions (D).

3.6 Clinical Monitoring of Inhalation Therapy

Most inhaled medications have known side-effects. For instance, hypertonic saline, colistin and tobramycin may all cause bronchospasm [105]. The British Thoracic Society Nebuliser Project Group [95] recommended that patients should be assessed in hospital for their first trial of isotonic colistin and should be pre-treated with a bronchodilator. This group also recommended that spirometry be performed before and after the test dose because bronchospasm can occur within 15 minutes in over 85% of people.

The European Respiratory Society recommends that patients should be re-assessed one month after commencing their treatment and then be re-assessed annually thereafter [93]. It has been demonstrated that the uptake of education in inhalation therapy techniques is improved if repeated educational sessions are performed and if the patient is asked to demonstrate their technique at these sessions [118].

Physiotherapy Practice

All new medications should be trialled in the presence of a suitably qualified health professional. Sections to be covered in this review should include: preparation of nebuliser equipment and medication, positioning and breathing technique and monitoring of potential side effects. An inhalation therapy review should be performed annually by a designated member of the CF health care team with appropriate and relevant knowledge in inhalation therapy.

During an inpatient admission or during a clinic visit it may be appropriate for a physiotherapist to review the patients' inhalation therapy technique including reviewing their positioning during inhalation therapy and making recommendations to improve the effectiveness of the therapy. All physiotherapists should be aware of the possible side effects of medication prescribed for inhalation therapy and the possible implications of ineffective use of inhaled medications.

3.7 Recommendations

1. **Positive expiratory pressure devices can be used whilst nebulising hypertonic saline, isotonic saline or bronchodilators but are not recommended whilst nebulising antibiotics or dornase alfa. (D).**

2. **Where possible, nebulized medication should be taken via a mouthpiece.**

The exception to this is young children who may be unable to coordinate the use of a mouthpiece effectively, when therapy is targeted at the sinuses or those acutely unwell with shortness of breath (C).

3. **Nebuliser and compressor combinations with demonstrated efficacy for specific medications should be used where possible (B).**

4. **An expiratory filter should be used when nebulising antibiotics. Where this is not possible, antibiotics should be administered in a well-ventilated room with the person alone (D).**

5. **Bronchodilators should be delivered by metered dose inhaler unless there is clinical need for nebulisation (C).**

6. **Metered dose inhalers with spacer should be used for the administration of inhaled corticosteroids. Patients should be encouraged to rinse their mouth and gargle with water afterwards to reduce the risk of thrush. (B).**

7. **Inhaled medications should not be routinely mixed (D).**

8. **Dornase alfa may be administered before or after airway clearance techniques with the regimen adapted to each individual. A minimum of 30 minutes should be allowed between completion of the nebuliser and commencing airway clearance (B).**

9. **Nebuliser equipment should be cleaned after every use according to methods approved by the local infection control department (C).**

10. **All new medications should be trialled in the presence of a suitably qualified health professional and inhalation therapy regimens should be reviewed annually (C).**

4 Exercise

Exercise is a cornerstone of therapy for patients with CF. Aerobic fitness is an independent predictor of survival [119, 120] and those with better physical fitness have better quality of life [121]. There is some evidence that structured exercise programs for people with CF improve fitness and slow the rate of pulmonary decline [122]. For this reason it is recommended that all patients should be encouraged to exercise several times per week [11]. The physiotherapist has an important role in both the assessment of exercise capacity and exercise prescription.

4.1 Assessment of exercise capacity

Assessment of exercise capacity is an important tool in the evaluation of functional capacity, response to treatment and disease progression [119, 123-125]. For physiotherapists, exercise tests also provide the basis for exercise prescription. Assessment of exercise capacity should be undertaken prior to the prescription of a new exercise regimen, and as a reassessment tool to assess the efficacy of the exercise prescription.

Tests of exercise capacity include formal laboratory assessments of maximum exercise capacity (cardiopulmonary exercise tests) and field tests. Maximal exercise testing on a cycle ergometer or a treadmill is a specialist role which is usually performed by respiratory scientists and is currently outside the scope of routine physiotherapy practice. This document focuses on field tests of exercise capacity which are in common use in the CF population. These are the six minute walk test, the three minute step test and the modified shuttle test.

4.1.1 Six-minute walk test

The six-minute walk test (6MWT) is an easy to administer, well tolerated, self-paced, sub-maximal exercise tolerance test, reflective of normal activities of daily living [126]. Patients are required to walk up and down a hallway as many times as they can in six minutes. The 6MWT is suitable for use in the assessment of response to introduction of a new intervention in patients with moderate to severe lung disease and is also suitable as a one-off assessment of exercise capacity and predictor of prognosis.

The 6MWT has traditionally been an important tool for preparation for lung

transplantation in CF. In a study reviewing 145 patients with lung disease (41 of these with CF) it was concluded that a distance of less than 400 metres achieved in the 6MWT is a reasonable indicator to consider referral for lung transplantation depending on review of other clinical variables [127]. The 6MWT has been shown to have a strong correlation with peak oxygen uptake in end-stage lung disease and in severely ill children [128].

Distance walked during a 6MWT is highly reproducible in children and adolescents with CF and is correlated with clinical variables such as expiratory muscle strength, maximum heart rate and dyspnoea scores [129]. The 6MWT is also a useful tool for assessing exercise-induced desaturation in adults with mild to moderate lung disease. The greatest degree of desaturation is seen in those with the lowest pulmonary function [130].

Physiotherapy Practice

The protocol for the 6MWT can be found in Appendix 7.

The 6MWT is extremely valuable as an indicator of limitation to activities of daily living and can be used to assess exercise-induced oxyhaemoglobin desaturation in patients across the spectrum of respiratory impairment [130]. The 6MWT is the recommended assessment tool for patients undergoing assessment for lung transplantation [127].

The main outcome of the 6MWT is distance walked. However, adults with mild to moderate CF lung disease cover a similar distance to healthy volunteers on a 6MWT [130]. This suggests that there may be a ceiling effect on this test which may limit its utility in assessing change following intervention in those with less severe pulmonary involvement. Another limitation of the 6MWT is that it is self-paced and thus dependent on the patient's motivation level. However it remains an extremely useful test to measure change over time following interventions such as exercise programs, especially in those with more severe lung disease.

Contraindications: The 6MWT is contraindicated in patients presenting with cardiac conditions that are unstable in the month prior to testing.

Precautions to be considered in the CF population include a resting heart rate of ≥120 beats per minute, systolic blood pressure of more than 180 mmHg, or a diastolic blood pressure of more than 100 mmHg.

4.1.2 The 3-minute step test

The 3-minute step test (3MST) is a submaximal test of exercise capacity used to determine exercise tolerance in individuals with CF [131-133]. It is an externally paced test which involves stepping on and off a 15cm step for three minutes at a rate of 30 steps per minute. The 3MST is highly reproducible, provokes a greater increase in heart rate and breathlessness than the 6MWT and equivalent levels of oxygen desaturation [131]. It is also responsive to change over the course of antibiotic treatment in children with CF [133] and therefore may be a useful alternative or adjunct to lung function tests to provide positive feedback during the course of the admission.

The 3MST is not dependent on the patient's motivation as it is an externally paced exercise test. It is quick, portable, reproducible and simple. It must be emphasised the 3 minute step test is not a maximal test, however it may be more sensitive to change in heart rate and oxygen saturation in patients with CF and moderate-severe lung disease than it is in those with mild disease [132].

To date, all the studies pertaining to the 3MST have been conducted in children and there has been no examination of the long-term predictive value of this test in CF. Further study is required to determine the sensitivity of the 3MST to clinical change over time in both the paediatric and adult setting. However if time and space are limited it may be appropriate to use the 3MST for annual review of exercise tolerance testing.

Physiotherapy Practice

The protocol for the 3MST can be found in Appendix 8.

The main outcomes of the 3MST are maximum heart rate, minimum oxygen saturation and breathlessness scores. Treatment of an acute exacerbation results in improvement in all these outcomes [133]. The 3MST should therefore be considered as a useful measure in the inpatient setting, particularly if lung function testing is not readily available, or the patient does not display significant changes in lung function.

The 3MST may be useful to assess the need for supplemental oxygen in individuals with moderate to severe lung disease as it is of sufficient intensity to provoke oxygen desaturation in this group [132]. The use of the 3MST in the evaluation of therapy for exercise-induced asthma has not been examined in the literature but clinically may prove to be a useful tool in these circumstances.

The 3MST is quick and easy to perform, has minimal space requirements and is independent of patient motivation. The portable nature of this test makes it ideal to perform across the many inpatient, outpatient and home-based settings where adults with CF receive treatment. However, it may not provide a sufficient exercise stimulus for patients with mild disease [132].

Contraindications: as for the 6-minute walk test

Precautions: The 3MST should be avoided in individuals with significant lower limb joint arthropathy [131].

4.1.3 Modified Shuttle test (walk/run)

The modified shuttle test (MST) is an externally paced, incremental test of maximum exercise capacity. The participant is instructed to walk or run around two cones placed nine metres apart in time to auditory cues from a pre-recorded tape. The required speed becomes progressively becomes faster as each level is completed. The test is terminated when the participant is no longer able to maintain the required pace or if they fail to complete the current shuttle before the 'bleep.'

The MST has similar sensitivity to change when assessing the effects of IV antibiotic treatment as does the 3MST [134], and is possibly more sensitive to change than changes in FEV_1 noted over the course of intravenous antibiotics. It is a valid measure of exercise tolerance in children [135]. The MST has been shown to have high validity, reproducibility and responsiveness in measuring exercise capacity in the adult population [123, 136].

Physiotherapy Practice

The protocol for the MST can be found in Appendix 9.

The MST is appropriate to use in both children and adult CF populations. It has the advantage of being a maximal test and therefore provides sufficient challenge for those with milder disease. In clinical practice this test could be used in an annual review setting (if time and space allows), during an inpatient admission for a patient with moderate to good lung function, and when determining oxygen requirements/desaturation patterns prior to prescribing an exercise program [136].

The outcomes of the MST are distance covered, peak heart rate and peak Borg scale of breathlessness. If there is a change of greater than 40 metres in the MST then it is likely that real clinical change has occurred [123].

Although the MST is externally paced it may still be influenced by patient motivation. If a patient has low motivation or is very unwell they may not perform the test to their full capacity. It may therefore not be suitable for patients at the beginning of an acute exacerbation or in those patients with severe lung disease [134].

4.1.4 Choosing a test of exercise capacity

Exercise tolerance testing should be considered as a standard element of CF care across the range of ages and disease severity. An exercise test should be performed at least annually to document changes in exercise capacity. The choice of test should take into consideration the following factors:

Age of patient – the 6MWT and MST have been validated in both adults and children with CF. The 3MST has been validated in children but to date its role in the assessment of exercise capacity in adults with CF has not been documented.

Lung function severity – The MST can be used in patients across the range of disease severity but may be overly challenging for those with severe disease. The 6MWT is an excellent choice for those with severe disease but may have a ceiling effect in those with mild to moderate lung disease with well preserved exercise tolerance. Likewise, the 3MST may be most sensitive to changes in heart rate and oxygen saturation in those with moderate to severe disease.

Clinic space – the 3MST has minimal space requirements. The MSWT requires a 10 metre track, whilst the 6MWT ideally requires a 30 metre track and therefore may not be practical in some settings.

Access to equipment – All tests require a pulse oximeter to measure oxygen saturation and heart rate. Equipment for the 3MST and the 6MWT are usually readily available. The MST requires a tape of standardised instructions and timed audio cues.

Patient's motivation level – Both the 3MST and the MST are externally paced and may be most suitable for patients with low motivation.

Time availability – the 3MST is very quick to perform. Both the 6MWT and the MST must be performed twice due to a learning effect.

Clinical status – The 3MST is easy to perform during a hospital admission and is sensitive to change in clinical status. The MST provides more feedback to the patient regarding increase in distance covered from admission to discharge and is also

sensitive to clinical change during hospitalisation. The 6MWT may not be practical at hospital admission in patients who are very unwell.

At present, the literature does not suggest that there is one 'best' exercise test for people with CF. It is therefore recommended that the choice of test be based on the patient's current health status, their motivation level, and space availability in the clinic area.

4.2 Exercise prescription in cystic fibrosis

The ideal exercise prescription for people with CF has not been established. Both aerobic training (endurance exercise) and anaerobic training (resistance training or high-intensity, short duration training) are beneficial [122]. Aerobic training results in improved maximum exercise capacity, strength and quality of life [137]. Anaerobic training has positive effects on lactate levels, peak power [138] and fat-free mass [137]. Both types of exercise may have positive effects on respiratory function [2, 137]. Exercise programs have beneficial effects both during admission for acute exacerbations [91, 137] and in the stable outpatient [2, 138, 139]. It is unclear whether home-based, unsupervised training programs are equally as effective as supervised programs.

Physiotherapy practice

Exercise should be considered and encouraged as part of overall physiotherapy management in CF. From time of diagnosis, irrespective of age, exercise and physical activity should be incorporated into the daily routine. As a young child, family and siblings should be encouraged to also be involved in activity and exercise to assist in normalising the activity and making it 'fun'. At puberty there is evidence of a drop in physical activity in girls with CF [140, 141]. This reduction is associated with a more rapid decline in respiratory function in girls compared to boys [141]. Particular care should therefore be taken during adolescence to tailor exercise programs to the individual's interests, environment, time availability and capabilities.

Aerobic exercise prescription should follow the same principles as those used in healthy individuals [142] and patients with other chronic respiratory diseases [143]:

- exercise at least 3 days per week
- duration of 30 minutes per session, consisting of shorter intervals if required
- an increase in heart rate to approximately 75% of maximum heart rate is safe

and beneficial during exercise

A low-weight, high repetition training strategy can effectively increase FEV_1, strength and body mass in hospitalised children with CF [137]. Resistance training should be performed on alternate days to allow for recovery. A combination of both aerobic and strength training is required to achieve maximum benefits from training [122].

Patients with CF may exhibit exercise-induced oxygen desaturation during training, even when pulmonary function is relatively well preserved [144]. Supplemental oxygen during training increases exercise duration [145] however whether this results in improved clinical outcomes is not clear. It is recommended that supplemental oxygen be used during training in patients whose oxygen saturation falls to below 90% during exercise [146].

Exercise prescription in CF may consist of working with the patient to devise a formal exercise program or may simply involve provision of guidelines for appropriate intensity, frequency and duration of training. Formal exercise prescription should be considered in the following settings:

- Reported reduction in exercise tolerance/involvement in normal activities
- Known reduction in muscle mass/strength
- Osteopenia/osteoporosis
- Onset of CF related diabetes
- Patients awaiting lung transplantation

Special consideration should be given to meeting the metabolic demands of exercise in CF and consultation with the dietitian may be required. Care should be taken to ensure adequate fluid and salt intake, particularly in warm climates. Specific infection control recommendations for exercise in gym settings are provided in Chapter 13.

Exercise prescription should be tailored to the individual. When prescribing exercise the following should be considered: age of patient, indications and contraindications to exercise, interests of the patient, resources at the patient's disposal upon discharge, realistic goals, appropriate dosage (frequency, duration, intensity), and guidelines for monitoring safe exercise levels.

Contraindications: Exercise should not be performed in patients who are febrile,

whose cardiovascular status is unstable or in patients who have had a cardiac event within the last month.

Precautions to exercise include pulmonary hypertension, cor pulmonale and haemoptysis. Some patients have exercise-induced bronchospasm and should always take their prescribed bronchodilators prior to exercising. Care should be exercised in patients with low bone mineral density, particularly with regard to resistance training. Arthropathy and other musculoskeletal issues should be considered prior to commencing an exercise program.

4.3 Recommendations

1. **Assessment of exercise capacity should be performed annually (C).**

2. **An exercise test should be considered to assess response to therapy in the inpatient and outpatient settings and as an assessment tool in the prescription of exercise training programs (C).**

3. **A six minute walk test should be performed as part of the initial assessment for lung transplantation (C).**

4. **Exercise is recommended for patients with CF throughout the lifespan (B).**

5. **Exercise prescription should be tailored to the individual and comply with recommended exercise guidelines (B).**

6. **Supplemental oxygen should be considered during training in patients with severe exercise-induced desaturation (C).**

5 Musculoskeletal Complications of Cystic Fibrosis

Musculoskeletal manifestations of CF are frequently characterised by acute or chronic pain and arise as a result of multi-factorial abnormalities in bone mineralization, altered respiratory mechanics and muscular imbalance secondary to pulmonary disease. As survival in CF improves, the prevalence of these complications is increasing and the resulting compromise to physical activity and airway clearance may deleteriously impact on quality of life (QOL).

5.1 Pain

Reported rates of spinal pain (thoracic, lumbar, cervical) in CF populations are high. The prevalence ranges from 64% to 94% and is both substantially higher than age-matched healthy control subjects and presents at a younger age [147-151]. In addition, the incidence of chest pain varies from 32% to 64% [147, 148, 152]. Although documentation of back pain is increased in those with increasingly severe lung disease, it is not proportional to the degree of pulmonary hyperinflation [153]. The high frequency of musculoskeletal pain is associated with decreased QOL, sleep disturbance, anxiety and depression together with a reduced ability to perform chest physiotherapy and exercise effectively [148, 152, 154, 155]. Approximately 25% of patients fail to seek treatment to alleviate their symptoms of pain [148].

5.2 Low Bone Mineral Density

Patients with CF have multiple risk factors for inadequate bone mineralisation - poor nutrition, pancreatic insufficiency and malabsorption, calcium and vitamin D deficiency, reduced weight bearing activity, delayed puberty, hypogonadism, diabetes mellitus and chronic infection. A significant proportion of musculoskeletal problems in CF arise secondary to low bone mineral density (BMD). Despite BMD appearing to be normal in studies of healthy well-nourished children with CF, it decreases in the first decade of life and accelerates during adolescence and early adulthood, with up to 66% of adults with CF reported to have low BMD [156-164].

Low BMD is associated with greater disease severity, low BMI, decreased physical activity and the need for increased intravenous antibiotic and oral corticosteroid use [159, 161-164]. The reporting of osteoporosis and osteopenia in one or more sites varies from 10% to 79% irrespective of gender, with the incidence proportional to the

severity of lung disease [159, 161, 165, 166].

5.3 Vertebral compression and rib fractures

Low BMD, osteoporosis and chronic steroid use increase the risk of fracture in people with CF. Vertebral compression fractures and rib fractures appear to be 100 times and 10 times respectively more common in CF compared to the age-matched population [164]. These data support the evidence of above normal fracture rates from the age of six years and increasing to patient reported levels of 35 to 50% in adults [160, 163, 164]. In addition, a significant proportion of spinal compression and rib fractures may be underestimated, with radiological investigations revealing 76 asymptomatic fractures in patients with severe lung disease [164].

5.4 Increased thoracic kyphosis

Studies have reported a high prevalence of abnormal kyphosis angles (>40 degrees), in CF subjects, varying from 15-74% compared to a normal, age-matched population [164, 167-169]. Although the aetiology of CF related kyphosis remains unclear, a number of concomitant factors appear to influence its development. A higher incidence of vertebral wedging, particularly >15% thoracic wedging, severity of pulmonary disease, age and loss of BMD have been related to the presence of thoracic kyphosis in patients with CF [164, 169, 170].

The significance of thoracic kyphosis may depend on the extent of reversibility and postural correction. While some studies found the presence of kyphosis to be stable and unrelated to pulmonary function in terms of lung volumes or maximal expiratory flowrates [171], other studies have concluded that the diagnosis of a thoracic kyphosis is an indicator of deteriorating lung function and a marker of poor prognosis in some patients [167. In some patients, the kyphotic deformity may be improved with postural correction, suggesting that in the absence of a structural kyphosis in CF, changes in soft tissue structures and muscular abnormality may contribute to the ‘habitual hunched posture’ secondary to increased work of breathing and excessive coughing {Rose J, 1987 #726, 172].

5.5 Muscle strength

Changes in muscle strength, length and neuromuscular recruitment have been

demonstrated in patients with CF. Reduced lean muscle mass in CF subjects is associated with malabsorption and deconditioning [173, 174]. The associated reduction in peripheral muscle strength and endurance in both children and adults with CF is primarily reflective of lower muscle mass rather than reduced force-generating capacity of muscle [175, 176]. Intrinsic abnormality of CF skeletal muscles including decreased efficiency of oxidative ATP with abnormal mitochondrial density and metabolism, have been reported [175]. Impaired respiratory muscle strength may occur in association with reduced respiratory muscle mass from nutritional impairment [173]. Chronic use of corticosteroids is associated with skeletal muscle weakness [177].

Conversely, preserved respiratory muscle strength despite chronic hyperinflation may represent relative training of respiratory muscles in response to chronic loading [178]. This hypothesis was supported by the work of Pinet and colleagues [179] who concluded that CF patients with FEV_1<60% predicted had thicker and stronger abdominal muscles than did control subjects. It was postulated that this was a consequence of the heavier respiratory work performed by these patients. de Jong and colleagues [180] reported reduced peripheral muscle strength in CF patients with airflow obstruction in the presence of preserved inspiratory muscle strength. In relatively healthy CF subjects (FEV_1 60-124% predicted) few differences were apparent in muscular performance compared to healthy controls of similar moderate-high activity levels [181].

5.6 Muscle length

Reductions in thoracic cage muscle lengths, in the presence of chronic accessory respiratory muscle recruitment and associated postural habits that splint the shoulder girdle, have frequently been hypothesised in CF [182]. However, investigative research is rare. Rose and co-workers [153] performed postural examinations on young adults with CF and aged matched controls, demonstrating three motions in which at least 45% of patients with CF fell below control measures: scapular retraction, trunk extension and chest mobility (expansion). Shoulder retraction and back extension were reduced in 71% and 48% of CF subjects respectively.

5.7 CF-related arthropathy

There are several CF-related arthritic conditions which frequently present with joint

pain and discomfort. The predominant types are CF arthritis (monoarthritis, polyarthritis), pulmonary hypertrophic osteoarthropathy and arthritis due to co-existent conditions and drug reactions [147, 150, 167].

CF arthritis (also known as CF arthropathy) occurs in 2-8.5% of patients [149]. It is a rare syndrome of unknown pathogenesis. [183]. Clinical presentation includes joint pain, long bone pain, arthralgia and joint effusions, particularly during infective exacerbations. Joint pains typically develop over 12-24 hours and last 4-7 days. The patient is asymptomatic between episodes.

Hypertrophic pulmonary osteoarthropathy (HPOA) is associated with respiratory failure, and is present in 2-7% of patients. HPOA presents with insidious onset of bone and joint pain; and evidence of periostitis on XRay of distal long bones. Clubbing is considered a form of HPOA and the degree of clubbing is linked to the degree of pulmonary disease [184].

Ciprofloxacin-associated arthropathy occurs infrequently in children with CF [185]. It is likely that ciprofloxacin can induce arthropathy in adult as well as paediatric patients [186].

Rheumatoid arthritis, vasculitis, spondyloarthropathies, sarcoidosis, amyloidosis all have been reported in association with CF. Rheumatoid factor titre is higher in CF than healthy controls. Rheumatic symptoms occur in 33% of adults with CF and arthritis in 2.5-12% of patients. [187].

5.8 Physiotherapy intervention for musculoskeletal problems

To date, no prospective studies have evaluated the efficacy of spinal joint mobilisation, massage, specific muscle strengthening exercises or postural advice on back pain, airway clearance, sputum expectoration or lung function in CF [188]. However, there is support advocating for the role of a variety of therapeutic approaches to optimise BMD, muscle strength, length and postural education as well as manual therapy to improve spinal mobilisation.

5.8.1 Optimise physical activity to maintain bone mineral density and muscle mass

Nixon and colleagues [189] reported children and adolescents with CF performed significantly fewer hours of vigorous activity than a normal age matched control

group (2 vs. 3.7 hours per week). Gains in BMD achieved through physical activity have been short lived in athletic populations [190] and intervention studies [191]. Exercise in pre-adolescence without CF produces higher gains in bone mass than does exercise in adulthood and should be high-impact, generating ground reaction forces greater than twice body weight, to maximise gain [192].

5.8.2 Optimise muscle strength

Habitual 'slouched' postures are common in CF patients and may predate structural change. Physiotherapy programs should thus include strengthening of thoracic extensor muscles and scapular stabilisers to improve endurance and limit persistent thoracic flexion. It is well established that strengthening programs are effective in the CF population [193]. The majority of reported home programs that apply a normal therapeutic training stimulus have yielded physiologic and psychological dividends [2, 139, 194, 195]. Improved adherence in CF patients is associated with supervision, individualised and flexible programs [193, 196], and knowledge of the condition and treatment rationale [197]. Additionally the work of Hodges and colleagues [198] have highlighted the impact of painful conditions resulting in ineffective neuromotor recruitment of the core trunk stabilisers thus postural correction should consider both relative strength and timing of muscle recruitment in conjunction with pain assessment.

5.8.3 Optimise muscle length

Thoracic stretches may have a role in the management of thoracic impairment to target identified shortened muscles in CF patients. A systematic review of the efficacy of muscle stretching demonstrated lasting increments in range of motion (ROM) in the presence of reduced muscle flexibility, in response to programs of greater than three weeks duration [199]. While evidence is restricted to long muscles a rationale exists in the thoracic region where restriction is present and appropriate muscle lengthening stimulus applied. Muscle length is particularly sensitive to the most extreme lengths experienced [200]. Additionally, education regarding postural correction should be included eg reduction of habitual postures that promote increased kyphosis, use of lumbar rolls, and active work pauses that include thoracic rotation and extension. This rationale reflects the close relationship between joint mobility and muscle flexibility in the presence of a relatively rigid thoracic cage.

5.8.4 Manual therapy and pain management

Spinal pain is troubling and warrants assessment in each individual to determine the likely source – be it intrapulmonary, pleural, bone (vertebral or rib fracture), joint (costovertebral, costotransverse, sternocostal) or muscular. A systematic review by van Tulder and colleagues [201] concluded strong evidence exists to support the use of manual therapy and exercise in the treatment of chronic musculoskeletal spinal pain. Home exercise programs were similar if not more effective in the management of chronic lower back pain particularly when combined with education and goal-directed [201]. Interestingly, unlike normal populations in which spinal pain is associated with abdominal weakness, CF patients have relatively increased abdominal muscle strength from chronic coughing [179]. Early reports regarding the use of manual therapy in the management of pain and restriction in thoracic patients is encouraging, but limited [202, 203]. In an analysis of service provision, symptoms of low back pain and poor posture in patients with CF improved or resolved in 66% following joint mobilisations, exercise and postural advice [204]. Despite the confounding issues of self-selection, this demonstrates that musculoskeletal pain may be reversible and emphasises the importance of prompt treatment to prevent respiratory deterioration as a result of compromised airway clearance and mobility. It is hypothesised that a home program that incorporates self/auto mobilisation with postural correction and stretching may gain the therapeutic effect of manual therapy. The primary clinical approach to CF-related arthropathy involves rheumatological management, which may include some degree of physiotherapy involvement, in terms of increasing physical approaches for pain relief and exercises for muscle strength.

Physiotherapy practice

Physiotherapy management of CF musculoskeletal impairment is warranted to relieve pain, promote physical activity, to optimise BMD and muscle mass, limit postural deformity and minimise the burden of CF disease.

The CF physiotherapist should provide prompt assessment and treatment of acute musculoskeletal pain. A concise screening tool for use in clinic may facilitate this process; an example is given in Appendix 10. Key components are:

- Subjective history, pain scales (Short-form McGill questionnaire)
- Functional scales with standardised items [205, 206] or patient-specific functional scale [207]
- Objective assessment, including posture

- Precautions & need for referral/medical investigation
- Likely structural source
- Evidence based interventions
- Reassessment
- Home program

When a patient with CF presents with a **swollen, hot, painful weight-bearing joint**, principles of management include:

- Rest affected joint/s
- Decrease impact or load in activity and exercise
- Reduce intensity and duration of exercise
- Encourage exercise of other joints; avoid exercise that increases pain
- Consult with other health care providers regarding optimal management of pain and inflammation
- When acute episode resolves, strengthening of muscles around the joint may be required.

When a patient with CF presents with a **painful but normal looking weight-bearing joint**, principles of management include:

- Reduce intensity and duration of exercise
- Encourage exercise of other joints; avoid exercise that increases pain
- When acute episode resolves, strengthening of muscles around the joint may be required.

When a patient with CF presents with problems in **non-weightbearing joint/s**, principles of management include:

- Modify exercise programs to reduce load on affected joint/s (eg walking rather than basketball)
- Consult with other health care providers regarding optimal management of pain and inflammation.

Additional physiotherapeutic interventions for patients with CF may include but are not limited to:

- Assessment for joint laxity, stability, or stiffness
- Maintain range of motion of affected joint/s and active exercise of other parts
- Local measures such as ice may be used for painful and inflamed jointsif warranted
- Manual therapy and therapeutic massage [208]
- Referral to medical colleagues and other physiotherapists with expertise in musculoskeletal issues

The optimal time to minimise or prevent musculoskeletal deformity may be in the pre-pubescent years (approximately 8-12 years of age) prior to significant structural change particularly of bone [182, 209, 210]. The European consensus regarding standards of care for patients with CF [211] includes the physiotherapists' assessment of "posture, chest mobility, muscle strength and endurance" every "1-3 months or at every outpatient clinic visit". This intensive approach is recommended in the presence of 0.5-1.0 (pediatric CF centre) / 1.0 (adult CF centre) physiotherapists per 50 CF patients.

The CF nutrition consensus statement [212] supports the periodic assessment of BMD from the age of eight years and then every three to five years if BMD is normal, every two years if BMD is moderately reduced and annually if BMD is severely reduced. More frequent scanning is recommended if significant new risk factors emerge.

Physiotherapists should promote physical activity to improve or maintain BMD and muscle strength.

Key components of home exercise programs for people with CF are:

- Individualised assessment. Exercise prescription should be patient specific in terms of muscle strengthening, stretches, self/auto mobilisation & postural correction.
- A muscle strengthening program should be included if muscle imbalance/weakness is contributing to postural impairment or pain with a normal training stimulus applied.
- A muscle stretching program should be included if muscle or joint stiffness is contributing to postural impairment or pain.

- Education regarding postural correction/health should be included eg reduction of habitual postures that promote increased kyphosis, use of lumbar rolls, and active work pauses that include thoracic rotation and extension.
- Standardised measures and reassessment should be included to determine and maintain program efficacy.

Musculoskeletal management in the presence of CF utilises diverse physiotherapy skills given the wide scope of presenting problems. These may include: acute sports injury, acute joint flares in the presence of CF related arthropathy, or acute pain associated with coughing. Physiotherapists will draw on skills in biomechanical assessment of posture and movement, exercise prescription (for the extremely deconditioned to elite athlete), management of pelvic floor dysfunction, and management of the musculoskeletal challenges of rapid body change during puberty, pregnancy, and post lung transplantation. Ultimately physiotherapists have an important role in the quantification of CF musculoskeletal impairment and the provision of effective musculoskeletal interventions, to enhance QOL for people with CF.

5.9 Recommendations

1. Prompt assessment and treatment of acute musculoskeletal pain should be provided (D).

2. A musculoskeletal assessment should be included at annual review from age eight (pre puberty). Earlier assessment is warranted if pain or functional impairment is reported or BMD risk highlighted (C).

3. The physiotherapist should provide musculoskeletal home programs based on individualised assessment (D).

4. The CF physiotherapist should contribute to the optimization of bone density (particularly in the pre-puberty period) (B) and optimise muscle mass (A) applying 'normal' training stimuli.

6 Physiotherapy management of the complex patient

Cystic fibrosis is a complex multi-system disease and patients often experience significant complications which may require alteration to their usual physiotherapy management. These complications include haemoptysis, pneumothorax, allergic bronchopulmonary aspergillosis and CF-related diabetes.

6.1 Haemoptysis

Haemoptysis is defined as the expectoration of blood from the lungs or bronchial tubes as a result of pulmonary or bronchial haemorrhage [213] p 701. Whilst the presence of occasional mild haemoptysis is common in cystic fibrosis (CF) and not life-threatening, severe haemoptysis can lead to asphyxiation, airway destruction, shock and exsanguination, and should be treated promptly [214].

Mild haemoptysis is very common, affecting approx 62% of all patients with CF [215]. The overall incidence of massive haemoptysis in CF has been reported as approx 1% in children [216], and between 4% and 10% in adults [215, 217]. Haemoptysis is unrelated to the severity of lung disease in children [216]. However massive haemoptysis is more prevalent in adults with severe lung disease, with approximately 60% of patients having an FEV_1<40% predicted [214, 217].

Medical management of mild haemoptysis consists of observation combined with antibiotic therapy to treat underlying infection [218] and the use of tranexamic acid [219]. For severe haemoptysis, the vessel may need to be occluded using bronchial artery embolisation [218, 220, 221]. Surgical ligation or excision of the affected segment/ lobe is recommended if embolisation is not successful [220].

Physiotherapy practice

There are no published data regarding physiotherapy management of patients with haemoptysis. The following recommendations are based on expert opinion and clinician consensus.

The physiotherapist should review ACTs and inhalation therapy in order to maximise secretion clearance and encourage gentle expectoration without exacerbating bleeding.

Blood streaked sputum, first episode:

- Reduce the force of coughing
- Cease highPEP
- Minimise head down tilt positions
- Provide reassurance and education

Blood-streaked sputum, recurrent episode:

- Normal airway clearance treatment
- Normal exercise routine

Moderate Haemoptysis (<250mls/ 24 hrs)

- Seek medical review
- Cease percussion, vibrations, oscillatory PEP techniques, hypertonic saline nebs and head down tilt positions
- Maximise controlled airway clearance and gentle coughing
- Ensure adequate humidification to ease sputum expectoration
- Encourage walking
- Cease vigorous exercise

Severe Haemoptysis (>250mls/ 24 hrs)

- Seek medical review
- If active bleeding, position into high sidelying with bleeding side down
- Cease airway clearance and exercise until active bleeding resolved, then continue as per moderate haemoptysis

Following Embolisation

- Ensure adequate analgesia and humidification
- Gentle mobilisation following surgeon/ radiologists advice, then gradually increase intensity of exercise
- Airway clearance using ACBT or AD initially
- Gradually reintroduce normal airway clearance regimen

6.1.1 Recommendations

When haemoptysis is present, the physiotherapist needs to maintain adequate airway clearance and exercise regimens whilst promoting vessel healing and minimising the risk of re-bleeding (D).

6.2 Pneumothorax

A pneumothorax is defined as the presence of air within the pleural space. In cystic fibrosis (CF), it is generally termed a secondary pneumothorax as it occurs as a result of underlying lung disease. A pneumothorax may occur in a patient with CF as a result of rupture of sub-pleural blebs on the visceral pleura [222, 223] or, less commonly, as a result of misplacement of a central line [222](ACPCF 2002). A pneumothorax can present a major problem in a patient with CF as the collapsed lung can be stiff and take a long time to re-expand [224].

The overall incidence of pneumothorax in patients with cystic fibrosis is 3.4% to 6.4% [223, 225, 226]. There is an equal risk for men and women [225]. Pneumothoraces occur more frequently in patients with more advanced disease [227], and hence the incidence increases to 18-20% in adults [215, 228, 229]. The vast majority of CF patients with spontaneous pneumothoraces have an FEV_1 less than 50% predicted normal [225, 228].

For small pneumothoraces in an asymptomatic patient, medical management usually involves observation and/ or aspiration. A large pneumothorax requires intercostal drainage. Intravenous antibiotics should be commenced at the same time to prevent infection and resultant sputum retention, which may delay re-expansion of the collapsed lung [224]. A recurrent pneumothorax requires more aggressive management, and hence a partial pleurectomy may be performed if the patient is fit to undergo surgery. If the patient is too unwell to undergo surgery, a talc pleurodesis is recommended [224].

Pleurodesis can make transplantation more difficult as it takes longer to remove the lungs and hence is not routinely performed in this population [224, 230]. The World Health Organisation guidelines state pleurodesis virtually rules out any prospect of future lung transplantation [220], however the current consensus is that pleurodesis is not an absolute contraindication [229].

Physiotherapy Practice

There are no published data regarding physiotherapy management of patients with pneumothorax. The following recommendations are based on expert opinion and clinician consensus.

Small Pneumothorax

- Monitor shortness of breath
- Cease PEP and other forms of positive pressure therapy
- Gentle coughing
- Ensure adequate humidification for ease of sputum expectoration
- Reduce exercise intensity
- Avoid upper limb resistance exercises

Large Pneumothorax

If pneumothorax is undrained, cease treatment and liaise with medical team.

If pneumothorax is drained:

- Review PEP and non-invasive ventilation
- Ensure adequate analgesia and humidification
- Maintain shoulder ROM
- Chest support during airway clearance
- Gentle coughing and huffing
- Avoid upper limb resistance exercises
- Submaximal exercise (walking, gentle cycling)
- Avoid positive pressure therapy while draining and for 1-2 weeks after to avoid pleural fistula and risk of recurrence

Pleurodesis:

- Ensure adequate analgesia
- Regular nebulisers
- Early mobilisation
- Commence ACBT/ AD with gentle coughing

6.2.1 Recommendations

When a pneumothorax is present, physiotherapists should ensure adequate airway clearance continues whilst minimising the amount of positive pressure generated inside the patient's lungs. Gentle exercise should continue (D).

6.3 Allergic Bronchopulmonary Aspergillosis

Allergic bronchopulnmonary aspergillosis (ABPA) is caused by a hypersensitivity response to *Aspergillus fumigatus* and other species). Aspergillus spores are trapped in the mucus of large segmental bronchi, germinate to form hyphae which elicits an immune response, and can lead to accumulation of focal pulmonary infiltrates, tissue damage and eventual destruction of lung tissue [231, 232]. It occurs in approximately 2 - 25% of CF patients, although it is more common in adult patients, those with lower FEV_1 and low body weight [231].

Detailed lung function testing in patients with ABPA shows abnormalities suggestive of airway narrowing, gas trapping and small airways disease [233]. The clinical features of ABPA are variable but can include increased cough, wheezing, focal pulmonary infiltrates, coughing up "plugs", frequent exacerbations and deteriorating lung function. A recent epidemiologic study also showed that some episodes of massive haemoptysis and pneumothorax were associated with ABPA [231].

Diagnosis is made via clinical features. There is usually also a rise in total IgE, increased aspergillus specific IgG and IgE and/or skin reactivity to aspergillus.

Medical management of ABPA involves oral steroids and/or antifungal agents as well as treatment of underlying infection.

Physiotherapy practice

There is no literature specifically pertaining to physiotherapy in ABPA. Some centres in Australia report successful use of hypertonic saline, with or without PEP, whilst closely monitoring lung function to ensure there are no adverse effects.

6.3.1 Recommendations

Physiotherapists should reassess the efficacy of usual airway clearance techniques in people with ABPA. Treatment should be modified based on response and symptoms (D).

6.4 Cystic fibrosis related diabetes

Cystic fibrosis related diabetes (CFRD) shares features of both Type 1 and Type 2 diabetes. Scarring of the exocrine pancreas leads to partial Islet cell destruction, causing disruption to the insulin secreting endocrine cells. Cystic fibrosis related diabetes manifests primarily as an insulin deficiency, and is best diagnosed via Glucose tolerance test (two hour blood glucose>11, further classified as "with or without fasting hyperglycemia").

Cystic fibrosis related diabetes has been associated with loss of weight and lung function for several years prior to diagnosis, and has been reported to increase whole body protein breakdown, as well as reduce lean body mass. It is the most frequent major co-morbidity in CF, occurring in 5-30% of patients, and is more common in patients with pancreatic insufficiency. Prevalence increases with age and is reported to be as high as 50% of patients aged over 30 years

The mainstay of medical treatment is insulin, usually in conjunction with specialist endocrinologists and much ongoing education. Specialist CF dietary advice is also necessary for optimal blood glucose level (BGL) control.

A literature review found no specific literature on physiotherapy in CFRD. However there is a wealth of literature on the role of exercise for type 1 and type 2 diabetes in non-CF patients. In type 1 diabetes, exercise can acutely lower blood glucose, improve glycaemic control and reduce HbA1c [234]. Exercise also improves vascular endothelial function [235]. In type 2 diabetes, exercise also improves glycaemic control and reduces insulin resistance [236]. Strength training has been demonstrated to be more effective than endurance training in this group [237]. Efforts should therefore be made to facilitate adherence to exercise programs in people with CFRD.

Physiotherapy practice

There are a number of important safety considerations in relation to diabetic patients and exercise.

Fast-acting carbohydrate snacks should be immediately accessible to all patients with CFRD during and after exercise. Patients with recurrent hypoglycemia may have poor hepatic glycogen stores, particularly where there is CF-related liver dysfunction. Carbohydrate intake pre-exercise is recommended in this situation to avoid hypoglycemia with exercise.

Consideration should be given to monitoring of BGLs levels before and after strenuous activity to determine BGL response to exercise. It is important to note that delayed hypoglycaemia can occur up to 24-36 hours after exercise as the muscles refuel. Monitoring will allow the CF team to take any necessary steps to prevent hypoglycemia.

If blood sugars are high prior to exercise then exercise can have a paradoxical effect on blood glucose causing it to rise. The high blood sugar is a reflection of inadequate insulin. Insulin is required during normal exercise to rapidly transport glucose into muscle. If there is insufficient insulin then hepatic glycogen stores will be released and blood sugar further elevated following exercise. It will however fall rapidly with use of insulin following exercise (causing delayed hypoglycemia).

Patients are frequently advised to select insulin injection sites that are away from areas used during the chosen form of exercise. Increased regional blood flow may result in faster absorption of insulin from such sites.

Consideration should be given salt supplementation and adequate hydration in people with CFRD. Attention should be paid to appropriate footwear and foot care to minimise the risk of diabetic ulcers.

6.4.1 Recommendations:

1. **Insulin injection sites should be away from areas used during the chosen form of exercise (D).**
2. **Fast acting carbohydrate snacks should be immediately accessible during and after exercise (D).**
3. **Consider monitoring BGLs before and after strenuous activity (D).**

7 Physiotherapy for pregnancy, labour and the post-natal period

7.1 Background

The improvement in health, quality of life and longevity in CF has increased the desire and possibility of adults becoming parents. In the 1980s, pregnancy was thought to be too risky for women with CF. However, increased survival means that pregnancy in women with CF is becoming more common and thus CF care teams can give better advice regarding likely outcomes. There are few published data that relate to the management of pregnancy in CF. Most literature reports the negative and positive outcomes of relatively small case series [238-241].

7.2 Physiological changes during pregnancy

The pregnant hormones of relaxin, progesterone, oestrogen and cortisols result in laxity of ligaments in preparation for the birth process. These effects are greater in mutigravidae than primagravidae women. It takes approximately 3-6 months for the body to return to the pre-pregnant state after the birth [242]. The maternal centre of gravity shifts posteriorly during pregnancy to accommodate the increased abdominal size resulting in changes in postural alignment and gait in later pregnancy. As thoracic and lumbar curves increase, so do strain on the vertebral joints. Back pain is common affecting more than 50% of women during pregnancy. Back pain is sometimes accentuated in women with CF especially during acute lung exacerbations and increased coughing.

Cardiac output increases by approximately 40% by 20 weeks. Blood volume increases by approximately 40%, with a peak at 30 weeks, secondary to new placental circulation. General vasodilatation occurs. This results in increased cardiac work during pregnancy [243]. Progesterone stimulates the respiratory centres of the brain to produce hyperventilation early in pregnancy. In late pregnancy secondary to hormonal changes relaxation of smooth muscle occurs in the tracheo-bronchial tree leading to a decrease in total pulmonary resistance. This may be beneficial to women with more obstructive lung disease. However, at the end of pregnancy, residual volume decreases secondary to elevation of the diaphragm. In the third trimester, especially with multiple foetuses, the enlarged uterus pushes upward and outward. The high abdominal wall tension raises the intra-abdominal pressure, even when the woman is

upright. The diaphragm does not descend appreciably, and therefore the FRC remains reduced. Expiratory reserve volume and FRC decrease by 15%. This may contribute to difficulty in removing respiratory secretions.

Oedema in the lower limbs is common in pregnancy and is caused by the effects of progesterone. When standing for long periods, gravity causes venous engorgement further exacerbating the problem. Carpal tunnel syndrome is caused by oedema in arms and hands compressing the distal segments of the median and ulnar nerves - generally later in pregnancy but sometimes occurs as early as 16 weeks.

7.3 Pre-pregnancy planning

It is widely recognised that a planned pregnancy is likely to result in fewer problems than an unplanned pregnancy. The multi-disciplinary team involved in the care of pregnant women should at least consist of a respiratory physician, obstetrician, physiotherapist, nutritionist and psychosocial practitioner, all experienced with CF. Inhaled, oral and intravenous medication and their potential for iatrogenic effects together with optimal nutrition and dietary supplementation should be reviewed [244].

All women with CF are advised to approach pregnancy with a regular airway clearance therapy routine. An optimal airway clearance therapy routine suitable for pregnancy should be developed. Modifications to physical exercise should also be planned. Domestic support during pregnancy and afterwards together with child care support once the baby has been born are necessary so that the mother has enough time and energy to carry out regular airway clearance, inhalation therapy and exercise [245].

7.4 Airway Clearance Therapy during pregnancy in CF

Head-down tilted postural drainage is not recommended during pregnancy because of the high prevalence of symptomatic and clinically silent gastro-oesophageal reflux (GOR) in adults with CF [246]. This is further compounded by the hormonal effects of progesterone during pregnancy resulting in a hypotonic lower oesophageal sphincter together with the growing weight of the developing foetus pressing against the stomach. Techniques that exacerbate nausea should be avoided.

Airway clearance techniques suitable during pregnancy include:

- Active Cycle of Breathing Technique
- Autogenic drainage
- Positive Expiratory Pressure (PEP) therapy
- Oscillating Positive Expiratory Pressure therapy (OscPEP)
- Effective huffing from different lung volumes avoiding dynamic collapse
- Physical exercise (appropriate to pregnancy) as airway clearance therapy

Mucolytic agents that may be used during pregnancy as adjuncts to airway clearance therapy include:

- Dornase alfa – may be continued if being used prior to pregnancy
- Hypertonic saline: 3 – 6%
- Saline 0.9%

Positioning during Airway Clearance Therapy

Because of the physiological changes of pregnancy, upright sitting is usually the most comfortable position for airway clearance. Consideration should be given to positioning during airway clearance to maintain a neutral lumbar spine for prevention and/or minimisation of urinary incontinence during treatment (see Appendix 11). Some women find left and right side lying horizontal or slightly head up to be more effective during ACT. The supine horizontal position should be avoided during the 2nd and 3rd trimesters because of pressure of the foetus on the inferior vena cava which may decrease venous return and cardiac output.

7.5 Pelvic floor function

Women with CF should be taught pelvic floor strengthening exercises to prevent and/or treat urinary incontinence (see Chapter 8). These exercises should be highlighted during pregnancy and in the post-natal period when urinary incontinence is a common problem. Increase in fluid intake and activity levels such as walking together with regular toilet habit help ease constipation.

7.6 Exercise during Pregnancy

Pregnant women are advised to modify their physical exercise program during

pregnancy. Contact sports should be avoided. Walking and swimming are appropriate forms of exercise. Women should avoid overheating and dehydration during exercise ensuring adequate water and electrolyte intake. Postural awareness, ergonomic advice, strengthening, mobilising and stability exercises and sometimes a lumbar sacral support belt assist in managing these normal pregnancy changes. Symphysis pubis, sacro-iliac joint and round ligament pain occur commonly around 29-32 weeks. An elastic binder, worn low below the belly to give support to the symphysis pubis and sacro-iliac joints while weight bearing, can provide significant relief. Diastasis of the recti muscles requires care in exercise.

7.7 Other physiotherapy interventions during pregnancy

Working and /or resting splints may be used to manage the symptoms associated with carpal tunnel syndrome. Contrast bathing to increase circulation and decrease oedema may also be helpful.

Lower limb oedema should be prevented by avoiding prolonged standing. Rest with feet elevated and muscle pump exercises and elastic support stockings are beneficial.

Physiotherapy advice about comfortable supported sleeping positions using extra pillows, relaxation and stress management techniques are useful strategies. Muscle cramps are common especially in later pregnancy. They may be caused by ischaemia and pressure of the uterus on the nerves or dietary issues. Calf stretches during the day, support stockings, medical advice on nutritional requirements such as calcium or salt and massage may relieve the problem. Plantar flexion should be avoided when waking up.

7.8 Physiotherapy during labour in CF

Pain, shortness of breath on exertion and low oxygen saturation are common in healthy women during labour. Oxygen saturation has been measured at 98% the day after delivery, whereas in labour it went as low as 87% in women without CF [243]. Thus desaturation may be marked in women with CF during labour. Oxygen therapy should be provided to maintain normal saturation. Bronchodilator therapy and assistance with sputum clearance may be required for some women during labour. Conservation of energy strategies should be employed. Adequate pain relief during labour is a high priority for women with CF, with normal vaginal delivery highly desirable in order to minimise post-delivery complications [245].

7.9 Physiotherapy post-Caesarian section in CF

Adequate post-operative pain relief, oxygen therapy (if required), appropriate inhalation therapy in the form of broncho-dilators and mucolytic agents together with optimal airway clearance therapy and early mobilisation are a priority after a Caesarian section.

7.10 Physiotherapy in the post-natal period

Physical support for the mother is a priority after birth. She needs to have time and energy to carry out appropriate airway clearance therapy, inhalation therapy and post-natal exercises.

7.11 Recommendations

1. **Postural drainage in head down tilted positions should not be used during pregnancy (D).**
2. **Exercise should be modified during pregnancy according to usual pregnancy guidelines (D).**
3. **During labour, appropriate pain relief, oxygen therapy, inhalational and airway clearance therapy should be provided as required (D).**
4. **Following delivery, adequate pain relief, oxygen therapy, appropriate inhalation and airway clearance therapy and early mobilisation should be considered (D).**
5. **Frequent contact with the multidisciplinary CF team and the obstetric team should be encouraged during pregnancy and the postnatal period (D).**

8 Physiotherapy management of continence

Urinary incontinence is the involuntary leakage of urine. There are two types of urinary incontinence, namely, stress incontinence and urge incontinence. The reported prevalence of urinary incontinence in girls and women with CF ranges from 22% to 64% [247-251] in comparison with 13% in healthy women aged 18-24 years [252]. In a recent study of urinary incontinence and bowel problems in women with CF compared to healthy controls, stress incontinence was significantly higher in women with CF (67%) compared to healthy controls (26%) [253]. Urinary incontinence in men with CF has received less attention in the literature but a recent report suggests a prevalence of 8% in males aged 16- 51 years, which is also higher than that found in healthy controls [254].

It is not known whether the cause of urinary incontinence in CF is chronic cough, paroxysms of prolonged coughing or demands placed on the pelvic floor during airway clearance therapy, huffing, coughing and physical exercise (all essential elements of recommended daily physiotherapy treatment), or underlying structural differences. It has recently been demonstrated that women with chronic lung disease did not differ from control subjects in pelvic floor muscle strength or timing of contractions; however women with chronic lung disease did have reduced endurance of pelvic floor musculature with prolonged coughing [255].

It has recently been demonstrated that treatment of urinary incontinence in women with CF by a qualified continence physiotherapist with exercise, electrical stimulation, biofeedback and bladder training resulted in significant improvements in pelvic floor strength, reduction in leakage and improvement in quality of life which were sustained for at least three months after the completion of treatment [256]. The recommended physiotherapy treatment is based on the results of this study.

Physiotherapy practice

Patients are embarrassed about incontinence and will seldom raise the topic with the health care team. However, if asked as part of routine assessment patients value the opportunity to discuss the problem and learn strategies to prevent and / or resolve the problem. All physiotherapists working with CF patients should include pelvic floor assessment and treatment as part of routine care, and if the problem persists should refer the patient on to a physiotherapist specialising in continence.

Patients should be taught “the knack”, a contraction of the pelvic floor prior to any

activity that increases the load to the pelvic floor (such as coughing, huffing, sneezing, laughing) to prevent leakage. This should become a lifelong habit.

Patients should be taught strength and endurance training of the pelvic floor and lower abdominal muscles for prevention of leakage during all activities that apply force to the pelvic floor such as exercise, airway clearance, huffing and coughing. Patients should also be taught optimal positioning during upright sitting for airway clearance therapy in positions that maintain a neutral lumbar spine and enhance pelvic floor function [257]. A protocol for pelvic floor training in CF is found in Appendix 11.

Trampoline jumping, a commonly prescribed form of physical exercise and airway clearance therapy is appropriate until the age of puberty. Thereafter, jogging on the trampoline is more appropriate to avoid excessive force on the pelvic floor.

Patients who continue to have a problem with bladder and bowel control should be referred for a course of specialised assessment and treatment using exercise, electrical stimulation, biofeedback and bladder training by a qualified continence physiotherapist.

8.1 Recommendations

1. Females with CF from puberty onwards should be taught "the knack", a way of bracing / preparing the pelvic floor to overcome the downward pressure during activities such as exercise, forced expirations and coughing (D).

2. Women should be taught preventative / rehabilitative strength and endurance exercises to provide better control of the pelvic floor (C).

3. Consideration should be given to positioning during airway clearance to maintain a neutral lumbar spine (C).

4. Patients who continue to have difficulties with bladder or bowel control should be referred to a qualified continence physiotherapist (D).

9 Physiotherapy management of the newly diagnosed patient

9.1 The newly diagnosed infant

Newly diagnosed infants with CF in Australia are generally asymptomatic and diagnosed via neonatal screening tests. Regardless of symptoms, all infants should meet with the CF multi-disciplinary team soon after diagnosis, either as an inpatient or a day stay outpatient [258, 259]. Physiotherapy intervention should begin immediately unless specifically delayed for a short period at a medical physicians discretion eg post bowel resection for meconium ilieus. Follow–up should occur frequently until the family is comfortable with the infant's routine and/or the infant is asymptomatic post acute infection.

The role of physiotherapy and airway clearance should be explained, demonstrated and practiced at initial education sessions regardless of symptoms [211, 260]. The rationale for airway clearance techniques should be explained with relation to:

Pathophysiology – Even in asymptomatic infants there is evidence of inflammation, infection and structural change in the airways [261, 262]. Treatment of early changes may preserve lung function and optimise long-term outcomes [263, 264].

Theory of airway clearance techniques - by improving mucociliary clearance, the development of chronic lung disease may be delayed [29, 263]

Adherence - routine may assist with adherence and teaches effective ACTs for when the infant is acutely unwell

Treatment of an acute chest infection - recognition of signs and symptoms so that necessary treatment can be started quickly.

Physiotherapy practice

Airway clearance for the newborn should fit in with the family's routine to aid adherence [1, 29, 260]. General consensus amongst Australian physiotherapists working with CF children suggests treatment of an asymptomatic infant should consist of 4-6 modified PD positions performed 1-2x/day. These positions should not include traditional gravity-assisted postural drainage in the infant due to the risk of GOR [58, 62, 64]. In each position percussion or thoracic compressions should be performed for 3-5 minutes with short rest intervals to allow for normal physiological

breathing. Vibrations are difficult to co-ordinate and not generally used with an infant. Total treatment time should be a maximum of 20 minutes per session. Some international centres also use PEP and assisted autogenic drainage [29] however these techniques are not in common use with infants in Australia.

Generally treatment should be encouraged before or at least one hour after feeds [29, 260] and be performed at a time that best suits the family routine. Some awake time treatment should be encouraged to aid future compliance. Coughing should not be induced in the asymptomatic infant, but imitation coughing should be encouraged from diagnosis.

If the child is unwell then treatment should be increased to 2-4 x/day and performed prior to antibiotic inhaled nebulisations. The teaching of inhaled medications may be performed by the CF Physiotherapist or Liaison nurse and differs in each centre. All members should promote a correct nebulisation technique with the family [265, 266].

On initial assessment the physiotherapist should encourage the parents to observe the infant's baseline signs and symptoms so they can identify possible signs of a chest infection. These signs and symptoms should be based on World Health Organisation (WHO) guidelines [267] and include changes in fever, cough frequency and/or sound, mood, stools, reflux patterns, work of breathing or breathing patterns, appetite or weight loss.

A cough swab, oropharyngeal suction or bronchoalveolar lavage (BAL) will be performed shortly after diagnosis, with or without a high-resolution computed tomography (HRCT) and chest X-ray (CXR). The physiotherapist may need to modify the individual program as these results become available. Attention should be paid to symptomatic segments of the lung affected by persistent atelectasis, inflammation, infection or abnormal anatomy.

General advice should be given to families on the need to protect their child from cigarette smoke, perform good hand-washing techniques and when to contact the CF team physiotherapist, particularly if the child becomes wheezy or breathless during treatment or has signs and symptoms of GOR.

It is important to establish a 'team' relationship with the family from diagnosis and emphasise the positive 'lifestyle' changes this experience may have [268]. Good parenting and behavioural management skills such as positive encouragement, the use of music/singing, regular routines, toys and pacifiers can be demonstrated and

encouraged to assist with future adherence with treatment [269]. Positions and methods with which to handle, distract and settle the child should be gently introduced and demonstrated throughout the session, particularly with first-time parents. Positive aspects of the importance of exercise and normal activity participation should be discussed. Normal developmental play and prone lying should be encouraged as the first steps towards an active physical life style and routine [29].

9.2 The newly diagnosed adult

Adults with a diagnosis of CF usually have milder disease than those diagnosed in infancy [211]. Symptoms are more subtle and initial sweat chloride tests are lower or equivocal. Only one system may be affected and there is a higher incidence of pancreatic sufficiency [211]. Often patients have a previous diagnosis of bronchiectasis and therefore may have had exposure to airway clearance techniques and possibly have established treatment regimens.

Education should be introduced slowly. Despite presentation with a milder form of disease adults with a CF diagnosis still have to accept living with a genetic and potentially severe chronic illness [263]. There should be no presumption of knowledge of the disease. Cystic fibrosis teams should assess what their adult-diagnosed patients know and what they need to learn. Specific problems should be addressed initially and further education introduced over a period of time in the outpatient or inpatient setting. The focus of treatment should be on self management but this may be dependent on disease severity and already established treatment regimens [263].

Education about CF and its management should consider the implications of the disease on established lifestyles [263]. Newly diagnosed adults may have unique needs regarding hospitalisation with significant impact on home, social and working lives. Establishing good communication and development of rapport are essential for a professional and supportive relationship [29]. Newly diagnosed adults may be active seekers of alternate sources for information, such as the internet. The CF team should ensure that patients are accessing reliable resources.

Care should be taken with early incorporation into a CF clinic until colonising organisms are established. Exposure to the multidisciplinary resources of CF clinic can optimise management of the diverse symptoms of adult CF disease.

Physiotherapy practice

Some newly diagnosed adults are very well; therefore physical exercise, huffing and coughing are appropriate stand-alone airway clearance techniques. However, it is still important that these patients are given information about other airway clearance techniques available to manage their respiratory symptoms. Comprehensive ongoing education about techniques and the rationale for their use may improve adherence in the future.

Those patients with established lung disease should be taught airway clearance and exercise regimens and educated about the role of nebulized drugs in their treatment.

9.3 Recommendations

1. Education by the physiotherapist should begin at diagnosis (D).

2. Routine treatment for newly diagnosed infants:

- **should be done before feeds, or at least 1 hour after feeds (C)**
- **should begin with the child awake (D)**
- **should be performed at a time that best fits in with family routine (D).**

3. The current treatment for infants is:

- **modified postural drainage in 4-5 positions (B)**
- **percussion for 3-5 minutes each position (C)**
- **vibrations do not need to be taught at diagnosis but can be introduced as control of breathing improves (D)**
- **cough should be spontaneous; however imitation of cough should be encouraged from the start of treatment (D).**

4. Physiotherapy treatment for the newly diagnosed adult should optimise airway clearance and encourage physical exercise (D).

10 Transition from paediatric to adult care – the physiotherapy role

Transition can be defined as the 'process of preparation for final transfer from paediatric to adult care systems; this transfer must be understood, ultimately, as success in aiding chronically ill children to start a productive life and achieve social integration as adults' [270].

It is well accepted that young adults with CF should receive their health care in adult settings [271, 272]. However, there is no doubt that transition is a stressful period for patients and families, with some being reluctant to consider transfer of care to an adult hospital [273]. Areas of most concern include potential exposure to infection; leaving a well-known physician; and meeting a new care team [274]. Parents also report significant concerns regarding the ability of their child to care for their CF independently as required in an adult setting [274, 275]. Age, gender and severity of lung disease do not predict the level of concern regarding transition [274]. Factors preventing the transfer of care from the paediatric to the adult team include patient and family resistance, medical severity and developmental delay [276].

There is no consensus regarding the best model of transition for patients with CF and there is little research on which to base recommendations. The most commonly used criterion for transfer to adult care is age [276] with 16 – 18 years being the preferred time [275]. However, the transition process must begin before this time. It has been suggested that discussions regarding transition should begin from the time of high school entry and no later than a year before transfer is expected [277]. Descriptive data indicate that meeting the adult team prior to transition is important in aiding the transition process [274, 278]. Patients report that provision of written information regarding the adult setting is useful [278] however it appears that if it is given around the time of transfer this information is not well retained [277]. Importantly it appears that the experience of transition impacts on future satisfaction with adult care [278].

Transition programmes differ between Australian centres. Many use a 'transfer clinic' where patients and families can meet with both the adult and paediatric teams prior to the transfer of care; the degree of preparation and coordination of the transfer process varies. The physiotherapist will work with the local team to facilitate a smooth transition between paediatric and adult services, regardless of the model utilised. However, there are some specific aspects of care that are important to address in the physiotherapy management of transfer.

Physiotherapy practice

During the transition process, physiotherapists from the paediatric and adult centres should communicate directly regarding the detailed aspects of each patient's treatment regimen [279]. The physiotherapist from the adult centre should meet the patient prior to transfer and opportunity should be provided to address the expectations and concerns of both patients and their parents regarding ongoing physiotherapy management. Infection control policies for physiotherapy in the adult setting should be discussed as part of the transition process [274]. Physiotherapists in the paediatric centre can assist the transition process by actively promoting self-management in the time leading up to transfer of care and providing positive information about the adult service.

The close liaison between paediatric and adult physiotherapy teams should not cease at the time of transfer but continue throughout the first year until the patient is well established in the adult clinic. This is particularly important if a patient becomes unwell soon after transfer, in which case the physiotherapists should communicate directly to ensure optimisation of physiotherapy care.

Transition should be a planned, coordinated and gradual process. The process must engage the young person with CF and their family in a non-confronting way. Cooperation between physiotherapy staff at adult and paediatric centres is essential for successful transition in CF.

10.1 Recommendations

1. During the process of transition, paediatric and adult physiotherapists should communicate directly regarding the detailed aspects of each patient's physiotherapy care (D).

11 Physiotherapy management for end-stage disease

11.1 Non-Invasive Ventilation in Cystic Fibrosis

The management of severe lung disease is an important component of care for patients with CF. With life expectancy now extending well into adulthood and many patients choosing to be listed for lung transplantation, maintaining optimum functioning in patients with end-stage lung disease is crucial. Non-invasive ventilation (NIV) has an expanding role in the management of CF-related acute respiratory failure and bridge to transplant; chronic respiratory failure; airway clearance; and exercise.

The physiological rationale for use of NIV in CF is that unloading of the respiratory muscles with positive pressure results in improved respiratory muscle performance, increased alveolar ventilation and improvement in gas exchange [280]. Support for this mechanism of action is provided by a number of short-term physiological studies. Reduced respiratory muscle work during NIV has been reported in both adults and children with CF, with reported reductions in work of breathing of 20– 60% [281-283]. This is associated with a 30% increase in minute ventilation and tidal volume, and reduction in transcutaneous carbon dioxide of 7% [283]. The results of these studies support the theoretical rationale for respiratory muscle unloading with NIV in CF, resulting in improved alveolar ventilation and better gas exchange. These effects are crucial to the clinical application of NIV in CF.

11.1.1 Acute respiratory failure and bridge to transplant

A number of descriptive studies report the successful use of NIV to stabilise patients with CF and acute respiratory failure [284-289]. In this group of patients with severe lung disease, NIV results in reduced $PaCO_2$, respiratory rate and dyspnoea. Although NIV does not reverse the respiratory deterioration inherent in end-stage disease, it may allow the patient to be stabilised for long enough for donor lungs to become available for transplantation. The use of NIV outside the group of CF patients awaiting lung transplantation has also been reported [289] where it may be useful for palliation of dyspnoea in end-stage disease (C).

Although there are no disease-specific guidelines for initiation of NIV during acute respiratory failure in CF, many useful principles can be taken from experience in

other lung diseases [290]. However, there are some special features of CF which should be taken into consideration when setting up NIV for this patient group.

1. Acid-base balance

Special care needs to be taken with analysis of arterial blood gases in CF patients with acute hypercapnic respiratory failure. As well as a respiratory acidosis, these patients frequently exhibit a metabolic alkalosis which may contribute to hypercapnia [291]. Metabolic alkalosis has been linked to chloride depletion and hypovolaemia, occurring secondarily to altered epithelial cell chloride transport in CF. Malnutrition, a common feature of end-stage CF, also contributes to metabolic alkalosis due to hypoalbuminemia. The presence of metabolic alkalosis may have implications for response to NIV in hypercapnic patients, and in some patients, electrolyte and volume correction may be required to restore acid-base balance (C).

2. Humidification

Non-invasive ventilation delivers air at high flow rates and with low relative humidity, which may overwhelm the capacity of the upper airway mucosa to warm and humidify inspired air [292]. The levels of humidity delivered during bilevel are lower than the levels reported to cause airway drying in users of CPAP [293]. This is of greatest concern in patients with excessive secretions, who are at high risk of sputum retention. Consideration should be given to heated humidification when NIV is used in CF.

3. Inhaled therapies

Patients with CF often require frequent and multiple inhaled therapies, such as bronchodilators and mucolytics. Consideration must therefore be given to the route of administration of these therapies in the patient using NIV. For some patients, breaks from NIV may be appropriate, at which time inhaled therapies can be given via their usual route. For NIV-dependent patients however, administration of inhaled therapies during NIV will be required. Connectors for metered dose inhalers (MDIs) are available; alternatively, a T-piece connector for nebulisation can be used. Ensure that the nebuliser is connected between the patient and the exhalation port.

11.1.2 Sleep disordered breathing and chronic respiratory failure

Hypoxia and hypercapnia occur commonly during sleep in moderate to severe CF [294, 295]. These alterations in gas exchange are frequently seen during sleep prior to

being evident in the daytime [144, 296]. Repeated deterioration in gas exchange during sleep may impair ventilatory drive and result in daytime respiratory failure [297]. Positive short-term effects of NIV during sleep in CF have been reported [296, 298]. NIV is more effective than either oxygen therapy or CPAP in treating sleep-related hypercapnia and prevents rapid eye movement (REM) related decreases in minute ventilation. The major benefit of NIV during sleep, therefore, is prevention of alveolar hypoventilation and hypercapnia whilst providing the same degree of correction of hypoxia as supplemental oxygen and CPAP.

Longer-term outcomes of NIV for chronic respiratory failure may include improvements in daytime $PaCO_2$, reduction in the number of days spent in hospital and improvement in symptoms [299, 300]. To date there is no evidence that NIV improves survival. Although little longer-term data is currently available, a trial of NIV in individual patients with symptomatic nocturnal ventilatory failure is indicated.

When initiating NIV for chronic respiratory failure in CF, care should be taken that effective ventilation is delivered. The rapid, shallow breathing pattern seen during REM sleep may be associated with impaired patient-ventilator synchrony, especially if a mouthleak is present. Attention should be given to selection of an appropriate interface, rectification of mouthleak and use of a back-up rate if required. In some patients full polysomnography may be indicated to ensure that effective ventilation has been achieved.

11.1.3 Non-invasive ventilation as an adjunct to airway clearance

Airway clearance techniques are an onerous aspect of CF treatment, especially when patients are unwell, due to increased ventilatory demand [70], adverse effects on respiratory muscle performance [301], alterations in gas exchange [65, 302] and dyspnoea [19]. Non-invasive ventilation has been reported to unload the respiratory muscles during airway clearance in both adults and children with CF, resulting in decreased dyspnea and preventing oxygen desaturation during treatment [301, 302]. Benefits are greatest in those with poor respiratory muscle strength or severe airflow obstruction, measured by FEV_1. However, the amount of sputum expectorated is not different to a session performed without NIV. Non-invasive ventilation may therefore be a useful adjunct to airway clearance for severely unwell patients in whom dyspnoea limits treatment effectiveness, or for NIV-dependent patients in whom it is crucial to maintain regular airway clearance.

The aim of NIV during airway clearance is to provide respiratory muscle unloading. Therefore when setting up NIV, the goal should be to provide as much pressure support as possible by increasing IPAP as tolerated. Anecdotal evidence suggests that high levels of expiratory pressure may interfere with coughing and expectoration and therefore EPAP should be kept relatively low. Coaching will be required so that the patient is able to perform forced expirations, cough and expectorate without removing the mask. A nasal mask will usually assist with ease of expectoration.

11.1.4 Exercise and non-invasive ventilation

Exercise capacity is correlated with survival in CF, and consequently exercise training forms an important part of CF management across the lifespan [119]. Listing for lung transplantation further increases the requirement to maintain good physical fitness to assist with post-transplantation rehabilitation. However, maintaining and improving exercise capacity poses significant challenges in patients with advanced lung disease where high work of breathing may limit exercise duration and patients may be NIV-dependent.

One study has examined the use of CPAP to reduce work of breathing during exercise in CF [303]. Patients who were more hyperinflated and had more severe lung disease showed improved exercise endurance, reduced oxygen consumption, reduced dyspnoea, improved oxygenation and reduced work of breathing with CPAP compared to exercise on room air. This is in contrast to subjects with mild disease who showed increased oxygen consumption and increased dyspnoea with CPAP. To date the use of bilevel during exercise has not been examined in CF, however studies in patients with COPD suggest a similar benefit from this modality [304]. These data indicate that NIV may have a role to reduce work of breathing during exercise in patients with advanced lung disease.

In clinical practice, NIV is used to assist exercise training in patients with CF where severe dyspnoea limits training duration, or in patients who are severely unwell and bridging to transplantation. In NIV-dependent patients training should not be commenced until arterial blood gases have stabilised. It is important to allow time for the patient to acclimatise to NIV at rest before beginning exercise training, particularly if NIV has not previously been used. The aim of NIV during exercise is to reduce work of breathing and therefore the patient should be given as much pressure support as possible by increasing IPAP as tolerated. This will often require titration during exercise. A full face mask may be required during exercise to prevent

mouthleak.

11.1.5 Recommendations

1. **Non-invasive ventilation should be considered in all patients with acute respiratory failure who are listed for transplantation (C).**

2. **In patients with symptomatic nocturnal ventilatory failure a trial of NIV may be undertaken (B).**

3. **NIV is a useful adjunct to airway clearance in patients with severe disease in whom dyspnoea and fatigue limits effective airway clearance (B).**

4. **NIV may be a useful adjunct to exercise in patients with severe disease in whom dyspnoea and fatigue contribute to deconditioning and limit effective training (C).**

5. **Heated passover humidification should be incorporated into the circuit for all applications of NIV in CF (C).**

6. **When selecting an interface, consideration should be given to ease of expectoration and prevention of mouthleak during sleep (D).**

11.2 Physiotherapy and Lung Transplantation

Lung transplantation is a well-established treatment which aims to improve the quality of life and survival of those patients with severe disease who are already managed optimally. Physiotherapists are key members of the transplant team, providing expertise in the physical and functional assessment, respiratory management and rehabilitation of patients both before and after surgery.

The following recommendations are largely based on expert opinion and current Australian clinical practice as there is a lack of published research in this area.

11.2.1 Transplant assessment

The assessment of potential recipients is performed by an experienced multidisciplinary team at a transplant centre with input from the usual CF treatment team. Extensive physiological, functional and psychological assessment is undertaken.

Physiotherapy assessment of the potential transplant candidate focuses on the impact of respiratory and musculoskeletal limitations on exercise, functional capacity and social performance. Functional exercise capacity is measured with the six-minute walk test. Musculoskeletal abnormalities such as reduced muscle mass, structural/postural thoracic kyphoscoliosis and shortened calf, hamstrings and psoas muscles are commonly seen in candidates with CF. Patients with co-morbidities that may seriously compromise the outcome of transplantation should be excluded.

The ability to adhere to treatments and to work together with the transplant team is considered essential for a successful long-term outcome following transplant.

11.2.2 Preparation for transplantation

Time on the waiting list can vary from weeks to years. Once on the waiting list, patients are monitored closely by the transplant team in order to ensure that candidates continue to meet selection criteria and are in optimal physical condition for surgery.

Most adult transplant centres offer dedicated pre-operative exercise training classes for transplant candidates. Supervised exercise training 2-3 times a week and a home exercise routine are encouraged. Patients who regularly attend other centres for

ongoing outpatient treatment should be supervised by their local physiotherapist and progress reported back to the transplant team.

11.2.3 Post-operative period

All physiotherapy interventions should be assessment-based and individualised for each patient.

Physiotherapy treatment in the post-operative period aims to:

- Optimise ventilation
- Clear retained lung secretions
- Promote independent function (ie bed mobility, transfers, ambulation)
- Improve fitness/ activity tolerance
- Facilitate self-management

The physiotherapy program is initiated in the intensive care unit (ICU) as early as the first postoperative day. Sufficient analgesia is needed to allow effective huffing, coughing and for early mobilisation. Lung transplant patients often have a poor ability to perceive the presence of secretions and this may persist in the long term. If sputum retention becomes a problem for a recipient, inhalation therapy and an appropriate airway clearance technique should be instituted.

On the ward, physiotherapy treatment focuses on achieving independence with activities of daily living, increasing endurance (walking, stationary cycling, stair climbing), and exercises addressing any specific musculoskeletal deficits. To allow chest wall healing, patients are advised not to lift weights greater than 5kg for 10 – 12 weeks. On discharge, supervised rehabilitation usually continues as an outpatient at the transplant centre for approximately 3 months.

11.2.4 Rehabilitation post transplant

Patients attend a formal outpatient rehabilitation program comprising of exercise training and education at the transplant centre. The primary goals in the rehabilitation phase are to:

- Improve the patient's physical condition (strength, endurance, posture)
- Promote independence in maintaining and monitoring their physical condition.

- Improve the patient's confidence in becoming involved in a full range of activities of daily living and appropriate exercise activities
- Nurture realistic expectations for employment, sport and leisure activities
- Facilitate the integration back into social and vocational roles

By approximately 12 weeks, most patients have achieved a good level of fitness and function and are able to be discharged from physiotherapy with a maintenance home exercise program to be undertaken independently. Patients are encouraged to maintain an active lifestyle. Those patients who require further rehabilitation are referred closer to their local area where access to services is more convenient.

11.2.5 Transplant-related problems

Lung transplant recipients commonly experience problems that may require physiotherapy intervention during hospital admission or outpatient follow up. These include:

- Acute or chronic respiratory tract infection
- Chronic graft dysfunction
- Musculoskeletal morbidities (osteoporosis, pathological fracture, myopathy)
- Reduced functional performance
- Declining exercise capacity
- Changes in social and vocational roles

Because of these ongoing issues, consideration should be given to yearly assessment of patients with CF who have undergone lung transplantation.

11.2.6 Recommendations

1. Patients with CF should be assessed for suitability for lung transplantation by a physiotherapist at the lung transplant centre in consultation with a physiotherapist from the treating CF team (D).

2. Patients with CF should undertake an exercise program designed to optimise their physical function while on the transplant waiting list (D).

3. Physiotherapy management following lung transplantation follows general

principles similar to the management of other thoracic surgery patients (D).

4. Patients with cystic fibrosis who have undergone lung transplantation should participate in a formal, supervised rehabilitation program post-operatively (D).

11.3 Palliative or end of life care in cystic fibrosis

The model of care for palliative/end of life care in CF differs from the model described for other diseases (eg cancer, AIDS) as there may not be a clear transition from active treatment to palliative care. The time it takes for a patient with CF to die varies considerably, is difficult to predict and can take many weeks or months. Treatment progresses from aggressive and invasive treatment to support care that makes comfort a priority (with some preventative/therapeutic treatment continuing), and finally to comfort care only [305, 306]. The likelihood of lung transplantation will influence decisions regarding when to move to another stage of care. Ninety percent of patients die of respiratory failure [307] and most patients die during a pulmonary exacerbation and/or viral infection [308].

The aim of end of life care is to help provide the best quality of life and comfortable death for the patient in accordance with his/her wishes. The care should focus on comfort and dignity and be tailored to each patient's goals and values [306]

It has been suggested that palliative care should be discussed earlier, rather than when patients are in the end stage of their disease [309]. This could occur at transition from the paediatric to the adult unit; during an annual review; at the consultant's discretion; or at a time when a patient's health declines, particularly when due to lack of adherence.

The palliative/end of life care management should be interdisciplinary and include:

- skilled management of the symptoms causing discomfort
- maximising quality of life
- family/carer education and training
- respite care for family and carers
- assessment and treatment of psychological, social and spiritual distress
- assistance to the patient, family and carers with planning for the end of life and after
- loss, grief and bereavement support [11].

Interdisciplinary care consists of continuing care from the CF team supplemented by the palliative care team and, if the patient chooses to die at home, the pastoral care personnel. In a study of all known CF deaths in Canada in 1995, 90% of patients

received on-going care from the CF physician and 7% received most of their care from a family physician [308].

Clinical indicators of short-term survival include:

- inability to maintain metabolic compensation for chronic respiratory acidosis
- increased rate of decline in pulmonary function tests
- lack of response to prolonged intravenous therapy
- weight loss that can't be halted with supplemental feeding / parental nutrition
- increases in headache and chest pain [310].

Symptoms that cause discomfort in patients with CF include:

- pain, including chest pain and headaches
- dyspnoea
- fatigue
- weight loss
- anxiety
- depression

11.3.1 When to switch from active treatment to palliative care

It is difficult for clinicians and family to decide when to change the focus of care. During their last year of life many patients have increased admissions for pulmonary exacerbations. During most of these admissions patients will respond to antibiotics +/- short-term non-invasive ventilation and it is difficult to determine which exacerbation is the final one. As a result preventative/therapeutic care (such as intravenous antibiotics, assisted ventilation, vitamins and airway clearance) often continues even within the last 24 hours of life [305]. The majority of patients will receive palliative care/comfort measures alongside these treatments [305, 308].

11.3.2 Physiotherapy treatment at end of life in CF

There is no published literature specifically pertaining to physiotherapy treatment in the terminal stages of CF.

The aims of treatment depend upon whether the patient is:

- actively waiting for transplant

- deteriorating whilst waiting for transplant
- unsuitable for transplant
- declines transplant listing

In the patient who is deteriorating but still waiting for transplantation, it may therefore be appropriate to continue with therapeutic care in the terminal stages if the patient wishes to do so. However in the dying patient in whom transplant is not a prospect, treatment should be used only to relieve symptoms. The patient's wishes regarding the amount of treatment should be respected and if the patient is tired or does not want treatment it should be omitted. Due to the long-term relationship of patients with their clinicians, it may be helpful for the CF physiotherapist to continue to see the patient in a support role even after active treatment is discontinued [7].

Airway clearance techniques

Minimising the work of breathing during airway clearance is an important consideration in those with end-stage disease. Airway clearance techniques result in increased ventilatory demand [70] and may compromise respiratory muscle performance in those with severe disease [301, 302]. Although many patients will be able to continue the use of independent techniques, some patients require therapist-assisted airway clearance such as percussion or thoracic compressions to minimise the respiratory work required. Non-invasive ventilation may also be useful to assist the respiratory muscles and relieve dyspnoea during airway clearance.

In the patient who is no longer receiving active treatment, airway clearance is often continued in order to relieve symptoms. The choice of technique should be based on patient preference and adapted according to the patient's tolerance and requests. The patient's wishes regarding the amount of treatment should be respected and if the patient is tired or does not want treatment, it should be omitted.

Other techniques

Towards the end of life, patients often report significant benefits from alternative techniques such as soft tissue massage [208], positioning for relaxation, trigger point release, music therapy and use of a fan to blow air on the face. These may be important physiotherapy roles for the dying patient. The physiotherapist can teach the family and carers to assist with many of these techniques, as well as to assist with cough support and airway clearance.

11.3.3 Recommendations

1. Physiotherapy treatment at the end of life should be tailored to each patient's wishes (D).

2. Airway clearance for patients with end-stage disease should aim to minimise work of breathing and maximise patient comfort (D).

3. Airway clearance may be continued even in the palliative stage if the patient finds it beneficial to relieve symptoms (D).

4. Comfort measures such as soft tissue massage and positioning should be considered in the palliative patient (D).

12 Adherence to physiotherapy in cystic fibrosis

Physiotherapists frequently encounter adherence problems in both inpatient and outpatient settings for clients with CF and their families. Adherence to physiotherapy has been reported at 53% [311]. This may vary according to the component of treatment - adherence to frequency of airway clearance has been reported at 51% whilst adherence to duration of airway clearance sessions was 64% [312]. Adherence for inhaled dornase alfa in children has been reported at 67-84% [313, 314] whilst in adults this varies from 24-82% [315]. Exercise therapy is perceived differently from other forms of treatment [311], with greater adherence to exercise than airway clearance techniques.

Parent and child self report give consistently higher adherence rates than other measurement methods [316]. For example, self report data of 50% adherence was objectively measured electronically as 27% and by diary as 46%. [312].

Clinical and demographic variables are poor predictors of treatment adherence. Greater level of worry about the disease and perception of having little personal control over the disease increased adherence to treatment. Knowledge and adherence are not correlated but more frequent contact with the health care team increases adherence [317].

The degree of adherence to treatment is influenced by a person's style of coping. Adherent clients scored higher on optimistic acceptance scale and hopefulness scale. Partially adherent clients used distraction as a way of coping. Non-adherent clients used avoidance as a coping strategy [318].

Consequences of poor adherence include increased morbidity and mortality, reduced quality of life and increased health care costs [319-321]. Strategies to maximise adherence are therefore important to long-term outcome in CF.

Physiotherapy practice

Adherence to prescribed ACTs, inhalation therapy and exercise should be explored openly and non-judgementally at each visit (D). Engaging in a partnership approach, to discuss barriers to adherence openly and normalise difficulties opens the way to facilitate behavioural change [322]. Strategies that may assist this approach include use of supportive, non-judgemental language; assessment of adherence over specific short periods (eg one week); use of contextual anchors in daily routines for better

recall of adherence behaviours; cognitive interviews with families to assess estimations of adherence; and frequent discussions with families and clients regarding the challenges of complex chronic disease management.

Many approaches to address individual adherence problems have been suggested, including use of effective resource materials for education; tailored treatment regimens to suit lifestyle; reduced complexity of home programs; and additional contacts in person, phone or email to support and encourage adherence.

For parental adherence with early treatment regimens, Davidson [323] reports that 'A five-position modified chest physiotherapy regimen can be used with infants and children, and it takes less time and may improve adherence'. Previous 'conventional chest physiotherapy' practice in some countries included a greater number of positions for chest drainage and longer time duration in each position.

In older patients, adherence does not significantly differ between 'conventional' chest physiotherapy and other ACTs but a trend exists for participants (particularly adults) to prefer self administered ACTs, which may promote adherence. [324].

Management of adherence problems needs to be individualised with regard to lifestyle, education needs, and multiple other influences. Multidisciplinary team involvement to develop client-focussed management plans is suggested as such problems may be outside the scope of core physiotherapy practice.

Age-appropriate approaches to encourage adherence include but are not limited to:

Infants: Role modelling and parent support in developing skills.

Toddlers: Incorporate play, songs, and routines in a dynamic and positive session.

Children 4-8 years: Develop a dynamic activity based routine that incorporates ACT and positive behavioural feedback for cooperation.

Children 9-12 years: Incorporate an airway clearance routine with some control given to the child, coached by parent, on the background of an active lifestyle which includes involvement in team sports, dance, or other preferred physical pursuits.

Adolescents: Identify individual goals and routines and how ACTs and exercise can fit in to their timetable. Encourage sports participation especially for those with less severe respiratory impairment; group exercise environments may still be appropriate

for those with greater functional impairment.

Adults 18-25 years: Explore individual goals and barriers to goal achievement; continue to educate and support positive aspects of actions.

Adults 25+: Continue to support and advise regarding enjoyed activities, participation options, and modifications if needed to ACT and exercise.

12.1 Recommendations

1. Adherence to prescribed airway clearance techniques, inhalation therapy and exercise should be explored openly and non-judgementally on a regular basis (D).

2. Management of adherence problems should be client-focussed and individualised (D).

13 Infection Control during physiotherapy in cystic fibrosis

Until the mid 1990's, cross-infection in cystic fibrosis was not of great concern. Patients were treated in multiple bed wards, social contact was not discouraged. Patients attended focus groups and conferences whilst summer camps for children and adults were popular all over the world. After outbreaks of Cepacia Syndrome in the USA, Canada and the UK, concern about patient-to-patient transmission of pathogens resulted in significant changes to these practices. Summer camps were disbanded, group meetings of patients with CF were no longer encouraged and segregation was introduced in different models in many CF centres around the world. Segregation and cohorting of inpatients and outpatients according to respiratory organisms are now practiced nationally and internationally [325, 326].

The following respiratory organisms are commonly found in CF and may require specific infection control practices: *Pseudomonas aeruginosa , Staphylococcus aureus* (including MRSA), *Burkholderia cepacia (B. cepacia), B. mallei* and *B. pseudomallei, Aspergillus* and *Acinetobacter fungi, Stenotrophomonas maltophilia, Heteroresistant vancomycin intermediate Staphylococcus aureus* (hVISA) and *Vancomycin Resistant Enterococci* (VRE) [327, 328].

Physiotherapy practice

A survey of infection control guidelines and practices amongst 19 CF centres across Australia indicated widespread awareness and recognition of the importance of practices to minimise the risk of transmission of organisms from patient to patient. However, there is significant variation in infection control policies between centres which reflects the lack of robust scientific evidence in this area. It is therefore important that physiotherapists familiarise themselves with local infection control guidelines. The following recommendations are based on consensus. Areas where there is no consensus are identified.

Airway clearance and inhalation therapy

Both *Pseudomonas aeruginosa* and *B. cepacia* may be spread in droplet form by coughing and that these organisms can survive on dry surfaces for a number of days [328, 329]. *B. cepacia* has been isolated from the hospital rooms and hands of patients following airway clearance [330-332] and has been isolated from the outside surfaces of sputum cups [330]. These findings reinforce the need to segregate patients whilst performing airway clearance and inhalation therapy, as well as the importance of hand

washing to prevent person to person transmission. Stethoscopes should be cleaned with alcohol wipes between patients (D).

Bacterial contamination of home nebulisers of CF patients has been documented and sharing equipment has been associated with transmission of *B. cepacia* [115, 333]. Under no circumstances should any respiratory equipment be shared between patients with CF. Recommendations for cleaning respiratory equipment can be found in Chapter 3. In most Australian centres (74%), responsibility for cleaning respiratory equipment lies with patients or families, with the advice and encouragement of physiotherapists and nursing staff.

There is no consensus regarding the use of gloves, gowns and masks during physiotherapy treatment in CF. Physiotherapists should consult their local infection control policy with regard to when these measures are required.

Gym Sessions and Exercise

Coughing is common during exercise in patients with CF and therefore droplet spread of organisms is likely. These droplets may be transmitted within three feet (one metre) of an infected patient [328]. It is therefore recommended that patients with different organisms do not exercise together (D). When people with the same organisms are sharing the gym, universal precautions should be practised. Patients should be educated and encouraged to maintain a two metre distance from other patients at all times; patients should be taught handwashing on entering and leaving the gym; and should be taught and encouraged to wipe down all exercise equipment with an alcohol-based solution before and after use. All patients should be encouraged to adopt behaviours which limit the spread and acquisition of organisms.

The consensus of Australian physiotherapists is that patients with *B. cepacia* and MRSA should exercise on their own in the hospital setting (D). Inpatients with VRE or hVISA should exercise in their own room or outdoors (D). In many centres exercise equipment is brought into the patient's room to facilitate exercise training.

13.1 Recommendations

1. Patients with different organisms should not carry out airway clearance physiotherapy together (C).

2. Patients should not share airway clearance therapy or inhalational therapy equipment under any circumstances (C).

3. Patients should clean their own airway clearance equipment at home and in hospital as advised by the CF team or manufacturer's instructions (D).

4. Patients with different organisms should not exercise in the same gym area at the same time. When people with the same organisms are in the gym, universal precautions should be practised (D).

5. Patients with *B.cepacia* and MRSA should exercise on their own in the hospital setting (D).

6. Inpatients with VRE / hVISA should exercise in their own room and outdoors (D).

7. Staff should practice strict handwashing between patients (C) and stethoscopes should be wiped before applying to patients (D).

14 Delivery of physiotherapy treatment to inpatients and outpatients with cystic fibrosis

There is little published research regarding the optimum structure of physiotherapy services for patients with CF. The following recommendations represent expert clinical opinion and reflect current Australian and international best practice [334].

14.1 Physiotherapy treatment for inpatients

Patients should be assessed and physiotherapy treatment started on the day of admission. The physiotherapy service should therefore be available seven days a week. The physiotherapy service should be led by a physiotherapy clinician with a special interest in CF in order to facilitate continuity of care.

Treatment should be tailored to the patient's clinical status and based on the clinical assessment findings. The physiotherapy treatment plan should specifically address inhalation therapy, airway clearance therapy and physical exercise.

Airway clearance therapy should be tailored to the patient's clinical status, considering the most efficacious regimen and each patient's personal preferences. Patients who are admitted with an acute exacerbation with increased and/or retained secretions will need to carry out more frequent airway clearance therapy sessions than their baseline daily regimen. The number of treatments will range from two to three or more treatments in 24 hours. Care should be taken to match the dosage (number and duration) of treatment sessions to each patient's condition. Physical exhaustion from too high a dose of physiotherapy should be avoided. Timely initiation of non-invasive ventilation should be considered where indicated. Ideally, an on call physiotherapy service should be available after hours to provide treatment to patients with severe respiratory insufficiency related to excessive and/or retained airway secretions who are at risk of deterioration overnight.

A graduated physical exercise program incorporating cardiorespiratory exercise as well as stretching, strengthening and mobilising exercises to normalize physical function should be commenced as soon as the patient is in a fit state to do so. Patients should not exercise while febrile or while they are requiring much of their physical strength and energy for work of breathing, airway clearance therapy and coughing. An objective measure of exercise tolerance using oximetry should be undertaken to assess baseline exercise capacity, to identify oxygen desaturation during exercise and to

assess whether supplemental oxygen is required.

During admission, age-appropriate assessment should be undertaken of comorbidities such as urinary incontinence and musculoskeletal limitations. Prior to discharge, an agreement should be made with the patient and / or family regarding airway clearance therapy and exercise to be undertaken at home.

14.2 Physiotherapy treatment for outpatients

Patients attending the outpatient department of the Cystic Fibrosis Service should have access to a physiotherapist with a special interest in CF at each clinic visit. It is suggested that each patient with CF be assessed by the physiotherapist three to six monthly so that their physiotherapy program can be reviewed and optimized. Complex patients (eg during pregnancy, those listed for transplantation) may require more frequent and detailed review.

Annually, each patient should:

- demonstrate their daily airway clearance therapy routine in a practical session with their physiotherapist
- go through their inhalational therapy program together with cleaning and replacement requirements of all respiratory equipment. Arrangements should be made for annual check and servicing of nebuliser pumps
- carry out an age-appropriate exercise tolerance test, especially in adulthood
- have a review of postural alignment, musculoskeletal and physical function. A preventative and/or rehabilitative exercise program should be instituted as appropriate to the age, condition and function of the patient
- an assessment of adherence to the physiotherapy program with modifications as necessary, always considering the patient's individual needs, lifestyle, economic status and personal preferences in order to achieve an optimum long term outcome.

14.3 Recommendations

1. Inpatients with CF should be assessed by a physiotherapist on the day of hospital admission and treatment commenced at the earliest opportunity (D).

2. The physiotherapy treatment plan for inpatients with CF should specifically address airway clearance therapy, inhalation therapy and physical exercise (D).

3. Outpatients with CF should be reviewed by a physiotherapist every three to six months (D).

15 References

[1] Desmond KJ, Schwenk WF, Thomas E, et al. Immediate and long-term effects of chest physiotherapy in patients with cystic fibrosis. *J Paediatr*. 1983;103:538-42.

[2] Schneiderman-Walker J, Pollock SL, Corey M, et al. A randomized controlled trial of a 3-year home exercise program in cystic fibrosis. *J Pediatr*. 2000;136:304-10.

[3] Elkins MR, Robinson M, Rose BR, et al. A controlled trial of long-term inhaled hypertonic saline in patients with cystic fibrosis. *N Engl J Med*. 2006;354:229-40.

[4] National Institutes of Health / National Heart LaBI. NHLBI/WHO Workshop Report. Global Initiative for Chronic Obstructive Lung Disease (GOLD): Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. April 2001.

[5] van der Schans CP, Postma DS, Koeter GH, et al. Physiotherapy and bronchial mucus transport. *Eur Respir J*. 1999;13:1477-86.

[6] Prasad A. Physiotherapy in cystic fibrosis. *J R Soc Med* 2000;93:27-36.

[7] Hodson ME. Treatment of cystic fibrosis in the adult. *Respiration*. 2000;67:595-607.

[8] Williams M. Chest Physiotherapy and Cystic Fibrosis. Why is the most effective form of treatment still unclear? *Chest*. 1994;106:1872-82.

[9] Robinson P. Cystic fibrosis. *Thorax*. 2001;56:237-41.

[10] van der Schans C, Prasad A, Main E. Chest physiotherapy compared to no chest physiotherapy for cystic fibrosis. *Cochrane Database Syst Rev*. 2003;3:3.

[11] Yankaskas JR, Marshall BC, Sufian B, et al. Cystic Fibrosis Adult Care: Consensus Conference Report. *Chest*. 2004;125:1S-39.

[12] Pryor J. Active cycle of breathing techniques. In: Gursli S, Ed. *Physiotherapy in the treatment of cystic fibrosis*. 3rd ed: International Physiotherapy Group/ Cystic Fibrosis 2003:8-11.

[13] Pryor J, Webber B, Hodson M, et al. Evaluation of the forced expiration technique as an adjunct to postural drainage in the treatment of cystic fibrosis. *Br Med J*. 1979;2:417-8.

[14] Hofmeyr JL, Webber BA, Hodson ME. Evaluation of positive expiratory pressure as an adjunct to chest physiotherapy in the treatment of cystic fibrosis. *Thorax*. 1986;41:951-4.

[15] Pryor JA, Webber BA, Hodson ME, et al. The Flutter VRP1 as an adjunct to chest physiotherapy in cystic fibrosis. *Respir Med*. 1994;88:677-81.

[16] Pike SE, Machin AC, Dix KJ, et al. Comparison of the flutter VRP1 and forced expirations with active cycle of breathing techniques in subjects with cystic fibrosis. *Netherlands J Med*. 1999;54:A125.

[17] Pryor JA, Parker RA, Webber BA. A comparison of mechanical and manual percussion as adjuncts to postural drainage in the treatment of cystic fibrosis in

adolescents and adults. *Physiotherapy*. 1981;67:140-1.
[18] Webber B, Hofmeyr J, Morgan M, et al. Effects of postural drainage, incorporating the forced expiration technique, on pulmonary function in cystic fibrosis. *Br J Dis Chest*. 1986;80:353-9.
[19] Cecins N, Jenkins S, Pengelly J, et al. The active cycle of breathing techniques - to tip or not to tip? *Respir Med*. 1999;93:660-5.
[20] Chevallier J. Autogenic Drainage (AD). In: Gursli S, Ed. *Physiotherapy in the treatment of cystic fibrosis (CF)*: International Physiotherapy Group/ Cystic Fibrosis 2003:12-5.
[21] Chevallier J. Autogenic drainage (A.D.). In: Lawson D, ed. *Cystic fibrosis: horizons*. Chichester: John Wiley 1984:235.
[22] Lapin CD. Airway physiology, autogenic drainage, and active cycle of breathing. *Respiratory Care*. 2002;47:778-85.
[23] Schoni MH. Autogenic drainage: a modern approach to physiotherapy in cystic fibrosis. *Journal of the Royal Society of Medicine*. 1989;82:32-7.
[24] Giles DR, Wagener JS, Accurso FJ, et al. Short-term effects of postural drainage with clapping vs autogenic drainage on oxygen saturation and sputum recovery in patients with cystic fibrosis. *Chest*. 1995;108:952-4.
[25] App EM, Kieselmann R, Reinhardt D, et al. Sputum rheology changes in cystic fibrosis lung disease following two different types of physiotherapy: flutter vs autogenic drainage. *Chest*. 1998;114:171-7.
[26] Miller S, Hall DO, Clayton CB, et al. Chest physiotherapy in cystic fibrosis: a comparative study of autogenic drainage and the active cycle of breathing techniques with postural drainage. *Thorax*. 1995;50:165-9.
[27] van der Schans CP. Forced expiratory manoeuvres to increase transport of bronchial mucus: a mechanistic approach. *Monaldi Arch Chest Dis*. 1997;52:367-70.
[28] Pfleger A, Theissl B, Oberwaldner B, et al. Self-administered chest physiotherapy in cystic fibrosis: a comparative study of high-pressure PEP and autogenic drainage. *Lung*. 1992;170:323-30.
[29] Lannefors L, Button BM, McIlwaine M. Physiotherapy in infants and young children with cystic fibrosis: current practice and future developments. *J R Soc Med*. 2004;97 Suppl 44:8-25.
[30] Falk M, Kelstrup M. Positive Expiratory Pressure (PEP). In: Gursli S, Ed. *Physiotherapy in the treatment of cystic fibrosis*. 3rd ed: International Physiotherapy Group/ Cystic Fibrosis 2003:18-9.
[31] Tonnesen P, Stovring S. Positive expiratory pressure (PEP) as lung physiotherapy in cystic fibrosis: a pilot study. *Eur J Respir Dis*. 1984;65:419-22.
[32] Falk M, Kelstrup M, Andersen JB, et al. Improving the ketchup bottle method with positive expiratory pressure, PEP, in cystic fibrosis. *Eur J Respir Dis*. 1984;65:423-32.
[33] Andersen JB, Falk M. Chest physiotherapy in the paediatric age group. *Respiratory Care*. 1991:546-54.
[34] Darbee JC, Ohtake PJ, Grant BJ, et al. Physiologic evidence for the efficacy of positive expiratory pressure as an airway clearance technique in patients with cystic fibrosis. *Phys Ther*. 2004;84:524-37.
[35] McIlwaine P, Wong L, Peacock D, et al. Long term comparative trial of

conventional postural drainage and percussion versus positive expiratory pressure physiotherapy in the treatment of cystic fibrosis. *J Pediatr*. 1997;131:570-4.

[36] McIlwaine PM, Wong LT, Peacock D, et al. Long-term comparative trial of positive expiratory pressure versus oscillating positive expiratory pressure (flutter) physiotherapy in the treatment of cystic fibrosis. *J Pediatr*. 2001;138:845-50.

[37] Newbold M, Tullis E, Corey M, et al. The flutter device versus the PEP mask in the treatment of adults with cystic fibrosis. . *Physiotherapy Canada*. 2005;57:199-207.

[38] Elkins MR, Jones A, van der Schans C. Positive expiratory pressure physiotherapy for airway clearance in people with cystic fibrosis. *Cochrane Database Syst Rev*. 2006:CD003147.

[39] AARC Clinical Practice Guideline: Use of Positive Airway Pressure Adjuncts to Bronchial Hygiene Therapy. *Respir Care*. 1993;38.

[40] Oberwaldner B. Hi-PEP. In: Gursli S, ed. *Physiotherapy in the treatment of cystic fibrosis*. 3rd ed: International Physiotherapy Group/ Cystic Fibrosis 2003:20-3.

[41] Oberwaldner B, Evans JC, Zach MS. Forced expirations against a variable resistance: a new chest physiotherapy method in cystic fibrosis. *Pediatr Pulmonol*. 1986;2:358-67.

[42] Oberwaldner B, Theissl B, Rucker A, et al. Chest physiotherapy in hospitalized patients with cystic fibrosis: a study of lung function effects and sputum production. *Eur Respir J*. 1991;4:152-8.

[43] Campbell T, Ferguson N, McKinlay RGC. The use of a simple self-administered method of positive expiratory pressure (PEP) in chest physiotherapy after abdominal surgery. *Physiotherapy*. 1986;72:498-500.

[44] Bjorkqvist M, Wiberg B, Bodin L, et al. Bottle-blowing in hospital-treated patients with community-acquired pneumonia. *Scand Journal Infect Dis*. 1997;29:77-82.

[45] Althaus P. Oscillating PEP - Flutter therapy. In: Gursli S, Ed. *Physiotherapy in the treatment of cystic fibrosis*. 3rd ed: International Physiotherapy Group/ Cystic Fibrosis 2003:24-6.

[46] Gondor M, Nixon PA, R. M, et al. Comparison of Flutter device and chest physical therapy in the treatment of cystic fibrosis pulmonary exacerbation. *Pediatr Pulmonol*. 1999;28:255-60.

[47] Homnick DN, Anderson K, Marks JH. Comparison of the flutter device to standard chest physiotherapy in hospitalized patients with cystic fibrosis: a pilot study. *Chest*. 1998;114:993-7.

[48] Konstan MW, Stern RC, Doershuk CF. Efficacy of the Flutter device for airway mucus clearance in patients with cystic fibrosis. *J Pediatr*. 1994;124:689-93.

[49] van Winden CM, Visser A, Hop W, et al. Effects of flutter and PEP mask physiotherapy on symptoms and lung function in children with cystic fibrosis. *Eur Respir J*. 1998;12:143-7.

[50] Volsko TA, DiFiore J, Chatburn RL. Performance comparison of two oscillating positive expiratory pressure devices: Acapella versus Flutter. *Respir Care*. 2003;48:124-30.

[51] Patterson JE, Bradley JM, Hewitt O, et al. Airway clearance in bronchiectasis: a randomized crossover trial of active cycle of breathing techniques versus Acapella. *Respiration*. 2005;72:239-42.
[52] Thoracic Society. The nomenclature of bronchopulmonary anatomy. *Thorax*. 1950;5.
[53] Reisman JJ, Rivington-Law B, Carey M, et al. Role of conventional physiotherapy in cystic fibrosis. *J Pediatr*. 1988;113:632-6.
[54] Sutton PP, Parker RA, Webber BA, et al. Assessment of the forced expiration technique, postural drainage and directed coughing in chest physiotherapy. *Eur J Respir Dis*. 1983;64:62-8.
[55] Verboon JM, Bakker W, Sterk PJ. The value of the forced expiration technique with and without postural drainage in adults with cystic fibrosis. *Eur J Respir Dis*. 1986;69:169-74.
[56] Mortensen J, Falk M, Groth S, et al. The effects of postural drainage and positive expiratory pressure physiotherapy on tracheobronchial clearance in cystic fibrosis. *Chest*. 1991;100:1350-7.
[57] Lannefors L, Wollmer P. Mucus clearance with three chest physiotherapy regimes in cystic fibrosis: a comparison between postural drainage, PEP and physical exercise. *Eur Respir J*. 1992;5:748-53.
[58] Button BM, Heine RG, Catto-Smith AG, et al. Postural drainage and gastro-oesophageal reflux in infants with cystic fibrosis. *Arch Dis Child*. 1997;76:148-50.
[59] Scott RB, O'Loughlin EV, Gall DG. Gastroesophageal reflux in patients with cystic fibrosis. *J Pediatr*. 1985;106:223-7.
[60] Ledson MJ, Tran J, Walshaw MJ. Prevalence and mechanisms of gastro-oesophageal reflux in adult cystic fibrosis patients. *J R Soc Med*. 1998;91:7-9.
[61] Vandenplas Y, Diericx A, Blecker U, et al. Esophageal pH monitoring data during chest physiotherapy. *J Pediatr Gastroenterol Nutr*. 1991;13:23-6.
[62] Button BM, Heine RG, Catto-Smith AG, et al. Postural drainage in cystic fibrosis: is there a link with gastro-oesophageal reflux? *J Paediatr Child Health*. 1998;34:330-4.
[63] Phillips GE, Pike SE, Rosenthal M, et al. Holding the baby: head downwards positioning for physiotherapy does not cause gastro-oesophageal reflux. *Eur Respir J*. 1998;12:954-7.
[64] Button BM, Heine RG, Catto-Smith AG, et al. Chest physiotherapy in infants with cystic fibrosis: to tip or not? A five-year study. *Pediatr Pulmonol*. 2003;35:208-13.
[65] McDonnell T, McNicholas WT, FitzGerald MX. Hypoxaemia during chest physiotherapy in patients with cystic fibrosis. *Ir J Med Sci*. 1986;155:345-8.
[66] Pryor JA, Webber BA, Hodson ME. Effect of chest physiotherapy on oxygen saturation in patients with cystic fibrosis. *Thorax*. 1990;45:77.
[67] Cross JH, Harrison CJ, Preston PR, et al. Postnatal encephaloclastic porencephaly--a new lesion? *Arch Dis Child*. 1992;67:307-11.
[68] McCarren B, Alison JA. Physiological effects of vibration in subjects with cystic fibrosis. *Eur Respir J*. 2006;27:1204-9.
[69] Sutton PP, Lopez-Vidriero MT, Pavia D, et al. Assessment of percussion, vibratory-shaking and breathing exercises in chest physiotherapy. *Eur J Respir Dis*. 1985;66:147-52.

[70] Williams MT, Parsons DW, Frick RA, et al. Acute respiratory infection in patients with cystic fibrosis with mild pulmonary impairment: comparison of two physiotherapy regimens. *Aust J Physiother*. 2001;47:227-36.
[71] Gallon A. The use of percussion. *Physiotherapy*. 1992;78:85-9.
[72] Purohit DM, Caldwell C, Levkoff AH. Letter: Multiple rib fractures due to physiotherapy in a neonate with hyaline membrane disease. *Am J Dis Child* 1975;129:1103-4.
[73] Hansen LG, Warwick WJ. High-frequency chest compression system to aid in clearance of mucus from the lung. *Biomedical instrumentation & technology*. 1990;24:289-94.
[74] Fink JB, Mahlmeister MJ. High-frequency oscillation of the airway and chest wall. *Respir Care*. 2002;47:797-807.
[75] Oermann CM, Sockrider MM, Giles D, et al. Comparison of high-frequency chest wall oscillation and oscillating positive expiratory pressure in the home management of cystic fibrosis: a pilot study. *Pediatr Pulmonol*. 2001;32:372-7.
[76] Scherer TA, Barandun J, Martinez E, et al. Effect of high-frequency oral airway and chest wall oscillation and conventional chest physical therapy on expectoration in patients with stable cystic fibrosis. *Chest*. 1998;113:1019-27.
[77] Arens R, Gozal D, Omlin KJ, et al. Comparison of high frequency chest compression and conventional chest physiotherapy in hospitalized patients with cystic fibrosis. *Am J Respir Crit Care Med*. 1994;150:1154-7.
[78] Braggion C, Cappelletti LM, Cornacchia M, et al. Short-term effects of three chest physiotherapy regimens in patients hospitalized for pulmonary exacerbations of cystic fibrosis: a cross-over randomized study. *Pediatr Pulmonol*. 1995;19:16-22.
[79] Kluft J, Beker L, Castagnino M, et al. A comparison of bronchial drainage treatments in cystic fibrosis. *Pediatr Pulmonol*. 1996;22:271-4.
[80] Phillips GE, Pike SE, Jaffe A, et al. Comparison of active cycle of breathing and high-frequency oscillation jacket in children with cystic fibrosis. *Pediatr Pulmonol*. 2004;37:71-5.
[81] AARC Clinical Practice Guideline. Postural Drainage Therapy. *Respiratory Care*. 1991;36:1418-26.
[82] Varekojis SM, Douce FH, Flucke RL, et al. A comparison of the therapeutic effectiveness of and preference for postural drainage and percussion, intrapulmonary percussive ventilation, and high-frequency chest wall compression in hospitalized cystic fibrosis patients. *Respir Care*. 2003;48:24-8.
[83] Homnick DN, White F, de Castro C. Comparison of effects of an intrapulmonary percussive ventilator to standard aerosol and chest physiotherapy in treatment of cystic fibrosis. *Pediatr Pulmonol*. 1995;20:50-5.
[84] Newhouse PA, White F, Marks JH, et al. The intrapulmonary percussive ventilator and flutter device compared to standard chest physiotherapy in patients with cystic fibrosis. *Clin Pediatr*. 1998;37:427-32.
[85] Hebestreit A, Kersting U, Basler B, et al. Exercise inhibits epithelial sodium channels in patients with cystic fibrosis. *Am J Respir Crit Care Med*. 2001;164:443-6.
[86] Salh W, Bilton D, Dodd M, et al. Effect of exercise and physiotherapy in

aiding sputum expectoration in adults with cystic fibrosis. *Thorax*. 1989;44:1006-8.
[87] Zach M, Oberwaldner B, Hausler F. Cystic fibrosis: physical exercise versus chest physiotherapy. *Arch Dis Child*. 1982;57:587-9.
[88] Bilton D, Dodd ME, Abbot JV, et al. The benefits of exercise combined with physiotherapy in the treatment of adults with cystic fibrosis. *Respir Med*. 1992;86:507-11.
[89] Loughlin GM, Cota KA, Taussig LM. The relationship between flow transients and bronchial lability in cystic fibrosis. *Chest*. 1981;79:206-10.
[90] Macfarlane PI, Heaf D. Changes in airflow obstruction and oxygen saturation in response to exercise and bronchodilators in cystic fibrosis. *Pediatr Pulmonol*. 1990;8:4-11.
[91] Cerny FJ. Relative effects of bronchial drainage and exercise for in-hospital care of patients with cystic fibrosis. *Phys Ther*. 1989;69:633-9.
[92] Thomas J, Cook, D.J., Brooks, D. Chest physical therapy management of patients with cystic fibrosis: a meta-analysis. *Am J Respir Crit Care Med*. 1995;151:846-50.
[93] Boe J, Dennis JH, O'Driscoll BR, et al. European Respiratory Society Guidelines on the use of nebulizers. *Eur Respir J*. 2001;18:228-42.
[94] Laube BL, Jashnani R, Dalby RN, et al. Targeting aerosol deposition in patients with cystic fibrosis: effects of alterations in particle size and inspiratory flow rate. *Chest*. 2000;118:1069-76.
[95] Nebulizer therapy. Guidelines. British Thoracic Society Nebulizer Project Group. *Thorax*. 1997;52 Suppl 2:S4-24.
[96] Laube BL, Geller DE, Lin TC, et al. Positive expiratory pressure changes aerosol distribution in patients with cystic fibrosis. *Respir Care*. 2005;50:1438-44.
[97] Frischknecht-Christensen E, Norregaard O, Dahl R. Treatment of bronchial asthma with terbutaline inhaled by conespacer combined with positive expiratory pressure mask. *Chest*. 1991;100:317-21.
[98] Stites SW, Perry GV, Peddicord T, et al. Effect of high-frequency chest wall oscillation on the central and peripheral distribution of aerosolized diethylene triamine penta-acetic acid as compared to standard chest physiotherapy in cystic fibrosis. *Chest*. 2006;129:712-7.
[99] Cegla UH, Jost JH, Harten A, et al. [RC-Cornet(R) improves the bronchodilating effect of Ipratropiumbromide (Atrovent(R)) inhalation in COPD-patients]. *Pneumologie*. 2001;55:465-9.
[100] Lannefors L. Inhalation therapy: practical considerations for nebulisation therapy. *Physical Therapy Reviews*. 2006;11:21-7.
[101] Raynor EM, Butler A, Guill M, et al. Nasally inhaled dornase alfa in the postoperative management of chronic sinusitis due to cystic fibrosis. *Archives of otolaryngology--head & neck surgery*. 2000;126:581-3.
[102] Cipolla D, Gonda I, Shire SJ. Characterization of aerosols of human recombinant deoxyribonuclease I (rhDNase) generated by jet nebulizers. *Pharmaceutical Research*. 1994;11:491-8.
[103] Webb AK, Dodd ME. Nebulised antibiotics for adults with cystic fibrosis. *Thorax*. 1997;52 Suppl 2:S69-71.
[104] Kamin W, Schwabe A, Kramer I. Inhalation solutions: which one are allowed

to be mixed? Physico-chemical compatibility of drug solutions in nebulizers. *J Cyst Fibros*. 2006;5:205-13.
[105] Australian Medicines Handbook (AMH): eAMH. www.amh.net.au; accessed December 2006.
[106] Delvaux M, Henket M, Lau L, et al. Nebulised salbutamol administered during sputum induction improves bronchoprotection in patients with asthma. *Thorax*. 2004;59:111-5.
[107] MIMS Drug Information System Online. CMPMedica www.mimsonline.com; accessed December 2006.
[108] van der Giessen LJ, de Jongste JC, Gosselink R, et al. RhDNase before airway clearance therapy improves airway patency in children with CF. *Pediatr Pulmonol*. 2007;42:624-30.
[109] Fitzgerald DA, Hilton J, Jepson B, et al. A crossover, randomized, controlled trial of dornase alfa before versus after physiotherapy in cystic fibrosis. *Pediatrics*. 2005;116:e549-54.
[110] Wilson CJ, Robbins LJ, Murphy JM, et al. Is a longer time interval between recombinant human deoxyribonuclease (dornase alfa) and chest physiotherapy better?: A multi-center, randomized crossover trial. *Pediatr Pulmonol*. 2007;42:1110-6.
[111] van der Giessen LJ, Gosselink R, Hop WC, et al. Recombinant human DNase nebulisation in children with cystic fibrosis: before bedtime or after waking up? *Eur Respir J*. 2007;30:763-8.
[112] Paul K, Rietschel E, Ballmann M, et al. Effect of treatment with dornase alpha on airway inflammation in patients with cystic fibrosis. *Am J Respir Crit Care Med*. 2004;169:719-25.
[113] Doring G, Conway SP, Heijerman HG, et al. Antibiotic therapy against Pseudomonas aeruginosa in cystic fibrosis: a European consensus. *Eur Respir J*. 2000;16:749-67.
[114] Zach MS, Oberwaldner B, Forche G, et al. Bronchodilators increase airway instability in cystic fibrosis. *Am Rev Respir Dis*. 1985;131:537-43.
[115] Hutchinson GR, Parker S, Pryor JA, et al. Home-use nebulizers: a potential primary source of Burkholderia cepacia and other colistin-resistant, gram-negative bacteria in patients with cystic fibrosis. *Journal of clinical microbiology*. 1996;34:584-7.
[116] Rosenfeld M, Joy P, Nguyen CD, et al. Cleaning home nebulizers used by patients with cystic fibrosis: is rinsing with tap water enough? *ournal of Hospital Infection*. 2001;49:229-30.
[117] Reychler G, Aarab K, Van Ossel C, et al. In vitro evaluation of efficacy of 5 methods of disinfection on mouthpieces and facemasks contaminated by strains of cystic fibrosis patients. *Journal of Cystic Fibrosis*. 2005;4:183-7.
[118] Kamps A, Brand PR, R. Determinants of correct inhalation technique in children attending a hospital-based asthma clinic. *Acta Paediatrica*. 2002;91:159-63.
[119] Nixon PA, Orenstein DM, Kelsey SF, et al. The prognostic value of exercise testing in patients with cystic fibrosis. *N Engl J Med*. 1992;327:1785-8.
[120] Pianosi P, Leblanc J, Almudevar A. Peak oxygen uptake and mortality in children with cystic fibrosis. *Thorax*. 2005;60:50-4.
[121] Orenstein DM, Franklin BA, Doershuk CF, et al. Exercise conditioning and

cardiopulmonary fitness in cystic fibrosis. The effects of a three-month supervised running program. *Chest*. 1981;80:392-8.
[122] Bradley J, Moran F. Physical training for cystic fibrosis. *Cochrane Database Syst Rev*. 2002:CD002768.
[123] Bradley J, Howard J, Wallace E, et al. Reliability, repeatability, and sensitivity of the modified shuttle test in adult cystic fibrosis. *Chest*. 2000;117:1666-71.
[124] Webb AK, Dodd ME, Moorcroft J. Exercise and cystic fibrosis. *J R Soc Med*. 1995;88 Suppl 25:30-6.
[125] Alison JA, Donnelly PM, Lennon M, et al. The effect of a comprehensive, intensive inpatient treatment program on lung function and exercise capacity in patients with cystic fibrosis. *Phys Ther*. 1994;74:583-91; discussion 91-3.
[126] Solway S, Brooks D, Lacasse Y, et al. A qualitative systematic overview of the measurement properties of functional walk tests used in the cardiorespiratory domain. *Chest*. 2001;119:256-70.
[127] Kadikar A, Maurer J, Kesten S. The six-minute walk test: a guide to assessment for lung transplantation. *J Heart Lung Transplant*. 1997;16:313-9.
[128] Nixon PA, Joswiak ML, Fricker FJ. A six-minute walk test for assessing exercise tolerance in severely ill children. *J Pediatr*. 1996;129:362-6.
[129] Cunha MT, Rozov T, de Oliveira RC, et al. Six-minute walk test in children and adolescents with cystic fibrosis. *Pediatr Pulmonol*. 2006;41:618-22.
[130] Chetta A, Pisi G, Zanini A, et al. Six-minute walking test in cystic fibrosis adults with mild to moderate lung disease: comparison to healthy subjects. *Respir Med*. 2001;95:986-91.
[131] Balfour-Lynn IM, Prasad SA, Laverty A, et al. A step in the right direction: assessing exercise tolerance in cystic fibrosis. *Pediatr Pulmonol*. 1998;25:278-84.
[132] Narang I, Pike S, Rosenthal M, et al. Three-minute step test to assess exercise capacity in children with cystic fibrosis with mild lung disease. *Pediatr Pulmonol*. 2003;35:108-13.
[133] Pike SE, Prasad SA, Balfour-Lynn IM. Effect of intravenous antibiotics on exercise tolerance (3-min step test)) in cystic fibrosis. *Pediatr Pulmonol*. 2001;32:38-43.
[134] Cox NS, Follett J, McKay KO. Modified shuttle test performance in hospitalized children and adolescents with cystic fibrosis. *J Cyst Fibros*. 2006;5:165-70.
[135] Rogers D, Prasad A, Doull IJ. Exercise testing in children with cystic fibrosis. *Journal of the Royal Society of Medicine*. 2003;96:23-9.
[136] Bradley J, Howard J, Wallace E, et al. Validity of a modified shuttle test in adult cystic fibrosis. *Thorax*. 1999;54:437-9.
[137] Selvadurai HC, Blimkie CJ, Meyers N, et al. Randomized controlled study of in-hospital exercise training programs in children with cystic fibrosis. *Pediatr Pulmonol*. 2002;33:194-200.
[138] Klijn PH, Oudshoorn A, van der Ent CK, et al. Effects of anaerobic training in children with cystic fibrosis: a randomized controlled study. *Chest*. 2004;125:1299-305.
[139] Moorcroft AJ, Dodd ME, Morris J, et al. Individualised unsupervised exercise training in adults with cystic fibrosis: a 1 year randomised controlled trial. *Thorax*. 2004;59:1074-80.

[140] Selvadurai HC, Blimkie CJ, Cooper PJ, et al. Gender differences in habitual activity in children with cystic fibrosis. *Arch Dis Child*. 2004;89:928-33.
[141] Schneiderman-Walker J, Wilkes DL, Strug L, et al. Sex differences in habitual physical activity and lung function decline in children with cystic fibrosis. *J Pediatr*. 2005;147:321-6.
[142] American College of Sports Medicine. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Ex*. 1998;30:975-91.
[143] Nici L, Donner C, Wouters E, et al. American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. *Am J Respir Crit Care Med*. 2006;173:1390-413.
[144] Bradley S, Solin P, Wilson J, et al. Hypoxemia and hypercapnia during exercise and sleep in patients with cystic fibrosis. *Chest*. 1999;116:647-54.
[145] Mallory GB, Fullmer JJ, Vaughan DJ. Oxygen therapy for cystic fibrosis. *Cochrane Database Syst Rev*. 2005:CD003884.
[146] Pulmonary Rehabilitation. British Thoracic Society Standards of Care Subcommitte on Pulmonary Rehabilitation. *Thorax*. 2001;56:827-34.
[147] Ravilly S, Robinson W, Suresh S, et al. Chronic pain in cystic fibrosis. *Pediatrics*. 1996;98:741-7.
[148] Festini F, Ballarin S, Codamo T, et al. Prevalence of pain in adults with cystic fibrosis. *J Cyst Fibros*. 2004;3:51-7.
[149] Botton E, Saraux A, Laselve H, et al. Musculoskeletal manifestations in cystic fibrosis. *Joint Bone Spine*. 2003;70:327-35.
[150] Parasa RB, Maffulli N. Musculoskeletal involvement in cystic fibrosis. *Bull Hosp Jt Dis* 1999;58:37-44.
[151] Tattersall R, Walshaw MJ. Back pain in adult patients with CF: effect of chronic steroid use and physiotherapy. *J Cyst Fibros* 2001;1.
[152] Koh JL, Harrison D, Palermo TM, et al. Assessment of acute and chronic pain symptoms in children with cystic fibrosis. *Pediatr Pulmonol*. 2005;40:330-5.
[153] Rose J, J G, A S, et al. Back pain and spinal deformity in cystic fibrosis. *Am Journal of Dis Child*. 1987;141:1313-6.
[154] Eksterowicz N. Pain management in cystic fibrosis. *Paediatr. Pulmonology*. 2000;Supplement 20:114-5.
[155] Chastain DC, Cook AJ. Chronic pain in CF: associated beliefs and behaviours. *Pediatr Pulmonology*. 2000;Supplement 20:116-7.
[156] Mortensen LA, Chan GM, Alder SC, et al. Bone mineral status in prepubertal children with cystic fibrosis. *J Pediatr*. 2000;136:648-52.
[157] Hardin DS, Arumugam R, Seilheimer DK, et al. Normal bone mineral density in cystic fibrosis. *Arch Dis Child*. 2001;84:363-8.
[158] Sood M, Hambleton G, Super M, et al. Bone status in cystic fibrosis. *Arch Dis Child*. 2001;84:516-20.
[159] Haworth CS, Selby PL, Webb AK, et al. Low bone mineral density in adults with cystic fibrosis. *Thorax*. 1999;54:961-7.
[160] Rossini M, Del Marco A, Dal Santo F, et al. Prevalence and correlates of vertebral fractures in adults with cystic fibrosis. *Bone*. 2004;35:771-6.
[161] Conway SP, Morton AM, Oldroyd B, et al. Osteoporosis and osteopenia in adults and adolescents with cystic fibrosis: prevalence and associated factors. *Thorax*. 2000;55:798-804.

[162] Buntain HM, Greer RM, Schluter PJ, et al. Bone mineral density in Australian children, adolescents and adults with cystic fibrosis: a controlled cross sectional study. *Thorax*. 2004;59:149-55.
[163] Elkin SL, Fairney A, Burnett S, et al. Vertebral deformities and low bone mineral density in adults with cystic fibrosis: a cross-sectional study. *Osteoporos Int*. 2001;12:366-72.
[164] Aris RM, Renner JB, Winders AD, et al. Increased rate of fractures and severe kyphosis: sequelae of living into adulthood with cystic fibrosis. *Ann Int Med*. 1998;128:186-93.
[165] Frangolias DD, Pare PD, Kendler DL, et al. Role of exercise and nutrition status on bone mineral density in cystic fibrosis. *J Cyst Fibros*. 2003;2:163-70.
[166] Bhudhikanok GS, Lim J, Marcus R, et al. Correlates of osteopenia in patients with cystic fibrosis. *Pediatrics*. 1996;97:103-11.
[167] Massie RJ, Towns SJ, Bernard E, et al. The musculoskeletal complications of cystic fibrosis. *J Paediatr Child Health*. 1998;34:467-70.
[168] Erkkila JC, Warwick WJ, Bradford DS. Spine deformities and cystic fibrosis. *Clinical orthopaedics and related research*. 1978:146-50.
[169] Denton JR, Tietjen R, Gaerlan PF. Thoracic kyphosis in cystic fibrosis. *Clinical orthopaedics and related research*. 1981:71-4.
[170] Fauroux B, Isabey D, Desmarais G, et al. Nonchemical influence of inspiratory pressure support on inspiratory activity in humans. *J Appl Physiol*. 1998;85:2169-75.
[171] Logvinoff MM, Fon GT, Taussig LM, et al. Kyphosis and pulmonary function in cystic fibrosis. *Clinical pediatrics*. 1984;23:389-92.
[172] Henderson RC, Specter BB. Kyphosis and fractures in children and young adults with cystic fibrosis. *J Pediatr*. 1994;125:208-12.
[173] Lands L, Desmond KJ, Demizio D, et al. The effects of nutritional status and hyperinflation on respiratory muscle strength in children and young adults. *Am Rev Respir Dis*. 1990;141:1506-9.
[174] Lands LC, Heigenhauser GJ, Jones NL. Respiratory and peripheral muscle function in cystic fibrosis. *Am Rev Respir Dis*. 1993;147:865-9.
[175] de Meer K, Gulmans VA, van Der Laag J. Peripheral muscle weakness and exercise capacity in children with cystic fibrosis. *Am J Respir Crit Care Med*. 1999;159:748-54.
[176] Elkin SL, Williams L, Moore M, et al. Relationship of skeletal muscle mass, muscle strength and bone mineral density in adults with cystic fibrosis. *Clin Sci (Lond)*. 2000;99:309-14.
[177] Barry SC, Gallagher CG. Corticosteroids and skeletal muscle function in cystic fibrosis. *J Appl Physiol*. 2003;95:1379-84.
[178] O'Neill S, Leahy F, Pasterkamp H, et al. The effects of chronic hyperinflation, nutritional status, and posture on respiratory muscle strength in cystic fibrosis. *Am Rev Respir Dis*. 1983;128:1051-4.
[179] Pinet C, Cassart M, Scillia P, et al. Function and Bulk of Respiratory and Limb Muscles in Patients with Cystic Fibrosis. *Am J Respir Crit Care Med*. 2003;168:989-94.
[180] de Jong W, van Aalderen WM, Kraan J, et al. Inspiratory muscle training in patients with cystic fibrosis. *Respir Med*. 2001;95:31-6.
[181] Sahlberg ME, Svantesson U, Thomas EM, et al. Muscular strength and

function in patients with cystic fibrosis. *Chest*. 2005;127:1587-92.
[182] Tattersall R, Walshaw MJ. Posture and cystic fibrosis. *J R Soc Med*. 2003;96 Suppl 43:18-22.
[183] Pertuiset E, Menkes CJ, Lenoir G, et al. Cystic fibrosis arthritis. A report of five cases. *British journal of rheumatology*. 1992;31:535-8.
[184] Nakamura CT, Ng GY, Paton JY, et al. Correlation between digital clubbing and pulmonary function in cystic fibrosis. *Pediatr Pulmonol*. 2002;33:332-8.
[185] Warren RW. Rheumatologic aspects of pediatric cystic fibrosis patients treated with fluoroquinolones. *The Pediatric infectious disease journal*. 1997;16:118-22; discussion 23-6.
[186] Samuelson WM, Pleasants RA, Whitaker MS. Arthropathy secondary to ciprofloxacin in an adult cystic fibrosis patient. *The Annals of pharmacotherapy*. 1993;27:302-3.
[187] Chi ZC, Ma SZ. Rheumatologic manifestations of hepatic diseases. *Hepatobiliary Pancreat Dis Int*. 2003;2:32-7.
[188] Dodd M, Prasad SA. Physiotherapy management of cystic fibrosis. *Chronic Respiratory Disease*. 2005;2:139-49.
[189] Nixon PA, Orenstein DM, Kelsey SF. Habitual physical activity in children and adolescents with cystic fibrosis. *Med Sci Sports Exerc*. 2001;33:30-5.
[190] Michel BA, Lane NE, Bjorkengren A, et al. Impact of running on lumbar bone density: a 5-year longitudinal study. *The Journal of rheumatology*. 1992;19:1759-63.
[191] Dalsky GP, Stocke KS, Ehsani AA, et al. Weight-bearing exercise training and lumbar bone mineral content in postmenopausal women. *Ann Int Med*. 1988;108:824-8.
[192] Heinonen A, Sievanen H, Kannus P, et al. High-impact exercise and bones of growing girls: a 9-month controlled trial. *Osteoporos Int*. 2000;11:1010-7.
[193] Smidt N, de Vet HC, Bouter LM, et al. Effectiveness of exercise therapy: a best-evidence summary of systematic reviews. *Aust J Physiother*. 2005;51:71-85.
[194] Gulmans VA, de Meer K, Brackel HJ, et al. Outpatient exercise training in children with cystic fibrosis: physiological effects, perceived competence, and acceptability. *Pediatr Pulmonol*. 1999;28:39-46.
[195] Blomquist M, Freyschuss U, Wiman LG, et al. Physical activity and self treatment in cystic fibrosis. *Arch Dis Child*. 1986;61:362-7.
[196] Prasad SA, Cerny FJ. Factors that influence adherence to exercise and their effectiveness: applications to cystic fibrosis. *Pediatric Pulmonology*. 2002;34:66-72.
[197] Gudas LJ, Koocher GP, Wypij D. Perceptions of medical compliance in children and adolescents with cystic fibrosis. *J Dev Behav Pediatr*. 1991;12:236-42.
[198] Hodges PW, Moseley GL, Gabrielsson A, et al. Experimental muscle pain changes feedforward postural responses of the trunk muscles. *Experimental brain research Experimentelle Hirnforschung*. 2003;151:262-71.
[199] Harvey L, Herbert R, Crosbie J. Does stretching induce lasting increases in joint ROM? A systematic review. *Physiotherapy Research International*. 2002;7:1-13.
[200] Williams PE. Use of intermittent stretch in the prevention of serial sarcomere

loss in immobilised muscle. *Annals of Rheumatic Disease*. 1990;49:316-7.
[201] van Tulder MW, Koes BW, Bouter LM. Conservative treatment of acute and chronic nonspecific low back pain. A systematic review of randomized controlled trials of the most common interventions. *Spine*. 1997;22:2128-56.
[202] El-Ansary D, Adams R, Ghandi A. Musculoskeletal and neurological complications following coronary artery bypass graft surgery: A comparison between saphenous vein and internal mammary artery grafting. *Aust J Physiother*. 2000;46:19-25.
[203] Vibekk P. Chest mobilization and respiratory function. In: Pryor JA, ed. *Respiratory Care*. Edinburgh: Churchill Livingstone 1991:103-20.
[204] McVean R, Langman H, Orr A, et al. Musculoskeletal problems in an adult CF unit. *Journal of Cystic Fibrosis*. 2002;1:S179.
[205] Roland M, Morris R. A study of the natural history of back pain. Part I: development of a reliable and sensitive measure of disability in low-back pain. *Spine*. 1983;8:141-4.
[206] Kopec JA, Esdaile JM, Abrahamowicz M, et al. The Quebec Back Pain Disability Scale. Measurement properties. *Spine*. 1995;20:341-52.
[207] Westaway M, Stratford P, Binkley J. The patient-specific functional scale: validation of its use in patients with neck impairment. *Journal of Orthopedic and Sports Physical Therapy* 1998;27.
[208] McQueen KL, Button BM, Heathcote CH. Massage and musculo-skeletal physiotherapy service for adults: effects on chest mobility, posture, muscle tension, pain, ease of breathing and well-being. *Pediatric Pulmonology*. 2003;Suppl 25:A240.
[209] Massery M. Musculoskeletal and neuromuscular interventions: a physical approach to cystic fibrosis. *J R Soc Med*. 2005;98 (Suppl 45):55-66.
[210] Lannefors L, Button BM, Mcllwaine M. Physiotherapy in infants and young children with cystic fibrosis: current practice and future developments. *J R Soc Med*. 2 2004;97 (Suppl 44):8-25.
[211] Kerem E, Conway S, Elborn S, et al. Standards of care for patients with cystic fibrosis: a European consensus. *J Cyst Fibros*. 2005;4:7-26.
[212] Dietitian's Association of Australia Cystic Fibrosis Interest Group. Australasian Clinical Practice Guidelines for Nutrition in Cystic Fibrosis 2006.
[213] Hensyl W. Stedman's Medical Dictionary. 25 ed. Baltimore MD: Williams and Wilkins 1990.
[214] Brinson GM, Noone PG, Mauro MA, et al. Bronchial artery embolization for the treatment of hemoptysis in patients with cystic fibrosis. *Am J Respir Crit Care Med*. 1998;157:1951-8.
[215] Penketh AR, Wise A, Mearns MB, et al. Cystic fibrosis in adolescents and adults. *Thorax*. 1987;42:526-32.
[216] Barben JU, Ditchfield M, Carlin JB, et al. Major haemoptysis in children with cystic fibrosis: a 20-year retrospective study. *J Cyst Fibros*. 2003;2:105-11.
[217] Flume PA, Yankaskas JR, Ebeling M, et al. Massive hemoptysis in cystic fibrosis. *Chest*. 2005;128:729-38.
[218] Schidlow DV, Varlotta L. CF lung disease: How to manage complications. *Journal of Respiratory Diseases*. 1997;18:489-91.
[219] Wilson JW, Kotsimbos ATC. The management of cystic fibrosis. In: Muers MA, ed. *Respiratory Diseases*. Oxford: Oxford University Press 2004:391-

410.
[220] De Abreu e Silva FA, Dodge JA. Guidelines for the diagnosis and management of cystic fibrosis: WHO Human Genetics Programme and the International Cystic Fibrosis Association 1996.
[221] King AD, Cumberland DC, Brennan SR. Management of severe haemoptysis by bronchial artery embolisation in a patient with cystic fibrosis. *Thorax*. 1989;44:523-4.
[222] Association of Chartered Physiotherapists in Cystic Fibrosis. Clinical guidelines for the physiotherapy management of cystic fibrosis. Recommendations of a Working Party. 2002.
[223] Rich RH, Warwick WJ, Leonard AS. Open thoracotomy and pleural abrasion in the treatment of spontaneous pneumothorax in cystic fibrosis. *J Pediatr Surg*. 1978;13:237-42.
[224] Henry M, Arnold T, Harvey J. BTS guidelines for the management of spontaneous pneumothorax. *Thorax*. 2003;58 Suppl 2:ii39-52.
[225] Flume PA, Strange C, Ye X, et al. Pneumothorax in cystic fibrosis. *Chest*. 2005;128:720-8.
[226] Luck SR, Raffensperger JG, Sullivan HJ, et al. Management of pneumothorax in children with chronic pulmonary disease. *J Thorac Cardiovasc Surg*. 1977;74:834-9.
[227] Flume PA. Pneumothorax in cystic fibrosis. *Chest*. 2003;123:217-21.
[228] Penketh AR, Knight RK, Hodson ME, et al. Management of pneumothorax in adults with cystic fibrosis. *Thorax*. 1982;37:850-3.
[229] Schidlow DV, Taussig LM, Knowles MR. Cystic fibrosis foundation consensus conference report on pulmonary complications of cystic fibrosis. *Pediatr Pulmonol*. 1993;15:187-98.
[230] Noyes BE, Orenstein DM. Treatment of pneumothorax in cystic fibrosis in the era of lung transplantation. *Chest*. 1992;101:1187-8.
[231] Mastella G, Rainisio M, Harms HK, et al. Allergic bronchopulmonary aspergillosis in cystic fibrosis. A European epidemiological study. Epidemiologic Registry of Cystic Fibrosis. *Eur Respir J*. 2000;16:464-71.
[232] Moss RB. Pathophysiology and immunology of allergic bronchopulmonary aspergillosis. *Med Mycol*. 2005;43 Suppl 1:S203-6.
[233] Kraemer R, Delosea N, Ballinari P, et al. Effect of allergic bronchopulmonary aspergillosis on lung function in children with cystic fibrosis. *Am J Respir Crit Care Med*. 2006;174:1211-20.
[234] Mosher PE, Nash MS, Perry AC, et al. Aerobic circuit exercise training: effect on adolescents with well-controlled insulin-dependent diabetes mellitus. *Arch Phys Med Rehabil*. 1998;79:652-7.
[235] Fuchsjager-Mayrl G, Pleiner J, Wiesinger GF, et al. Exercise training improves vascular endothelial function in patients with type 1 diabetes. *Diabetes care*. 2002;25:1795-801.
[236] Castaneda C, Layne JE, Munoz-Orians L, et al. A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes. *Diabetes care*. 2002;25:2335-41.
[237] Cauza E, Hanusch-Enserer U, Strasser B, et al. The relative benefits of endurance and strength training on the metabolic factors and muscle function of people with type 2 diabetes mellitus. *Arch Phys Med Rehabil*.

2005;86:1527-33.
[238] Fiel SB, Fitzsimmons S. Pregnancy in patients with cystic fibrosis. *Pediatr Pulmonol Suppl*. 1997;16:111-2.
[239] Frangolias DD, Nakielna EM, Wilcox PG. Pregnancy and cystic fibrosis: a case-controlled study. *Chest*. 1997;111:963-9.
[240] Gilljam M, Antoniou M, Shin J, et al. Pregnancy in cystic fibrosis. Fetal and maternal outcome. *Chest*. 2000;118:85-91.
[241] Jankelson D, Robinson M, Parsons S, et al. Cystic fibrosis and pregnancy. *The Aust & NZ J Obst Gynae* 1998;38:180-4.
[242] Beischer N, Mackay E, Purcal N. Care of the pregnant woman and her baby. 2nd ed. Sydney: W.B Saunders /Balliere Tindall 1989.
[243] De Swiet MTcs, in Hyten F and Chamberlain G (eds). Clinical Physiology in Obstetrics2nd edn, pp.3-38. Oxford: Blackwell scientific Publications. The cardiovascular system. In: Hyten F, Chamberlain G, eds. *Clinical Physiology in Obstetrics*. 2nd ed. Oxford: Blackwell Scientific Publishing 1991:3-38.
[244] Johannesson M, Carlson M, Brucefors AB, et al. Cystic fibrosis through a female perspective: psychosocial issues and information concerning puberty and motherhood. *Patient education and counseling*. 1998;34:115-23.
[245] Johannesson M. Effects of pregnancy on health: certain aspects of importance for women with cystic fibrosis. *J Cyst Fibros*. 2002;1:9-12.
[246] Button BM, Roberts S, Kotsimbos TC, et al. Gastroesophageal reflux (symptomatic and silent): a potentially significant problem in patients with cystic fibrosis before and after lung transplantation. *J Heart Lung Transplant*. 2005;24:1522-9.
[247] Cornacchia M, Zenorini A, Perobelli S, et al. Prevalence of urinary incontinence in women with cystic fibrosis. *BJU international*. 2001;88:44-8.
[248] White D, Stiller K, Roney F. The prevalence and severity of symptoms of incontinence in adult cystic fibrosis patients. *Physiotherapy Theory and Practice*. 2000;16:35-42.
[249] Orr A, McVean RJ, Webb AK, et al. Questionnaire survey of urinary incontinence in women with cystic fibrosis. *BMJ*. 2001;322:1521.
[250] Nixon GM, Glazner JA, Martin JM, et al. Urinary incontinence in female adolescents with cystic fibrosis. *Pediatrics*. 2002;110:e22.
[251] Moran F, Bradley JM, Boyle L, et al. Incontinence in adult females with cystic fibrosis: a Northern Ireland survey. *International journal of clinical practice*. 2003;57:182-3.
[252] Chiarelli P, Brown W, McElduff P. Leaking urine: prevalence and associated factors in Australian women. *Neurourology and urodynamics*. 1999;18:567-77.
[253] Button BM, Sherburn M, Chase J, et al. Incontinence (urinary and bowel) in women with cystic fibrosis compared to COPD and controls: prevalence, severity and bother. *Pediatr Pulmonol.* 2004;Suppl 27.
[254] Gumery L, Hodgson G, Humphries N, et al. The prevalence of urinary incontinence in the adult male population of a regional cystic fibrosis centre. *J Cyst Fibros*. 2002;1:S173.
[255] Button BM, Sherburn M, Chase J, et al. Pelvic Floor Muscle Function in Women with Chronic Lung Disease (Cystic Fibrosis and COPD) versus controls: Relationship to Urinary Incontinence. *Pediatr Pulmonol*. 2005;Suppl

28:A368.
[256] Button BM, Sherburn M, Chase J, et al. Effect of a Three Months Physiotherapeutic Intervention on Incontinence in Women with Chronic Cough Related to Cystic Fibrosis and COPD. *Pediatr Pulmonol.* 2005;Suppl 28:A369.
[257] Sapsford RR, Richardson CA, Stanton WR. Sitting posture affects pelvic floor muscle activity in parous women: an observational study. *Aust J Physiother*. 2006;52:219-22.
[258] Sawyer SM, Glazner JA. What follows newborn screening? An evaluation of a residential education program for parents of infants with newly diagnosed cystic fibrosis. *Pediatrics*. 2004;114:411-6.
[259] Merelle ME, Huisman J, Alderden-van der Vecht A, et al. Early versus late diagnosis: psychological impact on parents of children with cystic fibrosis. *Pediatrics*. 2003;111:346-50.
[260] The CF Trust's clinical standards and accreditation group. Standards for the clinical care of children and adults with cystic fibrosis in the UK. 2001.
[261] Armstrong DS, Grimwood K, Carlin JB, et al. Lower airway inflammation in infants and young children with cystic fibrosis. *Am J Respir Crit Care Med*. 1997;156:1197-204.
[262] Khan TZ, Wagener JS, Bost T, et al. Early pulmonary inflammation in infants with cystic fibrosis. *Am J Respir Crit Care Med*. 1995;151:1075-82.
[263] Merelle ME, Schouten JP, Gerritsen J, et al. Influence of neonatal screening and centralized treatment on long-term clinical outcome and survival of CF patients. *Eur Respir J*. 2001;18:306-15.
[264] Minasian C, McCullagh A, Bush A. Cystic fibrosis in neonates and infants. *Early human development*. 2005;81:997-1004.
[265] Hardy KA, Wolfson MR, Schidlow DV, et al. Mechanics and energetics of breathing in newly diagnosed infants with cystic fibrosis: effect of combined bronchodilator and chest physical therapy. *Pediatr Pulmonol*. 1989;6:103-8.
[266] Maayan C, Bar-Yishay E, Yaacobi T, et al. Immediate effect of various treatments on lung function in infants with cystic fibrosis. *Respiration*. 1989;55:144-51.
[267] World Health Organization (WHO). International Classification of Functioning, Disability and Health. Geneva: WHO 2001.
[268] Eiser C, Zoritch B, Hiller J, et al. Routine stresses in caring for a child with cystic fibrosis. *Journal of psychosomatic research*. 1995;39:641-6.
[269] Grasso MC, Button BM, Allison DJ, et al. Benefits of music therapy as an adjunct to chest physiotherapy in infants and toddlers with cystic fibrosis. *Pediatr Pulmonol*. 2000;29:371-81.
[270] Schidlow DV, Fiel SB. Life beyond pediatrics. Transition of chronically ill adolescents from pediatric to adult health care systems. *The Medical clinics of North America*. 1990;74:1113-20.
[271] Conway SP. Transition from paediatric to adult-orientated care for adolescents with cystic fibrosis. *Disability and rehabilitation*. 1998;20:209-16.
[272] Nasr SZ, Campbell C, Howatt W. Transition program from pediatric to adult care for cystic fibrosis patients. *J Adolesc Health*. 1992;13:682-5.
[273] Zack J, Jacobs CP, Keenan PM, et al. Perspectives of patients with cystic fibrosis on preventive counseling and transition to adult care. *Pediatr*

Pulmonol. 2003;36:376-83.
[274] Boyle MP, Farukhi Z, Nosky ML. Strategies for improving transition to adult cystic fibrosis care, based on patient and parent views. *Pediatr Pulmonol*. 2001;32:428-36.
[275] Westwood A, Henley L, Willcox P. Transition from paediatric to adult care for persons with cystic fibrosis: patient and parent perspectives. *J Paediatr Child Health*. 1999;35:442-5.
[276] Flume PA, Taylor LA, Anderson DL, et al. Transition programs in cystic fibrosis centers: perceptions of team members. *Pediatr Pulmonol*. 2004;37:4-7.
[277] Cowlard J. Cystic fibrosis: transition from paediatric to adult care. *Nurs Stand*. 2003;18:39-41.
[278] Brumfield K, Lansbury G. Experiences of adolescents with cystic fibrosis during their transition from paediatric to adult health care: a qualitative study of young Australian adults. *Disability and rehabilitation*. 2004;26:223-34.
[279] Webb AK, Jones AW, Dodd ME. Transition from paediatric to adult care: problems that arise in the adult cystic fibrosis clinic. *J R Soc Med*. 2001;94 Suppl 40:8-11.
[280] Fauroux B, Hart N, Lofaso F. Non invasive mechanical ventilation in cystic fibrosis: physiological effects and monitoring. *Monaldi Arch Chest Dis*. 2002;57:268-72.
[281] Fauroux B, Pigeot J, Polkey MI, et al. In vivo physiologic comparison of two ventilators used for domiciliary ventilation in children with cystic fibrosis. *Crit Care Med*. 2001;29:2097-105.
[282] Granton JT, Kesten S. The acute effects of nasal positive pressure ventilation in patients with advanced cystic fibrosis. *Chest*. 1998;113:1013-8.
[283] Serra A, Polese G, Braggion C, et al. Non-invasive proportional assist and pressure support ventilation in patients with cystic fibrosis and chronic respiratory failure. *Thorax*. 2002;57:50-4.
[284] Hodson ME, Madden BP, Steven MH, et al. Non-invasive mechanical ventilation for cystic fibrosis patients--a potential bridge to transplantation. *Eur Respir J*. 1991;4:524-7.
[285] Piper AJ, Parker S, Torzillo PJ, et al. Nocturnal nasal IPPV stabilizes patients with cystic fibrosis and hypercapnic respiratory failure. *Chest*. 1992;102:846-50.
[286] Padman R, Lawless S, Von Nessen S. Use of BiPAP by nasal mask in the treatment of respiratory insufficiency in pediatric patients: preliminary investigation. *Pediatr Pulmonol*. 1994;17:119-23.
[287] Caronia CG, Silver P, Nimkoff L, et al. Use of bilevel positive airway pressure (BIPAP) in end-stage patients with cystic fibrosis awaiting lung transplantation. *Clinical pediatrics*. 1998;37:555-9.
[288] Sprague K, Graff G, Tobias DJ. Noninvasive ventilation in respiratory failure due to cystic fibrosis. *South Med J*. 2000;93:954-61.
[289] Madden BP, Kariyawasam H, Siddiqi AJ, et al. Noninvasive ventilation in cystic fibrosis patients with acute or chronic respiratory failure. *Eur Respir J*. 2002;19:310-3.
[290] British Thoracic Society. Non-invasive ventilation in acute respiratory failure. British Thoracic Society Standards of Care Committee. *Thorax*. 2002;57:192-

211.
[291] Holland AE, Wilson JW, Kotsimbos TC, et al. Metabolic alkalosis contributes to acute hypercapnic respiratory failure in adult cystic fibrosis. *Chest*. 2003;124:490-3.
[292] Holland AE, Denehy L, Buchan CA, et al. Efficacy of a heated passover humidifier during noninvasive ventilation: a bench study. *Respir Care*. 2007;52:38-44.
[293] Wiest GH, Foerst MD, Fuchs FS, et al. In vivo efficacy of two heated humidifiers used during CPAP-therapy for obstructive sleep apnea under various environmental conditions. *Sleep*. 2001;24:435-40.
[294] Muller NL, Francis PW, Gurwitz D, et al. Mechanism of hemoglobin desaturation during rapid-eye-movement sleep in normal subjects and in patients with cystic fibrosis. *Am Rev Respir Dis*. 1980;121:463-9.
[295] Tepper RS, Skatrud JB, Dempsey JA. Ventilation and oxygenation changes during sleep in cystic fibrosis. *Chest*. 1983;84:388-93.
[296] Gozal D. Nocturnal ventilatory support in patients with cystic fibrosis: comparison with supplemental oxygen. *Eur Respir J*. 1997;10:1999-2003.
[297] Olson EJ, Simon PM. Sleep-wake cycles and the management of respiratory failure. *Curr Opin Pulm Med*. 1996;2:500-6.
[298] Milross MA, Piper AJ, Norman M, et al. Low-flow Oxygen and Bilevel Ventilatory Support. Effects on ventilation during sleep in cystic fibrosis. *Am J Respir Crit Care Med*. 2001;163:129-34.
[299] Hill AT, Edenborough FP, Cayton RM, et al. Long-term nasal intermittent positive pressure ventilation in patients with cystic fibrosis and hypercapnic respiratory failure (1991-1996). *Respir Med*. 1998;92:523-6.
[300] Granton JT, Shapiro C, Kesten S. Noninvasive nocturnal ventilatory support in advanced lung disease from cystic fibrosis. *Respir Care*. 2002;47:675-81.
[301] Fauroux B, Boule M, Lofaso F, et al. Chest physiotherapy in cystic fibrosis: improved tolerance with nasal pressure support ventilation. *Pediatrics*. 1999;103:1-9.
[302] Holland AE, Denehy L, Ntoumenopoulos G, et al. Non-invasive ventilation assists chest physiotherapy in adults with acute exacerbations of cystic fibrosis. *Thorax*. 2003;58:880-4.
[303] Henke KG, Regnis JA, Bye PT. Benefits of continuous positive airway pressure during exercise in cystic fibrosis and relationship to disease severity. *Am Rev Respir Dis*. 1993;148:1272-6.
[304] van 't Hul A, Gosselink R, Hollander P, et al. Training with inspiratory pressure support in patients with severe COPD. *Eur Respir J*. 2006;27:65-72.
[305] Robinson WM, Ravilly S, Berde C, et al. End-of-life care in cystic fibrosis. *Pediatrics*. 1997;100:205-9.
[306] Tonelli MR. End-of-life care in cystic fibrosis. *Curr Opin Pulm Med*. 1998;4:332-6.
[307] Ramsey BW. Management of pulmonary disease in patients with cystic fibrosis. *N Engl J Med*. 1996;335:179-88.
[308] Mitchell I, Nakielna E, Tullis E, et al. Cystic fibrosis. End-stage care in Canada. *Chest*. 2000;118:80-4.
[309] Chapman E, Landy A, Lyon A, et al. End of life care for adult cystic fibrosis patients: facilitating a good enough death. *J Cyst Fibros*. 2005;4:249-57.

[310] Robinson W. Palliative care in cystic fibrosis. *Journal of Palliative Medicine*. 2000;3:187-92.
[311] Abbott J, Dodd M, Webb AK. Health perceptions and treatment adherence in adults with cystic fibrosis. *Thorax*. 1996;51:1233-8.
[312] Modi AC, Lim CS, Yu N, et al. A multi-method assessment of treatment adherence for children with cystic fibrosis. *J Cyst Fibros*. 2006;5:177-85.
[313] Zindani GN, Streetman DD, Streetman DS, et al. Adherence to treatment in children and adolescent patients with cystic fibrosis. *J Adolesc Health*. 2006;38:13-7.
[314] Suri R, Wallis C, Bush A, et al. A comparative study of hypertonic saline, daily and alternate-day rhDNase in children with cystic fibrosis. *Health technology assessment (Winchester, England)*. 2002;6:iii, 1-60.
[315] Burrows JA, Bunting JP, Masel PJ, et al. Nebulised dornase alpha: adherence in adults with cystic fibrosis. *J Cyst Fibros*. 2002;1:255-9.
[316] Quittner AL, Espelage DL, Levers-Landis CE, et al. Measuring adherence to medical treatments in childhood chronic illness. *J Clin Psychol Med Settings*. 2000;7.
[317] Conway SP, Pond MN, Hamnett T, et al. Compliance with treatment in adult patients with cystic fibrosis. *Thorax*. 1996;51:29-33.
[318] Abbott J, Dodd M, Gee L, et al. Ways of coping with cystic fibrosis: implications for treatment adherence. *Disability and rehabilitation*. 2001;23:315-24.
[319] Bauman LJ, Wright E, Leickly FE, et al. Relationship of adherence to pediatric asthma morbidity among inner-city children. *Pediatrics*. 2002;110:e6.
[320] Berg JS, Dischler J, Wagner DJ, et al. Medication compliance: a healthcare problem. *The Annals of pharmacotherapy*. 1993;27:S1-24.
[321] Weiss KB, Gergen PJ, Hodgson TA. An economic evaluation of asthma in the United States. *N Engl J Med*. 1992;326:862-6.
[322] Modi AC, Quittner AL. Utilising computerised phone diary procedures to assess health behaviours in family & social contexts. *Child Health Care*. 2006;35:29-45.
[323] Davidson KL. Airway clearance strategies for the pediatric patient. *Respir Care*. 2002;47:823-8.
[324] Main E, Prasad A, Schans C. Conventional chest physiotherapy compared to other airway clearance techniques for cystic fibrosis. *Cochrane Database Syst Rev*. 2005:CD002011.
[325] Cystic Fibrosis Australia, Infection Control and Hygiene Guidelines. 2000.
[326] Cystic Fibrosis Foundation. Infection control recommendations for patients with cystic fibrosis. 2001.
[327] Saiman L, Siegel J. Infection control recommendations for patients with cystic fibrosis: microbiology, important pathogens, and infection control practices to prevent patient-to-patient transmission. *Infect Control Hosp Epidemiol*. 2003;24:S6-52.
[328] Saiman L, Siegel J. Infection control in cystic fibrosis. *Clinical microbiology reviews*. 2004;17:57-71.
[329] Zimakoff J, Hoiby N, Rosendal K, et al. Epidemiology of Pseudomonas aeruginosa infection and the role of contamination of the environment in a

cystic fibrosis clinic. *The Journal of hospital infection*. 1983;4:31-40.
[330] Moore JE, McIlhatton B, Buchanan J, et al. Occurrence of Burkholderia cepacia in the hospital environment. *Ir J Med Sci*. 2002;171:131-3.
[331] Ensor E, Humphreys H, Peckham D, et al. Is Burkholderia (Pseudomonas) cepacia disseminated from cystic fibrosis patients during physiotherapy? *The Journal of hospital infection*. 1996;32:9-15.
[332] Pegues DA, Schidlow DV, Tablan OC, et al. Possible nosocomial transmission of Pseudomonas cepacia in patients with cystic fibrosis. *Archives of pediatrics & adolescent medicine*. 1994;148:805-12.
[333] Estivariz CF, Bhatti LI, Pati R, et al. An outbreak of Burkholderia cepacia associated with contamination of albuterol and nasal spray. *Chest*. 2006;130:1346-53.
[334] Button BM, Wulfsohn V, Wilson JW, et al. Benchmark Parameters of international physiotherapy services to inpatients and outpatients with cystic fibrosis. *Pediatric Pulmonology*. 2000;Supplement 20 A450.
[335] ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med*. 2002;166:111-7.
[336] Borg G. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc*. 1982;14:377-81.

APPENDICES

Appendix 1 Performance of the Active Cycle of Breathing Technique

Thoracic Expansion Exercises (TEEs) are deep inspirations toward total lung capacity. Lower chest expansion is usually encouraged. With an increase in lung volume the resistance to airflow via the collateral channels is reduced. Mobilisation of secretions can be facilitated by air passing along these channels and behind secretions. A three second hold (inspiratory pause through an open glottis) at the end of inspiration may augment this effect.

The Forced Expiration Technique (FET) is a combination of one or two forced expirations (huffs) and periods of breathing control. During a forced expiratory manoeuvre (for example a huff) there is compression of the airways downstream (towards the mouth) of the equal pressure point. This squeezing action, which moves peripherally with decreasing lung volume, facilitates the movement of secretions. Huffing to low lung volumes will assist in mobilizing the more peripherally situated secretions. When secretions have reached the larger, more proximal airways, a huff or cough from moderate or high lung volume can be used to clear them.

Breathing Control (BC) is gentle, relaxed breathing around tidal volume, encouraging use of the lower chest and relaxation of the upper chest and shoulders. Breathing control is considered an essential part of the ACBT in order to prevent any increase in airflow obstruction [13] or oxyhaemoglobin desaturation [66]; however this evidence comes only from uncontrolled trials.

During the ACBT, BC is followed by TEE. Breathing control is then repeated followed by the FET. The entire ACBT is repeated until the huff sounds dry and is non-productive, or it is time for a rest. A minimum of ten minutes in a productive position is recommended. If more than one position is needed, two positions are usually sufficient for one treatment session. The total treatment time is between ten and thirty minutes.

Appendix 2: Technique for Autogenic Drainage

Breathing IN:

- Commence the breath in from a low lung volume, close to residual volume
- Slowly breathe in the necessary volume of air through the nose
- Hold the breath for approximately 2-3 seconds

Breathing OUT:

- Breath out preferably through the nose, or mouth to hear bronchial noises
- Do not slow down the expiratory flow
- The expired volume should rarely be larger than the volume which has been inhaled previously
- Movement of mucus should be heard distinctly during expiration.

Repeat until the mucus can be heard moving more centrally. Tidal volume and end-expiratory lung volume should then be increased in a step-wise fashion, with the aim of gradually moving the mucus into the large airways. Once the mucus reaches the central airways it can be evacuated using a high lung volume huff or cough.

Appendix 3: Technique for administering Positive Expiratory Pressure (PEP)

PEP therapy can be delivered through a face mask system or a mouthpiece system. In both systems, PEP is created by expiring through a narrow opening, providing resistance to expiration. The resistor should provide a steady PEP of 10-20cmH_20 during the middle of expiration.

The basic technique to be used with PEP therapy is as follows:

- Patient in sitting, with elbows on a table, feet on the floor and a neutral lumbar spine, with the mask sealed around the nose and mouth or the mouthpiece sealed by the lips while wearing a nose clip
- The patient takes a breath slightly larger than tidal volume
- Slightly active expiration is then performed through the PEP device for at least 3 seconds, maintaining a steady PEP of 10-20 cmH_20
- This is repeated 10-15 times consecutively without losing the seal of the mask or the mouthpiece in order to increase resting lung volumes
- At the end of the cycle of 10-15 breaths, the forced expiratory technique is used to bring up secretions and expectorate if possible. Patients should be discouraged from premature coughing and instead repeat the cycles until sputum has reached the upper airways where gentle coughing will clear it.

The frequency and duration of each treatment is adapted to the needs of the individual patient. For example in a clinically stable person with CF, 10 cycles of 10 breaths with FET between each cycle, performed twice daily is generally recommended for regular airway clearance. The addition of inhalation therapy may be used in clinical practice to reduce treatment time and promote adherence (see Chapter 3).

Appendix 4: Technique for administering high pressure PEP

High pressure PEP is administered through a face mask, using the same patient positioning as for PEP. The patient is seated with elbows resting on a table.

The patient performs PEP breathing (moderately increased tidal breathing) for eight to ten breaths.

Inhalation to total lung capacity is performed, followed by a forced expiratory manoeuvre through the mask down towards residual volume, reaching pressures of 40-100cm H_2O. Mobilisation of secretions usually results in coughing at low lung volume, through the mask against the resistor. Care must be taken not to terminate these forceful expirations before reaching residual volume.

Appendix 5: Assembling Bottle PEP

Equipment consists of:

- a plastic bottle (1 or 2 litre size)
- tubing 20-30cm in length and 5mm in diameter (suction tubing is suitable).

The bottle should be filled with water to a depth of 3.5 – 10 cm, depending on individual patient requirements. A manometer can be included in the circuit for measurement of pressures and for teaching / patient education. The bottom of the tubing should be located close to the bottom of the bottle throughout treatment.

The patient is instructed to undertake slightly larger than tidal volume breath with a slightly active breath out against the resistance of the column of water. The top of the bottle should not be sealed as this will alter resistance and pressure. A permeable material, eg face washer, held loosely over the top can be used to stop bubbling out of the top.

Paediatrics: A two litre milk bottle with handle is useful. The tubing can be fed through the inside of the handle to maintain its position at the bottom of bottle. Detergent and/or food colouring can be added to increase patient co-operation and participation.

Appendix 6: Technique for Oscillating PEP

A. Flutter®

To use the Flutter®, the patient should sit comfortably, then inspire to approx ½ to ¾ total lung capacity. The Flutter® is then placed in the mouth with lips closed firmly around the mouthpiece. The breath is held for 2-3 seconds. The patient then exhales through the Flutter® at a reasonably fast but not too forceful speed with the cheeks held in firmly using the other hand until the buccal muscles have developed to take over this role. This is repeated 5-15 times followed by huffing/coughing. The patient should suppress the urge to cough until the end of each cycle. At the end of each cycle, the patient should perform huffing and coughing to clear sputum. This is repeated until good clearance is achieved (usually 10-15 minutes). Patients should be taught to avoid unproductive coughing by going on to the next cycle and repeat huffing until secretions have accumulated in the upper airway. This will avoid side effects associated with paroxysmal coughing.

The performance of the Flutter® is gravity-dependent such that the device must be positioned upright in order to produce oscillation. The frequency can be modulated by changing the inclination of the device either slightly up (higher frequency) or slightly down (lower frequency). An optimal angle and frequency in the midrange will result in vibrations felt lower down towards the abdomen. It requires practice and skill to use the Flutter® in positions other than sitting. Because of the complexity of the technique, children may need supervision to use the Flutter® effectively.

B. Acapella®

To use the Acapella®, the mouthpiece should be placed in the mouth and a tight seal formed with the lips. The patient should inspire to approx ½ to ¾ of total lung capacity. The breath should be held for 2-3 seconds. The patient should then exhale actively, but not forcefully through the Acapella® for 3-4 seconds. This is repeated 10-20 times followed by huffing/coughing. The patient should suppress the urge to cough until the end of each cycle. The cycle is repeated until good clearance is achieved.

The Acapella® produces a PEP range of 7-35 cmH_20, and a frequency of airflow oscillation of 0-30Hz. Adjusting the dial clockwise increases the resistance of the vibrating orifice, which will allow the patient to exhale at a lower flow rate and with increased PEP. The Acapella® is not gravity-dependent and can be used in any body

position.

C. RC Cornet®

The RC Cornet® can be held at any angle during treatment, so it may be used with the patient in sitting or in recumbent positions. The patient is to create a firm seal around the mouthpiece with their lips. This is followed by inspiration to approx ½ to ¾ total lung capacity, followed by expiration through the device. This is repeated 8-10 times before huffing/coughing. The patient should suppress the urge to cough until the end of each cycle. The cycles should be repeated for approximately 15 minutes or until good clearance is achieved.

Appendix 7: Six-minute walk test protocol

The six-minute walk test (6MWT) should be conducted according to American Thoracic Society guidelines [335], from which this protocol is adapted.

The primary outcome of the 6MWT is distance walked. However, it is recommended pulse rate, oxygen saturation and perceived level of breathlessness is also recorded at the beginning and the end of the test as they provide important clinical information. Pulse oximetry may be performed continuously throughout the test to evaluate the degree of exercise-induced desaturation.

Equipment and setting
The equipment required for a 6MWT is:

- 25 m walking track, marked each 5m
- stopwatch
- pulse oximeter
- Borg scale
- recording sheet on a clipboard
- cones to mark the turn-around points

The test should be performed indoors, preferably in a wide corridor with minimal traffic. It is recommended the course be 30 metres in length; however other studies have shown the same outcomes with distances of 20 – 29 metres so it may depend on availability of space. There should be visible lines or markers at the beginning and the end of the course and it is helpful if there is some reference for the patient at certain points along the course.

It is recommended that the six minute walk test (6MWT) is performed at the same time of the day on each testing occasion and should be performed without a warm-up period. If the patient is routinely prescribed bronchodilators prior to exercise this should be administered prior to the test but note this in the assessment documentation. If the patient is receiving oxygen therapy this should be continued throughout the test at the same flow rate – if it is increased through the test due to desaturation this should also be noted on the assessment sheet.

Safety
It is recommended that there be a chair available in case the patient needs to rest

during the test and you should have easy access to oxygen supplies and emergency assistance staff if required. The ATS recommends that the person performing the test should have training in CPR. Reasons for immediately stopping a 6MWT include the following: (1) chest pain, (2) intolerable dyspnea, (3) leg cramps, (4) staggering, (5) diaphoresis, and (6) pale or ashen appearance, (7) SpO_2 <80%.

Procedure

The patient should remain sitting 10 minutes prior to commencing the walk test to allow for baseline measures to be recorded. Pulse rate, oxygen saturation and perceived breathlessness on the Borg scale should be recorded with the patient at rest.

The instructions given to the patient prior to commencing the test should be standardised and the verbal encouragement throughout the test should be minimal and standardised. The following is recommended by the ATS [335]:

'The object of this test is to walk as far as possible for 6 minutes. You will walk back and forth in this hallway. Six minutes is a long time to walk, so you will be exerting yourself. You will probably get out of breath or become exhausted. You are permitted to slow down, to stop, and to rest as necessary. You may lean against the wall whilst resting, but resume walking as soon as you are able. You will be walking back and forth at the finish and start marks. You should pivot briskly and continue back the other way without hesitation. Now I'm going to show you. Please watch the way I turn without hesitation'.

Demonstrate walking one lap yourself. 'Walk and pivot around the course briskly. Are you ready to do that? I am going to use this counter to keep track of the number of laps you complete. I will click it each time you turn around the starting line. Remember the object is to walk as FAR AS POSSIBLE for 6 minutes, but don't jog or run. Start now or whenever you are ready.'

Avoid walking with the patient during the test as this will influence the pacing of the patient. The encouragement provided during the six minutes also needs to be standardised. The following phrases are suggested by the ATS

At one minute: "You are doing well. You have 5 minutes to go."

At two minutes: "Keep up the good work you have 4 minutes to go."

At three minutes: "You are doing well. You are half-way done."

At four minutes: “Keep up the good work you only have 2 minutes to go.”

With one minute remaining: “You are doing well. You only have one minute to go.”

If the patient stops during the test let them know that they are able to lean against the wall if they need to, then continue walking whenever they feel able. Do not stop the timer. If the patient stops before the six minutes is up and refuses to keep walking then discontinue the test, note the time and the reason for the patient stopping on the assessment sheet.

With 15 seconds to go, inform the patient the time is almost up – let them know you will shout “stop” when the time is up and the patient should stop right where they are.

At the conclusion of the test, patients should rate their degree of breathlessness on the Borg scale and repeat measures of oxygen saturation, pulse rate and perceived breathlessness should be recorded. Ask the patient what they perceived to be the main limitation to the distance covered – breathing, legs or other symptoms. Congratulate the patient on a good effort.

It is recommended that two 6MWTs separated by at least 15 minutes are performed to ensure that a maximum result is achieved.

The Borg scale of perceived breathlessness [336]:

0	Nothing at all
1	Very slight
2	Slight (light)
3	Moderate
4	Somewhat severe
5	Severe (heavy)
6	
7	Very severe
8	
9	
10	Very, Very, severe (maximal)

Appendix 8: Three-minute step test protocol

Equipment

- Standard 6 inch (15 cm) step
- Stopwatch
- Metronome
- Pulse oximeter
- Borg scale
- A non-stick mat is optional and may be advised if the patient has any lower limb joint pain

Safety

Oxygen saturation should be recorded continually and the test ceased if saturation drops below 80% (or as indicated by respiratory physician).

Procedure

Set the metronome to 120 beats per minute, giving a stepping rate of 30 steps per minute.

The test should be explained to the patient prior to commencement. Patients should be given opportunity to practise the technique, rhythm and timing of stepping to the metronome and the technique for changing the leading leg should be demonstrated. Allow adequate time for return to resting pulse rate and oxygen saturation levels following practice. The patient should be told that they can stop the test at any time if they are unable to continue.

Baseline pulse rate, oxygen saturations and Borg breathlessness rating should be recorded prior to commencing the test. To reduce the interference when stepping, tape the oxygen probe lead to the forearm.

Standard encouragement should be given at 1, 1.5 and 2 minutes. 'You are one minute / half way / two minutes through the test and you are doing well'.

At the conclusion of the test, record the lowest value of SpO_2 and the highest value of pulse rate and note the times these occur. Ask the patient to rate their perceived breathlessness on the Borg scale. If the patient stops stepping or the test is stopped before the three minutes is completed, record the duration of stepping, number of

steps, reason for stopping as well as pulse rate and saturation at the time of stopping.

Appendix 9: Modified shuttle test protocol

The modified shuttle test is a 15 level walk/run shuttle test performed at increasing speeds back and forth on a 10 metre course with an audio signal to indicate the times the marker cones should be reached.

Equipment

- Shuttle tape *(*available from Dr Sally Singh, Dept of Respiratory Medicine, Glenfield Hospital NHS Trust, Groby Road, Leicester LE3 9QP, UK)
- Pulse oximeter
- Borg scale
- recording sheet on a clipboard
- cones to mark the turn-around points

Procedure

Patients should be familiarised with the procedure by conducting a practice test. Baseline measures should be taken prior to commencing the test and these should include resting pulse rate, oxygen saturation and perceived level of breathlessness using the Borg breathlessness scale. These measures should be repeated at the completion of the test. If you need to determine levels of desaturation the probe should remain on the patient throughout the test with the lead taped to their forearm to reduce interference. If the patient voluntarily stops the test, document the reason why, for example pain, breathlessness or other.

There should be standardised verbal encouragement at the end of each level: "good, keep going, you are doing well" and remind them they can run at any time if they need to keep up the beeps.

The patient should continue the test until they are unable to do so or fail to maintain the set pace (0.5m away from the cone when the beep sounds).

The distance covered should be recorded at the end of the test. Pulse rate, oxygen saturation and perceived level of breathlessness using the Borg breathlessness scale should also be recorded

Appendix 10: Musculoskeletal Screening Tool

A. Does pain limit your functional activities on more than two occasions per week?

☐ No

☐ Yes - VAS/10_____

Source

☐ Thoracic

☐ Lumbar

☐ Other_____

B Bone Mineral Density

☐ Not applicable

☐ Normal

☐ Z score < -1

☐ Z score < -2

☐ # in last 12 months, site and mechanism_____

C Thoracic kyphosis? (√ for Yes)

☐ Head to wall

☐ Radial styloid to wall

☐ Clasp hands behind back with wrists together

Appendix 11: Pelvic floor exercises for people with CF

1. Teach patients 'the knack' to protect them from leaking during increased load to the pelvic floor during coughing, huffing, sneezing, laughing etc.

'The knack' is a contraction of the pelvic floor (a form of bracing of the pelvic floor) prior to any activity that increases pelvic floor loading. This should become a lifelong habit similar to the lifting strategy of bending the knees and keeping the back straight during heavy lifting to prevent back injury.

2. Teach patients to carry out strength and endurance training of the pelvic floor and lower abdominal muscles. These should be taught to those who experience leaking during sneezing, nose blowing, coughing and huffing.

Instructions for the patient:

- Pull the pelvic floor up towards the diaphragm
- Hold for 3-5 seconds
- While holding, superimpose three quick contractions – 'pull up, up,up'

Dosage is 3 x 10 sets per day.

3. Teach optimal positioning for airway clearance therapy

Airway clearance should be carried out in positions that enhance pelvic floor function (Sapsford et al 2006).

In sitting, the lumbar spine should be held in a neutral or extended position to help lower abdominal and pelvic floor muscle activity to provide maximum protection against urinary leaking during all forms of airway clearance therapy.

If airway clearance is done sitting on a chair, the feet should be flat on the floor with a 90° angle at the hips and knees to further improve pelvic floor control and guarding against leaking during physiotherapy treatment.

Use "the knack" (pre-contraction) and "straighten the back" before increasing stress to the pelvic floor including during huffing and coughing regardless of the circumstances. If leaking feels imminent apply manual pressure over the pelvic floor region or cross the legs if in a standing position.

Patients who continue to have a problem with bladder and bowel control need to be

referred to a specialist continence physiotherapist for a course of treatment.

Appendix 12: Writing group declarations

Jenny Bishop	Research support, Roche Pharmaceuticals, 1998-2001
Jenny Busch	Solvay Allied Health Travel Scholarship 2007
	Conference support, Roche Pharmaceuticals 2003, 2006, 2007
Brenda Button	Conference support, Roche Pharmaceuticals, 1999-2007
Rosie Day	Solvay Allied Health Travel Scholarship 2006
	Conference support, Roche Pharmaceuticals, 2005-2007
Anne Holland	Solvay Allied Health Travel Scholarship 2002
Rachael McAleer	Solvay Allied Health Travel Scholarship 2006
	Conference support, Roche Pharmaceuticals, 2003-2007
Jenny Murphy	Conference support, Roche Pharmaceuticals, 2005, 2007
Nathan Ward	Conference support, Roche Pharmaceuticals, 2007
Christine Wilson	Research support for equipment and staffing, Roche Pharmaceuticals, 2005
Michelle Wood	Conference support, Roche Pharmaceuticals, 2005-2007

The Solvay Allied Health Travel Scholarship is awarded each year according to a competitive process using independent assessors who are not associated with Solvay.