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PHYSIOTHERAPY FOR CYSTIC FIBROSIS IN AUSTRALIA AND NEW ZEALAND

A Clinical Practice Guideline

Comprehensive Version*

July 2016

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FOREWORD

This Clinical Practice Guideline has been written by physiotherapists who are experienced in the management of cystic fibrosis in Australia and New Zealand.

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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 in arterial blood
PEFR	peak expiratory flow rate
PD	postural drainage
QOL	quality of life
TEE	thoracic expansion exercises
WHO	World Health Organisation

OVERVIEW

Physiotherapy management is a key element of care for people with cystic fibrosis (CF). Airway clearance techniques, exercise and inhalation therapy are cornerstones of treatment and are associated with improved long-term outcomes. As survival improves, complications associated with 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 considerable evidence exists to support physiotherapy management in CF, there is considerable variation in clinical practice. The need for physiotherapy guidelines which were applicable to the Australian and New Zealand 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 and New Zealand.

The Guideline 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, end of life care and infection control. This Supplement provides more detail of the evidence underpinning the recommendations and application of the physiotherapy techniques.

The Guideline will be due for review in 2019. Responsibility for organising the review process will be taken by the incumbent chairperson of the Australian chapter of the International Physiotherapy Group/Cystic Fibrosis (IPG/CF) and country contact person for Australia in the IPG/CF.

1 INTRODUCTION

Background to the Clinical Practice Guideline

Physiotherapy management is a key element of care for people with cystic fibrosis (CF). Airway clearance techniques, exercise and inhalation therapy are cornerstones of treatment and are associated with improved long-term outcomes (1-3). The Clinical Practice Guideline provides recommendations for the key areas of physiotherapy management for people with CF, including airway clearance techniques (ACTs), inhalation therapy, exercise and musculoskeletal management. The recommendations are graded according to National Health and Medical Research Council (NHMRC) guidelines (4) and based on evidence up to and including June 2014. Elements of clinical practice that were considered important but lacking research evidence, and not likely to have research evidence in the future, were highlighted as 'Practice Points'.

Purpose and Scope

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

The aims of the guideline are:

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 and reflects the best available knowledge
3. To standardise the physiotherapy care of people with CF across 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.

Process

This Clinical Practice Guideline is an update of 'Physiotherapy for Cystic Fibrosis: A Consensus Statement', which was endorsed by the Thoracic Society of Australia and New Zealand in 2008.

All known physiotherapists who regularly care for people with CF across paediatric and adult settings in both Australia and New Zealand were invited to participate in this update. A call for volunteers was made via email and at the 9th Australian and New Zealand Cystic Fibrosis Conference in Melbourne in 2011. Participants were invited to nominate their areas of interest for the update. Group leaders were appointed to coordinate the update of each chapter

Updates of each chapter were prepared by the writing group and circulated to the whole group for comment and revision. The document was compiled into one editorially consistent text by the editor and circulated to the group for review.

All writing group members were invited to attend a workshop held in conjunction with the 10th Australian and New Zealand Cystic Fibrosis Conference in Auckland in 2013. At this time, feedback was sought from group members on all sections of the document, especially the recommendations. The draft document was then offered to stakeholders for comment, including CF physicians, CF consumers, allied health professionals and expert physiotherapists who were not part of the writing group.

Methods

The literature search for this document was conducted systematically using electronic databases including MEDLINE, CINAHL, EMBASE and PEDro. Separate searches were undertaken for each chapter and each search strategy was documented. Manual search of relevant conference proceedings was undertaken. Searches were limited to articles in English. Literature up to and including June 2014 was included. Both randomised controlled trials and research conducted with less robust designs were included. Groups were encouraged to make use of existing systematic reviews when they were available.

One or more individuals from each group decided which studies should be included in the update. Data from every included study were extracted into an evidence table by one reviewer and checked by a second reviewer. Data extracted were study identifier, number and characteristics of participants, design, intervention details where appropriate, results and study limitations. The quality of each study was graded according to the NHMRC evidence hierarchy and recommendations formulated (4). Recommendations were formulated based on the quality, quantity and level of the evidence; the consistency of the body of evidence; the likely clinical impact; and generalisability and applicability to physiotherapy practice in Australia and New Zealand (4). Elements of clinical practice that were considered important but lacking research evidence, and not likely to have research evidence in the future, were highlighted as 'Practice Points'.

Dissemination

The evaluation of the 2008 Consensus Statement (5) showed that physiotherapists used and preferred a wide range of methods for accessing the document, including hard copy, soft copy and via the internet. This Clinical Practice Guideline will be disseminated amongst physiotherapists working in CF centres throughout Australia and New Zealand in hard copy and soft copy. It will also be made available on the Thoracic Society of Australia and New Zealand (TSANZ) website. Evaluation findings also showed that knowledge of the previous Consensus Statement treatment recommendations were lower outside specialist CF centres and in specialist areas of CF practice. This will be addressed by active dissemination of the guidelines to non-CF centres in metropolitan regions, as well as regional centres and all known physiotherapists involved in CF care outside of specialist centres. We will also prioritise the provision of education in specialist areas of CF practice at CF, respiratory and general physiotherapy conferences. A copy will also be provided to all university physiotherapy schools in Australia and New Zealand. The guideline will be published in *Respirology*.

Review process

The guideline will be due for review and updating in 2019. The process will be coordinated by the incumbent chairperson of the Australian chapter of the International Physiotherapy Group – CF (IPG/CF) and the contact physiotherapist for the IPG/CF in Australia and New Zealand. Prior to this update, an evaluation of the document will be undertaken via a survey of physiotherapy practice across all centres in Australia, consistent with our evaluation of the 2008 Consensus Statement (5). Update of the document will incorporate the findings of the evaluation, as well as new evidence from the scientific literature.

Table 1: Definition of National Health and Medical Research Council grades of recommendations (4)

Grade of recommendation	Description
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations.
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendation must be applied with caution

Disclosure statement

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Development of the 2008 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.

Declarations of interest were made by each author according to the policies of the TSANZ. Any perceived conflicts of interest were managed by the Editor. Declarations of interest are outlined in Appendix 6.

2 AIRWAY CLEARANCE TECHNIQUES

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 manifested 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' (6). 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' (7).

Airway clearance techniques (ACTs) are usually commenced as soon as the diagnosis of CF is made, often soon after birth. In infants ACTs are performed by the parents, however as children grow older they are taught techniques that can be performed independently of an assistant (8). People with CF undertake this treatment both during acute exacerbations and prophylactically between infections (9).

It has been stated that 'physiotherapy has a major influence in limiting the adult consequences of CF' (10) p240. This is based on the assumption that ACTs have both short-term beneficial effects, and are able to slow the rate of pulmonary deterioration over time, via physical compensation for decreased mucociliary clearance. A Cochrane review has concluded that ACTs have short-term beneficial effects on mucus transport in CF however there was no evidence regarding long-term effects (11). One uncontrolled study has evaluated the effects of withdrawing ACTs 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 controlled trial could be conducted, especially in adults with established lung disease (7).

A Consensus Conference Report on Cystic Fibrosis Adult Care describes airway clearance as a 'cornerstone' of treatment (12) p5S. As such it is the role of physiotherapists to ensure that the ACTs prescribed have a sound

basis in physiology and can be effectively performed across the lifespan. This chapter discusses the various ACTs that a physiotherapist may perform or prescribe for a person with CF. Several systematic reviews note that no single ACT is superior, nor is one approach suitable for all patients (13-15), such that treatments should be individualised.

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) (16). Studies using the ACBT have shown it to be an effective technique for the mobilisation and clearance of airway secretions (17), and is as effective as other widely used ACTs (13). Previous studies demonstrated that ACBT is not further improved by the adjuncts of positive expiratory pressure (18), oscillating positive expiratory pressure (19, 20) or mechanical percussion (21). An improvement in lung function following the instigation of the ACBT has been shown in an uncontrolled study (22).

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 weblink to the protocol for ACBT can be found in Appendix 1.

The ACBT regimen is flexible and can be 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 CF and 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 (23). 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. In young children (from 2-3 years), blowing games and huffing can be commenced to educate the elements of ACBT, as foundations for incorporation when developmentally and clinically appropriate. 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.

During forced expirations, 69% of 40 adult patients studied had tracheomalacia visible on dynamic CT, causing marked reductions in tracheal cross-sectional luminal area (24). In assessment of cough sound, a barking, brassy, or vibratory cough (25) is a strong indicator of airway malacia, and is associated with slower resolution of infective exacerbations. Implications for practice include careful teaching and modification of forcefulness of huffing and coughing to avoid early closure of unstable airways.

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 (26). It was introduced by Chevaillier (27), 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 (28).

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 weblink to a description of the protocol for AD can be found in Appendix 1.

Greater expiratory flow is generated in smaller airways with AD compared to forced expirations (29). Short-term studies have shown that AD is as effective as postural drainage and percussion (30), oscillating PEP (31) and the ACBT (32). In a long term comparative study in adolescents with CF, AD was as effective as postural drainage and percussion, and participants showed strong preference for AD (33).

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 (34). As such it is likely to be useful in patients who have unstable airways or evidence of airway hyperreactivity (35). 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. More details about the execution of AD can be found via the weblink in Appendix 1.

The technique of AD may be adapted for infants and young children, where it is known as assisted AD. The therapist places his or her hands on the child's chest to manually increase expiratory flow and prolong expiration towards residual volume (36). 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. This approach also requires specific training for the physiotherapist, as the small closing volumes in infants increase the risk of early airway closure and worsening gas exchange (37).

Positive Expiratory Pressure (PEP) Therapy

Positive expiratory pressure (PEP) therapy is defined as breathing against a positive expiratory pressure of 10 – 20 cmH_2O (38). 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, temporarily increasing functional residual capacity (FRC). The pressure gradient across the obstructed region will force secretions centrally toward the larger airways, from where they can be expectorated (39, 40). 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 (41). Improvement in gas mixing and oxyhaemoglobin saturation following PEP support this rationale (42).

In an early study by Falk et al (40), PEP was shown to be superior to postural drainage in terms of sputum clearance. In comparison to conventional chest physiotherapy over a 12 month period, McIlwaine et al (43) found that children who performed PEP had better pulmonary function. Over a similar time period, McIlwaine (44) found a significantly greater rate of decline in lung function in children using oscillating PEP compared to PEP. However Newbold (45) found no significant difference in decline of lung function between adults using the two therapies, and West et al (46) found no significant difference in lung function, exercise tolerance, sputum expectoration or patient satisfaction in children during a two week hospital admission. In a crossover trial comparing a single session of PEP to one of PEP to high frequency chest wall intervention, Fainardi et al found no significant difference in lung function, sputum expectoration or exertion, however significantly more patients preferred PEP (47). A Cochrane review concluded that PEP was no more or less effective than other forms of ACT and that there was some evidence of patient preference for PEP over other techniques (15). Patients with non-CF tracheomalacia may benefit from PEP therapy by increasing cough expiratory flow (25).

Physiotherapy Practice

Positive expiratory pressure therapy can be delivered through a face mask or a mouthpiece. Most studies are based on mask PEP. If a mouthpiece is used, a noseclip may be necessary during the training phase. In both systems, PEP is created by exhaling through a narrow opening, providing resistance to expiration. The resistor should provide a steady PEP of 10-20cmH20 during the middle of expiration. When teaching PEP to a child, it is may be helpful to delay the use of a manometer or pressure indicator until the process of PEP breathing is practiced and a regular rhythm is established; thereafter check for correct pressure plateau. A weblink to a description of the protocol for PEP can be found in Appendix 1.

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

Precautions: 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 (48).

High Pressure PEP

High pressure PEP therapy is a modification of PEP therapy which includes a full forced expiration against a fixed mechanical resistance (49). 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 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 (FVC) manoeuvres with different resistors. The resistor that provides the greatest increase in FVC over baseline values, along with a sustained plateau in expiratory flow and avoiding early airway closure, is chosen for use during treatment (49).

Studies on the use of high pressure PEP have been limited and mainly conducted at one centre where it is regularly used. 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 (35, 50, 51), but quality of the evidence is low to moderate.

Physiotherapy practice

High pressure PEP is effective in patients with collapsible airways, tracheomalacia, bronchomalacia or respiratory muscle weakness. A weblink to a description of the protocol for high pressure PEP can be found in Appendix 1.

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.

Oscillating PEP

Oscillating PEP refers to a variety of devices that combine PEP with oscillation of airflow. The addition of oscillation is thought to loosen secretions and thus facilitate airway clearance (52). When the resonance frequency of the pulmonary system is achieved, the pressure variations are amplified, maximising the vibrations of the airway wall. Three 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 intracranial pressure, haemodynamic instability, recent facial, oral or oesophageal surgery, acute sinusitis or middle ear pathology (48).

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, PEP 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. A laboratory study (53) demonstrated that a positive incline optimises PEP, oscillation and flow amplitude effects. Short term clinical trials indicate that the Flutter® is at least as effective as other ACTs (31, 54-57) and that it significantly reduces sputum viscoelasticity (31). 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 (44). However, a more recent study over 13 months showed no difference in lung function between groups randomly assigned to PEP or Flutter® (45). Turboforte® is marketed as having similar indications to Flutter®.

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 (52). 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 practise 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. A weblink to a description of the protocol for Flutter® can be found in Appendix 1.

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® (58). However, there are limited data regarding its clinical efficacy. In a randomised crossover trial of ACBT versus Acapella® in non-CF bronchiectasis, no differences were found between weight of sputum expectorated, although a greater proportion of patients preferred the Acapella® (59). In children with CF, the Acapella® appears equally effective as PEP mask therapy during treatment of an acute respiratory exacerbation (46).

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 Acapella® was compared to no treatment (3 month crossover, 1 month washout) in 20 adults with non-CF bronchiectasis, with significant improvements in quality of life, exercise capacity and sputum volume (60). Whilst caution must be used in extrapolation to CF, this study provides some support for its use in chronic suppurative lung disease. A weblink to a description of the protocol for the Acapella® can be found in Appendix 1.

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.

Pryor et al (61) compared two oscillating PEP devices (Flutter® & RC Cornet® with PEP, AD, and ACBT in adolescents and adults with CF. This 12 months study was completed by 53 of 75 recruits, with no significant differences between ACTs for any outcome. 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 recumbent positions. A weblink to a description of the protocol for RC Cornet® can be found in Appendix 1.

Postural Drainage

Postural Drainage in gravity-assisted positions

Postural drainage was first introduced for the treatment of CF in the 1950s and remained the cornerstone of therapy until the 1980s. Postural drainage consists of placing the patient in a position that allows gravity to assist in draining mucus from the periphery of the lungs. The recognised postural drainage positions were published in 1950 (62).

Many studies use postural drainage as the comparison for the 'newer' techniques. Reisman et al (63) 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 (64, 65). However, Mortensen et al (66) demonstrated no advantage of postural drainage over PEP. Lannefors et al (67) 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. Rather, different positions result in ventilation changes which can make ACT more effective.

A growing body of research has challenged the efficacy and safety of the traditional head-down postural drainage positions in infants. Gastro-oesophageal reflux (GOR) is common in infants, children and adults with CF (68-70). A number of studies have demonstrated provocation of GOR during head-down tilted postural drainage in infants, children and adolescents with CF (68, 71, 72). Two additional studies did not reproduce these results in infants, with no significant differences in GOR between modified and traditional postural drainage (73, 74); however the head-down position utilised was not as steep, older infants were studied and they avoided the prone head down tilted position (73). Multiple episodes of GOR extending into the upper airway were shown using pH multichannel intraluminal impedance in both head-down and horizontally positioned children, with the potential for aspiration during treatment (74). Studies to determine the individual contributions and safety profiles of various techniques (positions, chest percussion and vibration) are urgently needed.

The longitudinal relationships between PD, GOR and clinical outcomes have been examined in a number of studies. 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 (75). Similarly, children who performed PEP had superior respiratory function at 12 months compared to those who undertook postural drainage and percussion (43). The association between GOR, postural drainage and reduced respiratory function has not yet been studied in adults. Using pH MII recording, Palm et al (76) have shown an association between higher reflux burden and Pseudomonas infection, however the studies were unable to demonstrate a causal relationship, with further prospective studies needed to clarify this issue.

Alternatives to PD are available. A long-term study comparing postural drainage and autogenic drainage (AD) (33) showed significant differences in the secondary outcome of Huang score (p=0.04) in favour of AD and strong patient preference for AD. Other measures including respiratory function tests, exacerbations, and hospitalisations showed no significant between-group differences.

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 (23). Oxygen desaturation during postural drainage with FET has been demonstrated (77), 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 (78).

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 (68, 71, 72). There is no consensus as to whether postural drainage has a role in management of other patients. Clinically silent GOR has been reported in 40% of 11 adults with CF awaiting lung transplantation (79). The majority of Australian and New Zealand 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 necessary. 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.

Modified postural drainage

Modified postural drainage involves positioning for airway clearance without use of head-down tilt. Positioning to facilitate changes in airflow and breath volumes is conceptually aligned with contemporary approaches that rely less on gravity and manual techniques, with greater emphasis on changes in airflow, ventilation, and active participation of the patient. The recommended positions for infants include: supine 30o head up, prone horizontal, left and right horizontal side lying, and upright chest position for apical segment of upper lobes, leaning against therapist/carer shoulder and avoiding slumped sitting which increases intra-abdominal pressure (68). A schematic of these positions can be found via the weblink in Appendix 1.

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 (75). 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 (23).

Physiotherapy practice

In infants and small children when active participation is not possible, modified PD is the optimal treatment choice (75). The infant's head should be well supported, avoiding shaking movements during treatment which has been associated with adverse outcomes in premature infants (80). Treatment should be commenced at least 1- 2 hours after a feed. A maximum of 20 minutes per treatment session is recommended.

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 (6). 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 similar frequency of oscillation to percussion but produces higher expiratory flow rates than PEP or oscillating PEP (81). These effects may increase mucus transport.

The clinical effects of percussion and vibration on airway clearance are unclear. Sutton and colleagues (82) did not find any increase in tracheobronchial clearance when manual percussion and vibration were added to postural drainage (82). However, addition of percussion and vibration to a regimen that included postural drainage and the ACBT 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 (83). Percussion may increase hypoxemia (40) but this may be prevented if combined with thoracic expansion exercises (78). Tannenbaum et al (84) demonstrated a short-term decline in respiratory function immediately after manual techniques were applied to children with CF undergoing anaesthesia. A literature review by Gallon (85) 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 being undertaken. 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 ACT 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 (86).

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

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 often used in clinical practice with CF in Australia or New Zealand. The evidence and indications for these techniques are presented in this section.

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 (87). It has been proposed that HFCWO assists sputum removal by increasing airflow 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 (88).

A recent, large multi-centre randomised controlled trial conducted in Canada compared the effects of PEP and HFCWO over 12 months in adults and children with CF (89). In the HFCWO group the number of pulmonary exacerbations was significantly greater and the time to first exacerbation was significantly shorter. The groups were similar for lung function and quality of life (90-94).

Physiotherapy practice

High quality data does not support the use of HFCWO as a routine airway clearance technique for the majority of individuals with CF.

If used for individuals who are not able to perform other ACTs, HFCWO 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. Newer models have built in settings to ensure pauses for forced expiration and coughing. The cost of HFCWO is prohibitive for many patients and thus it is in use by a small proportion of patients with CF.

Contraindications: Unstable neck injury, intravenous 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), intravenous port under the vest (not currently accessed), recent oesophageal surgery, distended abdomen, bronchospasm, osteoporosis, coagulopathy (95).

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 cmH20. 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 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 (91, 96, 97). It has similar short-term efficacy to the Flutter® (98). 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

Physical Exercise as Airway Clearance

Physical exercise that increases minute ventilation leads to the mobilisation of pulmonary secretions and enhances airway clearance (67, 99-101). It is acknowledged that some people with mild lung disease and good lung function use exercise together with forced expiration (huffing), coughing and expectoration as stand-alone ACT. Others with more extensive lung disease and larger volumes of sputum use exercise as an adjunct to a formal airway clearance therapy regimen.

Recent publications lend physiological support to the contribution of exercise to airway clearance. The contribution of exercise to airway clearance was evaluated in 14 adults with CF (102). Reduced mechanical impedance of sputum was reported with treadmill exercise but not cycle exercise, however both forms of exercise improved ease of expectoration. The authors postulated that this positive effect of treadmill exercise may have been influenced by increased trunk oscillations with walking. A transient increase in FEV_1 and peak expiratory flow rate (PEFR) following exercise has been demonstrated in CF (103-105), 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 ACT (106). 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 (107).

Whether exercise can be used as the sole alternative to other ACTs is less clear. In a crossover trial, 34 children with CF participated in repeated bouts of whole body exercise combined with expiratory manoeuvres (experimental intervention) compared with breathing exercises and manual expiratory compressions (control). Sputum clearance was the same for both conditions. The mean improvement in lung function was significantly greater for the exercise group. Treatment satisfaction also favoured the exercise group, suggesting that bouts of vigorous and age-appropriate exercise combined with forced expiration strategies may be a suitable alternative for airway clearance in some children with CF (108). In hospitalised subjects with CF, treatment using conventional chest physiotherapy resulted in greater weight of expectorated sputum than exercise alone (100). In contrast, Cerny and colleagues (106) 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 (67). 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:

- reduce mechanical impedance of mucus
- 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 ACT, as it mobilises secretions and makes ACT more effective, where as those with advanced bronchiectasis and large volumes of daily sputum need to do ACTs before being able to enjoy exercise. Use of short interval training (eg circuits) can be beneficial for effective changes in airflow combined with pauses for breathing control, forced expirations, and coughing if needed.

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, snowboarding, 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 be interspersed with physical exercise in order to optimise ACT. More detail regarding exercise assessment and prescription can be found in Chapter 4.

Clinical Decision Making regarding Airway Clearance Techniques

There are a number of evidence based ACTs available for use in CF. 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. This has the benefits of allowing the individual with CF to take ownership of their health and fosters engagement

with the team. The individualised program should include ACTs 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, culture, and clinical status.

RECOMMENDATIONS

1. **Airway clearance techniques should be performed across the lifespan in CF (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).**

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

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

5. **Physical exercise may be used to reduce mechanical impedance of sputum (B), achieve short term improvements in respiratory function (A) and improve ease of expectoration (B).**

PRACTICE POINTS

- **Active cycle of breathing technique may be useful in patients where other techniques are contraindicated, eg haemoptysis.**

- **PEP therapy and oscillating PEP should be avoided if there is suspected untreated pneumothorax.**

- **When physical exercise is used as an airway clearance technique it should be accompanied by modulated forced expirations and coughing to optimize cephalad movement of secretions and evacuation from the bronchial tree.**

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 multidisciplinary 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. As a result, physiotherapists should be adequately skilled in the area of inhalation therapy in order to maximise the effectiveness of both treatments.

Inhalation Therapy Technique (including Adjuncts to Inhalation Therapy)

The main determinants of deposition pattern for nebulized medications are breathing pattern during inhalation, droplet size and age/condition of the lung (109). It is widely accepted that a quicker breath results in greater central deposition (109). A slower breath results in a more peripheral deposition pattern, improved homogeneity of the deposition pattern and increased overall drug deposition (110). Slow steady breaths with occasional deep breaths have therefore been traditionally recommended to promote improved deposition (111). The specific device being utilised however may affect the optimal breathing pattern (112). Adaptive aerosol delivery (AAD) devices have the ability to alter their output in response to the patient's breathing pattern. By tailoring the inhalation time to the individual patient's ability, there is better lung deposition, reduced expiratory loss, reduced treatment times and better adherence (113, 114). Physiotherapists need to be aware of the differences between nebuliser types (eg jet vs mesh) and their impact on inhalation technique, dose received and deposition pattern.

A study reported in abstract form suggests that the uniformity of drug deposition is not substantially altered by side lying in healthy participants or people with CF (115). This study confirmed that the upper lobes are relatively under dosed, receiving approximately 40% of the density of deposition in the non-apical regions. Alternate side lying during inhalation therapy can improve apical deposition in healthy lungs (13%) and to a lesser extent in mild CF lung disease (4%).

Combining ACTs 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. A study presented in abstract form has reported that inhaling hypertonic saline during AD compared to prior, shortened the treatment session without compromising the quantity of sputum clearance (116).

Combining 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 (117). 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. A small study by O'Connell and colleagues (118) with four participants previously intolerant of hypertonic saline demonstrated improved tolerance in terms of chest tightness, cough and sore throat with the addition of PEP in combination with hypertonic saline inhalation.

Frischknecht-Christensen et al (119) explored the introduction of a PEP device (facemask PEP) with the use of inhaled β2 agonists via a metered dose inhaler (MDI). The study showed improved bronchodilation, dyspnoea, cough and mucus production when compared to administration of the β2 agonist alone. Stites et al (120) reported that the use of HFCWO 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 chronic obstructive pulmonary disease (COPD), addition of the RC-Cornet® oscillating PEP device during nebulisation of ipratropium bromide resulted in improved bronchodilation (121). These conflicting results highlight the need for further research into the combination of ACTs and inhalation therapy.

Physiotherapy Practice

There is no negative impact on lung deposition if people with CF nebulise in side lying, using two minute intervals on each side. In clinical practice it is likely that patients will choose to nebulise a full dose on one side and lie on the other side for the next dose, or alternate the starting side and change when half the nebulisation time has been completed. In the second scenario care must be taken to alternate the starting side, in light of the known bias towards greater initial nebuliser output. Given that many patients prefer to nebulise in side lying due to comfort and convenience, permitting nebulisation in side lying may improve treatment adherence.

The combination of PEP with inhalation therapy (hypertonic or isotonic saline and occasionally salbutamol) is commonly prescribed by physiotherapists around Australia and New Zealand. Some physiotherapists also combine inhalation therapy with positioning, and breathing techniques such as the ACBT or AD. 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 a large number of nebulized medications are prescribed. The incorporation of physiotherapy adjuncts to inhalation therapy also has the potential to improve therapy compliance. This may include positioning other than upright and the inclusion of ACTs during inhalation therapy. It is recommended that the incorporation of adjuncts within inhalation therapy be reviewed regularly and written instructions be provided.

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 (109). 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) (109).

Lannefors (122) recommended that when a medication may be administered via either a dry powder inhaler, MDI 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 MDI 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 MDI and spacer should be chosen. For antibiotics, Tobramycin Inhalation Powder (TIP) achieves a faster delivery time, greater portability and convenience, with low systemic absorption and equivalent efficacy to Tobramycin Inhaled Solution (TIS); however it may be associated with a greater incidence of cough (123).

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 (109). A mouthpiece may not be appropriate if the sinuses are a target of therapy (124).

Ultrasonic nebulisers should not be used for dornase alfa as they can alter its physico-chemical properties, rendering it ineffective (125). A list of recommended nebulisers is provided in the dornase alfa consumer medicine information sheet. Disposable jet nebulizers may not be as effective, with respect to inhalable mass and output rate, as reusable jet nebulizers for the administration of tobramycin (126). Vibrating mesh nebulizers may reduce treatment time compared to jet nebulizers (112, 127).

It is often recommended that patients use an expiratory filter when nebulising antibiotics (111). 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 (128).

Physiotherapy Practice

Where possible, nebulized medication should be taken via a mouthpiece to maximise delivery of the drug to the airways and avoid nasal filtration (129). The exceptions to this are: 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 MDI and spacer (109) 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 (129).

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 (109) 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 (130). A European Consensus Statement has published very limited data regarding physico-chemical stability of combinations of inhalation solution (112).

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.

Timing and Order of Inhaled Medications

A Cochrane systematic review investigated whether changing when dornase alfa is inhaled in relation to ACT or time of day impacts the overall effect of the airway clearance session in people with CF (131). The searches identified 4 eligible trials that examined inhalation of dornase alfa before versus after ACT . Meta-analysis of all the available data showed that inhalation after instead of before airway clearance did not change FEV_1 (mean difference -0.03 litres, 95% CI -0.08 to 0.03 litres). Similarly, FVC and quality of life were unaffected. However, FEF25 was significantly better with dornase alfa inhalation before ACT, based on the pooled data from two small studies in children with well preserved lung function (132, 133).

It has 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 (134). There appear to be no detrimental effects on sleep quality or nocturnal cough associated with administering dornase alfa before bedtime (135). Given the long-term beneficial effects of dornase alfa on lung inflammation in CF (136), 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 (111) 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 ACTs should precede the delivery of other inhaled medications (137). 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 (128). 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 (138).

The timing of hypertonic saline inhalation in relation to ACT (before, during or after) does not appear to have a substantial effect on lung function after a single treatment session (139). However, participants were more satisfied with the entire treatment session when hypertonic saline was inhaled before or during ACT and perceived these timing regimens as more effective. Participants who repeated the study tended to retain their preferred timing regimen. .

Physiotherapy Practice

Bronchodilators should be administered prior to ACTs 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.

Children with well preserved lung function who use dornase alfa could be advised to inhale it 30 minutes before ACT because this may be more beneficial for small airway function, although other outcomes may not be affected. Apart from this, the timing of dornase alfa inhalation can be largely based on pragmatic reasons or individual preference with respect to the time of ACTs and time of day. 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.

For people with CF who use hypertonic saline, clinicians should encourage inhalation before or during ACT. It is likely that a patient's preferred timing regimen remains constant over time and does not require repeated review once the daily routine is established.

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.

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 (140).

There is no one method which has been recommended for cleaning home nebulisers. Rosenfeld et al (141) 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. A small study reported that cleaning frequency was linked to home nebuliser contamination (i.e. cleaning after each use was associated with a lower rate of nebuliser contamination) but that there was no significant difference in contamination with respect to cleaning or drying technique (142). Reychler et al (143) found that cleaning via a dishwasher (temperature of 70°C) or immersion for 20 minutes in a litre of Hexanios 0.5% hypochlorite solution or hot water (40°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. 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.

Clinical Monitoring of Inhalation Therapy

Most inhaled medications have known side-effects. For instance, hypertonic saline, mannitol, colistin and tobramycin may all cause bronchospasm (144). The British Thoracic Society Nebuliser Project Group (111) 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. There is a detailed trial regimen that needs to be adhered to for patients commencing inhaled mannitol due to the potential for bronchospasm (145).

The European Respiratory Society recommends that patients should be re-assessed one month after commencing their treatment and then be re-assessed annually thereafter (109). 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 (146).

Physiotherapy Practice

All new medications should be trialled in the presence of a suitably qualified health professional. 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.

RECOMMENDATIONS

6. **Where possible, nebulized medication should be taken via a mouthpiece (C). The exceptions to this are: young children who may be unable to coordinate the use of a mouthpiece effectively, or when therapy is targeted at the sinuses, or those acutely unwell with shortness of breath.**
7. **To optimise dose delivery and treatment time, inhalation technique should be adapted to the specific device being used, including consideration of body position and concurrent ACTs (C)**
8. **Bronchodilators should be delivered by MDI unless there is clinical need for nebulisation (C).**
9. **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).**
10. **Hypertonic saline may be administered before or during ACTs (B).**

PRACTICE POINTS

- **Positive expiratory pressure devices can be used whilst nebulising hypertonic saline, isotonic saline or bronchodilators. Positive expiratory pressure devices are not suitable for nebulising antibiotics or dornase alfa.**
- **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.**
- **Nebuliser and compressor combinations with demonstrated efficacy for specific medications should be used where possible.**
- **Inhaled medications are not routinely mixed.**
- **Efforts should be made to maximise the time interval between administration of dornase alfa and ACT; this may involve administration before bedtime if acceptable to the patient, although timing should be individualised to optimise adherence.**

4 EXERCISE

Exercise is a cornerstone of therapy for people with CF. Measures of exercise capacity predict survival in children and adults with CF (147, 148) and those with better physical fitness have better quality of life (149). There is some evidence that structured exercise programs for people with CF improve fitness, thoracic mobility, maintain bone mineral density and preserve or slow the rate of pulmonary decline (150-156). For this reason it is recommended that all patients should be encouraged to exercise on most days of the week (12). More recently it has become apparent that structured exercise programs may not be the only approach to achieving these benefits. A study in over 200 people with CF conducted over nine years showed that patients with higher levels of physical activity in daily life (encompassing all activities, not just exercise programs) had a slower rate of decline in FEV_1 than those who were less active (157).

The physiotherapist has an important role in the assessment of exercise capacity, exercise prescription and facilitation of physical activity. Research has shown exercise testing and training, both in inpatient and outpatient settings, to be safe (158).

Assessment of exercise capacity

Assessment of exercise capacity is an important practice for the evaluation of functional capacity, response to treatment and disease progression (147, 159-161). 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. It has been suggested that an exercise test should be performed at least annually to document changes in exercise capacity (162). However studies indicate that exercise testing is currently underutilised by physiotherapists (163, 164).

Tests of exercise capacity include formal laboratory assessments of maximum exercise capacity (cardiopulmonary exercise tests) and field tests. Maximal exercise testing is a specialist role which is usually performed by respiratory scientists and is currently outside the scope of routine physiotherapy practice. Field tests are useful alternatives which provide relevant clinical information regarding exercise capacity (163, 165). 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.

Six minute walk test

The six-minute walk test (6MWT) is an easy to administer, well-tolerated, self-paced exercise tolerance test, reflective of functional exercise capacity (166). Patients are required to walk as far as they can in six minutes. In patients with severe disease the 6MWT is suitable for assessment of response to a new intervention and as a one-off assessment of exercise capacity or predictor of prognosis (166).

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 (167). The 6MWT is also a useful tool for assessing exercise-induced oxygen desaturation (168) and has a strong correlation with peak oxygen uptake in end-stage lung disease (169) and in severely ill children (170).

The 6MWT has limited utility in assessing exercise tolerance in people with mild CF lung disease. Distance walked is poorly correlated with maximal exercise capacity for those with mild lung disease (171) and adults with mild to moderate CF lung disease cover similar distance to healthy volunteers (168, 172). This suggests in those with mild lung disease there may be a ceiling effect for the 6MWT. Another limitation of the 6MWT is that it is self-paced and thus dependent on the patient's motivation.

Physiotherapy Practice

The protocol for the 6MWT has been published (166).

The 6MWT can be performed in both paediatric and adult CF populations. The main outcome of the 6MWT is the distance walked, however it is not yet known what minimum change in distance is required to represent a real clinical change in patients with CF. It is recommended that the same track is used when re-assessing a 6MWT in the same individual, as distance can be affected by the track layout. Two 6MWTs are needed on each measurement occasion in order to reliably measure exercise capacity in adolescents and adults with CF and overcome the known learning effect (173). Normative values for 6MWT distance are available for children, adolescents and adults (168, 174, 175); however as normative values may differ according to population and region, local reference values are preferable.

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

Precautions 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.

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 (176-178). 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. It is a quick, portable and simple exercise test. The 3MST is highly reproducible, provokes a greater increase in heart rate and breathlessness than the 6MWT and equivalent levels of oxygen desaturation (176).

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 (177, 179). It is also responsive to change over the course of antibiotic treatment in children with CF (178) 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 a maximal test and it may be more sensitive to change in heart rate and oxygen saturation in patients with CF and moderate-severe lung disease than in those with mild disease (177, 179).

The 3MST may also be helpful to use as a screening test for patients at risk of poorer outcomes. In a study reviewing 101 adult CF patients, those who experienced oxygen desaturation on testing showed a greater decline in FEV_1 and had more hospitalised days over 12 months than their peers who did not experience desaturation on 3MST (179). In addition, the 3MST can be effectively assessed using remote telemonitoring (180), which may create opportunities for exercise assessment of geographically isolated patients or during periods of home-based intravenous antibiotic therapy

To date, most studies pertaining to the 3MST have been conducted in children, with only one study examining the predictive value of this test in adults with CF. Further study is required to determine the sensitivity of the 3MST to clinical change in both the paediatric and adult setting.

Physiotherapy Practice

The protocol for the 3MST can be found in Appendix 2.

The 3MST can be performed in both paediatric and adult CF populations. The main outcomes of the 3MST are maximum heart rate, minimum oxygen saturation and breathlessness scores. If the entire test is unable to be completed, the time or number of steps completed should also be recorded. Due to its simplicity, short time and minimal space requirements, the 3MST is suitable to perform across inpatient, outpatient and home-based settings. There are no normative values for the 3MST (177, 178).

Contraindications: As for the 6-minute walk test

Precautions: The 3MST should be avoided in individuals with significant lower limb joint arthropathy (176).

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 pre-recorded auditory cues. The required speed becomes progressively 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 be within 0.5 metres of the marker cone, at the time of the 'beep' on two consecutive shuttles. The original 15-level MST (181) has been extended to a 25-level MST (182), as 15% of CF adults and 46% of healthy volunteers completed the 15-level MST (183), however to date information on the MST-25 is only available in abstract form.

The MST is sensitive to change when assessing the effects of intravenous antibiotic treatment (184), and was shown to be more sensitive to change than FEV_1 following a hospital admission in adults with CF (159). It is a valid measure of exercise tolerance in children (165, 185) and adults (181). The MST has been shown to have high reproducibility and responsiveness in measuring exercise capacity in the adult CF population (159).

The MST has the advantage of being an incremental test and therefore provides sufficient challenge for those with milder disease. In clinical practice this test could be used in an annual review setting, during an inpatient admission and when determining oxygen requirements/desaturation patterns prior to prescribing an exercise programme (181).

Physiotherapy Practice

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

The MST is appropriate to use in both paediatric and adult CF populations. The main outcomes of the MST are distance covered, peak heart rate, minimum oxygen saturation and breathlessness. If there is a change of greater than 40 metres in the MST then it is likely that real clinical change has occurred (159). As the MST is an incremental exercise test that elicits peak or near-peak exercise responses, it may not be suitable for unwell patients. There are no normative values for the MST, however, estimates of peak oxygen consumption can be made for adults with CF from distance covered in the 15-level MST (159, 181, 184).

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. 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 there are limited data regarding its role in the assessment of exercise capacity in adults with CF.

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. Likewise, the 3MST may only be 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 MST 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 recording 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. The 6MWT may require two tests to be performed 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 in paediatric patients. The MST provides more feedback to the patient regarding increase in distance covered from admission to discharge and is 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, time, staffing and space availability in the clinic area (172).

Exercise prescription in CF

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 (150). Aerobic training results in improved maximum exercise capacity, strength and quality of life (186, 187). Anaerobic training has positive effects on lactate levels, peak power (188) and fat-free mass (187). Both types of exercise may have positive effects on respiratory function (2, 187). Exercise programs have beneficial effects both during admission for acute exacerbations (106, 187, 189) and in the stable outpatient (2, 188, 190). It is unclear whether home-based, unsupervised training programs are 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. For young children, their family and siblings should also be encouraged to 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 (190-192). This reduction is associated with a more rapid decline in respiratory function in girls compared to boys (191). 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 (193) and patients with other chronic respiratory diseases (194): In order to improve aerobic capacity, exercise training must:

- occur on at least 3 days (preferably 5 or more days) per week
- have a duration of 30 minutes per session, consisting of shorter intervals if required
- increase heart rate to approximately 75% of maximum heart rate.

Peripheral muscle force is reduced in people with CF (195). A low-weight, high repetition training strategy can effectively increase FEV_1, strength and body mass in hospitalised children with CF (187). 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 (150).

People with CF may exhibit exercise-induced oxygen desaturation during training, even when pulmonary function is relatively well preserved (181). Supplemental oxygen during training increases exercise duration (196) 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 (197).

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

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, patient motivation, resources at the patient's disposal upon discharge, realistic goals, appropriate dosage (frequency, duration, intensity), and guidelines for monitoring safe exercise levels. In children with CF significant differences in oxygen uptake (VO2) and heart rate (HR) at rate of perceived exertion (RPE) levels 4 and 7 using the OMNI scale have been demonstrated (198). This indicates children can discriminate between exercise training intensities and that regulation of exercise training can be successfully achieved using the OMNI scale.

With the emergence of new technologies, alternative training stimuli may be considered in addition to 'traditional' training approaches. Undertaking exercise using a gaming console has been found to be comparable to both treadmill and cycle exercise in regards to peak heart rate, achieved workload, oxygen saturation and levels of perceived exhaustion and fatigue (189) and can provide high intensity work in adults with CF (199). Gaming console exercise was rated favourably in terms of patient enjoyment, which may in turn aid patient compliance and motivation with long term exercise (189).

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.

Contraindications: Exercise training should not be performed in patients who are febrile, or whose cardiovascular status is unstable.

Precautions to exercise training 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 taken 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.

Facilitating physical activity in people with CF

To date there are only a few studies that have examined strategies to increase physical activity in daily life in people with CF (200). Most studies have used a structured exercise program and measured its impact on physical activity, with variable results. The limited data available suggest that exercise training programs of longer duration (more than six months) and those that require self-directed behaviours may have a greater impact on physical activity in daily life (200). Whether other types of interventions, such as behavioural and motivational strategies, may have a greater impact on physical activity has not yet been explored.

The Australian guidelines for physical activity provide the following recommendations (201):

- Children and young people (ages 5 – 17 years) should engage in 60 minutes of moderate to vigorous physical activity each day. On 1 – 3 days per week they should also engage in activities that strengthen muscle and bone.

- Adults (aged 18 to 64 years) should accumulate 150 – 300 minutes of moderate intensity physical activity, or 75 – 100 minutes of vigorous intensity physical activity, or an equivalent combination of the two, each week. Adults should do muscle strengthening activities on at least two days per week.

Specific physical activity recommendations for people with CF have not yet been published.

RECOMMENDATIONS

11. **Exercise is recommended for patients with CF throughout the lifespan (B).**
12. **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).**
13. **A 6MWT should be performed as part of the initial assessment for lung transplantation (C).**
14. **Exercise prescription should be tailored to the individual and comply with recommended exercise guidelines (B).**
15. **Supplemental oxygen should be considered during training in patients with severe exercise-induced desaturation (C).**

PRACTICE POINT

- **An annual assessment of exercise capacity is useful to document changes in exercise capacity and exercise responses (eg desaturation) over time.**

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 and suitability for transplant.

Pain

Reported rates of spinal pain (thoracic, lumbar, cervical) in CF populations are high. The prevalence ranges from 43% to 94% (202-213), irrespective of clinical status, and is both substantially higher than age-matched healthy control subjects and presents at a younger age (203-205, 210, 214). Pain is generally reported to be of moderate intensity (207-209, 211-213). The prevalence of pain does not appear to be influenced by disease severity or gender (209). The incidence of chest pain varies from 16% to 64% (203, 208-210, 212, 215) with 30% to 77% reporting pain in more than one location (209, 212). Although documentation of back pain is increased in those with increasingly severe lung disease, it is not proportional to the degree of pulmonary hyperinflation (216). The high frequency of musculoskeletal pain is associated with decreased quality of life, respiratory symptoms, sleep disturbance, anxiety and depression together with a reduced ability to perform chest physiotherapy and exercise effectively (207, 209-213) (203, 217-219). Whilst some patients report

seeking pharmacological and non-pharmacological management to alleviate their symptoms, approximately 25% of patients with CF fail to seek treatment of pain (203, 208, 210, 213).

Low Bone Mineral Density

Patients with CF have multiple risk factors for inadequate bone mineralisation - poor nutrition, pancreatic insufficiency and malabsorption, deficiencies in calcium and vitamins D and K, abnormal fatty acid status, liver dysfunction, reduced weight bearing activity, delayed puberty, hypogonadism, CF-related diabetes, reduced lung function, chronic infection, increased intravenous antibiotic use, glucocorticoid therapy and immunosuppression, CFTR dysfunction in bone cells (220-222) and abnormal bone remodelling favouring bone resorption (223-227). A significant proportion of musculoskeletal problems in CF arise secondary to low bone mineral density (BMD). Studies in children reveal conflicting results about BMD abnormalities. While several studies suggest normal BMD in healthy well-nourished children with CF, other studies have shown low BMD in young children with mild lung disease and normal nutritional status with osteoporosis reported in 20-34% of children and osteopenia in 28-47% (227). These differing results may support the role for a dysfunction in bone metabolism from an early age (228, 229) or may reflect difficulties in the interpretation of DXA scans in growing children (222). Longitudinal studies show bone gains during puberty are decreased in CF adolescents compared to healthy controls resulting in decreased attainment of peak bone mass (222, 224, 225, 230-234). Loss of bone mineralisation begins in late adolescence and is accelerated throughout adulthood (222, 224, 235-237) . A meta-analysis found the prevalence of osteoporosis in adults in CF to be 24% and osteopenia 38% (238) but ranges from 9-70% across studies (224).

Adolescents and adults who had higher physical activity levels and better aerobic capacity had higher BMD at the hip and lumbar spine than their less active and less fit counterparts (226, 233, 234, 236, 239, 240). Duration and intensity of physical activity is positively correlated with BMD in adolescents and adults with CF (240). Individuals with more severe lung disease, decreased physical activity and low aerobic capacity had the lowest BMD, higher prevalence of vertebral fractures and more severe kyphosis (240).

Vertebral compression and rib fractures

Low BMD, osteoporosis and chronic steroid use increase the risk of fracture in people with CF. Increased rates of long bone, rib and vertebral fractures have been reported (234). 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 (241). While the majority of the literature suggests fracture risk is normal in children with CF (242), fracture risk is increased by late adolescence (224, 226). A meta-analysis found the prevalence of vertebral fractures in the adult CF population was 14% and non-vertebral fractures 20% (238), however rates have been reported to be higher (38%) in more recent studies (240). Patient reported fracture rates occur in up to 50% of adults with CF (241, 243, 244). The prevalence of vertebral fractures was higher in adolescents and adults with severe lung disease compared to mild lung disease (226, 240). Studies have not found any association between fracture rates and BMD (233, 240, 245, 246) In addition, a significant proportion of spinal compression and rib fractures may be underestimated, with radiological investigations revealing 76 asymptomatic fractures in 70 patients with severe lung disease (241).

Chest wall fractures and kyphosis may impair airway clearance, reduce pulmonary function, reduce mobility, accelerate decline in heath status, contribute to pulmonary exacerbation, decrease quality of life and may affect eligibility for transplantation (225, 233, 240, 247).

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 (241, 248-250) and in 7% of children under 10 years (251). 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 (226, 240), age and loss of BMD have been related to the presence of thoracic kyphosis in patients with CF (241, 250, 252). The development of thoracic kyphosis may also contribute to rib and vertebral fractures and reduced lung function (226)

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 (253), other studies have concluded that the diagnosis of a thoracic kyphosis is an indicator of deteriorating lung function and a marker of poor prognosis (248, 251). 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 (216).

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 (254, 255). 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 (256, 257). Intrinsic abnormality of CF skeletal muscles including decreased efficiency of oxidative ATP with abnormal mitochondrial density and metabolism, have been reported (256). Peripheral muscle impairment is also noted in response to systemic inflammation and lack of moderate to vigorous physical activity (258, 259). Impaired respiratory muscle strength may occur in association with reduced respiratory muscle mass from nutritional impairment (254). Chronic use of corticosteroids is associated with skeletal muscle weakness (260).

Conversely, preserved respiratory muscle strength despite chronic hyperinflation may represent relative training of respiratory muscles in response to chronic loading (261). This hypothesis was supported by the work of Pinet and colleagues (262) 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 (263) 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 (264).

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 (265). However, investigative research is rare. Rose and co-workers (216) report that the habitual flexed posture caused by altered breathing mechanics are reinforced by chronic coughing and result in further tightening of muscles and restriction of movement of the shoulder, trunk and chest. They 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. A more recent study in children (7-14 years) found that those with CF had significantly shorter pectoralis major, pectoralis minor and gastrocnemius-soleus muscles than age-matched controls (266).

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 (202, 205, 248).

CF arthritis (also known as CF arthropathy) occurs in 2-9% of patients (204). It is a rare syndrome of unknown pathogenesis. (267). 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 (268).

Ciprofloxacin-associated arthropathy occurs infrequently in children with CF (269). It is likely that ciprofloxacin can induce arthropathy in adult as well as paediatric patients (270).

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 (271).

Gout appears to occur with greater frequency in the CF population, 2.5% compared to 0.6% in a healthy population under 54 years of age. Gout should be considered in individuals with recurrent or single joint arthritis. In cases of confirmed gout or extreme hyperuricaemia pancreatic enzyme intake should be reviewed (272).

Physiotherapy intervention for musculoskeletal problems

Recently, two prospective studies have evaluated the efficacy of a combined approach including spinal joint mobilisation, massage, specific muscle strengthening and postural advice, with results suggesting short-term reduction in musculoskeletal pain and improvement in respiratory symptoms (273, 274). The findings of these pilot studies require confirmation in larger trials, however they lend preliminary support to use of a package of therapeutic approaches to optimize BMD, muscle strength, length and postural education as well as manual therapy to improve spinal mobilisation.

Optimise physical activity to maintain bone mineral density and muscle mass

Nixon and colleagues (275) 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). Weight bearing exercise is the most effective non-pharmacological method to improve BMD in the healthy population by stimulating bone accretion during growth and after bone loss, preventing bone loss and improving bone structural qualities (234). Physical activity has also been shown to increase bone formation markers in premenopausal women (276).

Weight bearing exercise during childhood and adolescence appears to be particularly osteogenic and a variety of weight bearing exercise programs have increased bone mineral accrual in healthy children at different pubertal stages (225, 233, 234, 237, 277-279). As the foundation of bone health begins in childhood, and there is some evidence of a sustained benefit from early vigorous physical activity (279, 280), children and adolescents should engage in regular high impact and intensity weight bearing exercise for 30 minutes three times a week. The pre-pubertal and early pubertal years are particularly important to help maximise peak bone mass (222, 281, 282) as approximately one quarter of peak bone mass is gained in the two years around the pubertal growth spurt (281, 283). Children who are more physically active have higher bone mass than more sedentary children and the emphasis is on high impact vigorous activities as light to moderate physical activity does not have the same osteogenic effect (284).

High impact weight-bearing exercise continues to have benefits into adulthood in the healthy population. A meta-analysis has shown that in women 18-50 years, brief high impact jumping exercises improved BMD at the hip (285).Weigh- bearing exercise is also beneficial in maintaining or increasing BMD in postmenopausal populations (234, 281, 282, 286, 287) and therefore is likely to be beneficial in maintain BMD in adults with CF. Adults should perform regular individualised weight-bearing, high impact and resistance exercises, the combination of which appears to have additional benefits(222, 278, 282, 288, 289). When admitted in hospital individuals with CF should be encouraged to continue their usual exercise program where possible (222).

Weight-bearing exercises should include force generating activities that provide loading of the skeleton above that of normal ADLs and should be of sufficient magnitude to generate ground reaction forces greater

than two times body weight, impose an unusual strain distribution and have a high strain rate (e.g hopping, jumping, skipping, trampolining, circuit training, resistance training, aerobics, gymnastics) (281-283, 287, 289). Shorter, more frequent exercise sessions are more beneficial as rest periods enhance bone adaptation and restore mechanosensitivity (234, 285). The most successful interventions included 2-3 session of 30 minutes a week (234) with exercises aimed at regions with low BMD (289) and progression of intensity and impact (282, 289).

Optimise muscle strength

Habitual 'slouched' postures are common in CF patients and may predate structural change. Physiotherapy programs should consider inclusion of 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 (290). The majority of reported home programs that apply a normal therapeutic training stimulus have yielded physiologic and psychological dividends (2, 190, 291, 292). Improved adherence in CF patients is associated with supervision, individualised and flexible programs (290, 293), and knowledge of the condition and treatment rationale (294).

In CF, strength training programs of moderate to high intensity have produced significant leg strength gains in programs of short and long duration (19 days – 12 months) (295-297). A combined circuit weight and aerobic training program generated significant muscle strength gains in upper and lower limbs, with gains that were maintained following a four week detraining period (298). Strength training for children is still a novel area with protocols not clearly defined. This is an area for future research (297).

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 (299). 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 (300) and thus the effectiveness of stretching is affected by the muscle length when the stretch is applied. Additionally, education regarding postural correction could 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

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. Recent studies in other populations have concluded that strong evidence exists to support the use of manual therapy and exercise in the treatment of chronic musculoskeletal spinal pain (301) (302). Home exercise programs were similar if not more effective in the management of chronic lower back pain particularly when goal-directed and combined with education (302). Early reports regarding the use of manual therapy in the management of pain and restriction in this population is encouraging, with preliminary reports supporting the role of a combined approach of manual therapy and exercise prescription in patients with CF (273, 274). The primary clinical approach to CF-related arthropathy involves rheumatological management, which may include physiotherapy interventions targeting pain reduction and muscle strengthening.

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 4. Key components are:

- Subjective history, pain scales (eg Short-form McGill questionnaire)
- Functional scales with standardised items (303, 304) or patient-specific functional scale (305)
- Objective assessment, including posture
- Precautions and need for referral/medical investigation
- Likely structural source
- Evidence based interventions
- Reassessment
- Home program
- Analgesia and commencement of additional mucolytic and IV treatments should be considered if fractures (vertebral/rib) interfere with ACT (222)

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 joints if warranted
- Manual therapy and therapeutic massage (306)
- 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 (265, 307, 308). The European consensus on standards of care for patients with CF (162) 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 (309) 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 and 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 quality of life for people with CF.

RECOMMENDATIONS

16. **A musculoskeletal assessment should be included at annual review from approximately age eight (pre puberty). Earlier assessment is warranted if pain or functional impairment is reported or BMD risk highlighted (C).**
17. **Regular physical activity, including weight-bearing exercise, should be encouraged throughout the lifespan in order to optimise BMD (C).**
18. **Strength training programs should be prescribed in order to optimise muscle mass (B)**

PRACTICE POINTS

- **Prompt assessment and treatment of acute musculoskeletal pain should be provided to people with CF.**
- **Consider provision of a musculoskeletal home program for individuals with CF, based on individualised assessment.**

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 (ABPA) and CF-related diabetes.

Haemoptysis

Haemoptysis is defined as the expectoration of blood from the lungs or bronchial tubes as a result of pulmonary or bronchial haemorrhage (310). Whilst the presence of occasional mild haemoptysis is common in CF and not life-threatening, massive haemoptysis can lead to asphyxiation, airway destruction, shock and exsanguination (311).

Mild haemoptysis affects approximately 62% of all patients with CF (312). The overall incidence of massive haemoptysis in CF has been reported as around 1% in children (313), and between 4% and 10% in adults (312, 314). Increasing age is the greatest risk factor for the development of massive haemoptysis. Other risk factors include moderate to severe lung function impairment, concurrent infection with Staphylococcus aureus, vitamin K deficiency and diabetes (315).

Medical management of mild haemoptysis consists of observation combined with antibiotic therapy to treat underlying infection (316) and the use of tranexamic acid (317). For massive haemoptysis, the vessel may need to be occluded using bronchial artery embolisation (316, 318, 319). Surgical ligation or excision of the affected segment/ lobe is recommended if embolisation is not successful (318).

Physiotherapy practice

The CF Foundation Pulmonary Therapies Committee (USA) have developed guidelines for the management of haemoptysis based on expert opinion using a Delphi process (320).

Scant (<5mL) haemoptysis, first episode:

- Seek medical review (320)
- Continue with ACTs and inhaled therapies (320)
- Modify ACTs:
    - Reduce the force of coughing
    - Cease highPEP
    - Minimise head down tilt positions
- If active bleeding, position into high sidelying with bleeding side down (321)
- Provide reassurance and education
- Do not withhold non-invasive ventilation

Scant haemoptysis, recurrent episode:

- Normal ACTs and inhaled therapies
- Normal exercise routine

Mild to Moderate Haemoptysis (<250mls/ 24 hrs)

- Seek medical review (320)
- Cease percussion, vibrations, oscillatory PEP techniques and head down tilt positions
- Consider ACBT, AD (320) and gentle huffing and coughing
- Continue inhaled therapies in most situations (320)
- Ensure adequate humidification to ease sputum expectoration
- Cease vigorous exercise, encourage low intensity exercise

Massive Haemoptysis (>250mls/ 24 hrs)

- Seek medical review (320)
- If active bleeding, position into high sidelying with bleeding side down (321)
- Cease ACTs, hypertonic saline (320) and exercise until active bleeding resolved,
- Cease other inhaled therapies if considered to provoke bleeding
- Cease non-invasive ventilation
- Once active bleeding contained, 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 ACT regimen

PRACTICE POINT

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

Pneumothorax

A pneumothorax is defined as the presence of air within the pleural space. A pneumothorax may occur in an individual with CF as a result of rupture of sub-pleural blebs on the visceral pleura (322, 323) or, less commonly, as a result of misplacement of a central line (322). 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 (324). This may affect

the ability to perform ACTs and lead to secondary complications related to sputum retention.

The overall incidence of pneumothorax in patients with cystic fibrosis is 3.4% to 6.4% (323, 325, 326). There is an equal risk for men and women (325) and 72% are adults (327). Pneumothoraces occur more frequently in patients with more advanced disease (327), with 75% of affected patients having an FEV_1 less than 40% predicted (327). Recurrence rates of 41% ipsilaterally (328) and 46% contralaterally (323) are reported.

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 (324). A recurrent pneumothorax requires more aggressive management, including either a partial pleurectomy or a talc pleurodesis (324).

There is concern that pleurodesis can make transplantation more difficult as it impedes lung removal, however the current consensus is that pleurodesis is not an absolute contraindication to transplantation (329).

Physiotherapy Practice

There are no published data regarding physiotherapy management of patients with pneumothorax. The following recommendations are based on expert opinion (320) and clinician consensus.

Small Pneumothorax

- Monitor shortness of breath
- Cease PEP and other forms of PEP therapy and liaise with medical team
- Review use of hypertonic saline for nebulisation, especially if it causes coughing
- 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:

- If patient uses PEP or non-invasive ventilation, consider cessation or reduction in pressures while draining and for 48 hours afterwards, to avoid pleural fistula and risk of recurrence
- Review use of hypertonic saline for nebulisation, especially if it causes coughing
- Ensure adequate analgesia and humidification
- Maintain shoulder range of motion
- Chest support during airway clearance
- Gentle huffing and coughing
- Avoid upper limb resistance exercises
- Submaximal exercise (walking, gentle cycling)

Pleurodesis:

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

PRACTICE POINT

- **When a pneumothorax is present, physiotherapists aim to ensure that adequate airway clearance continues, whilst minimising the amount of positive pressure generated inside the patient's lungs. Gentle exercise can continue.**

Allergic Bronchopulmonary Aspergillosis

Allergic bronchopulmonary 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 elicit an immune response, and can lead to accumulation of focal pulmonary infiltrates, tissue damage and eventual destruction of lung tissue (330, 331). It occurs in approximately 7-9% of individuals with CF (332), although it is more common in adults, those with lower FEV_1 and low body weight (330).

Detailed lung function testing in patients with ABPA shows abnormalities suggestive of airway narrowing, gas trapping and small airways disease (333). 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 (330).

Diagnosis is made via clinical features. There is usually also a rise in total immunoglobulin E (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.

PRACTICE POINT

- **Physiotherapists should reassess the efficacy of usual ACTs in people with ABPA. Treatment should be modified based on response and symptoms.**

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. CFRD 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.

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 (334). Exercise also improves vascular endothelial function (335). In type 2 diabetes, exercise also improves glycaemic control and reduces insulin resistance (336). Strength training has been demonstrated to be more effective than endurance training in this group (337). The American Diabetes Association Clinical Care Guidelines for CFRD (338) recommend that people with CFRD should be advised to perform moderate aerobic exercise for at least 150 minutes per week (level of evidence – expert consensus or clinical experience). They also suggest that people with CFRD be counselled to monitor blood glucose levels (BGLs) before vigorous physical activity and 'potentially consume extra carbohydrate or alter their insulin dose, depending on the glucose level and the intensity and duration of the planned exercise" (338), page 2705).

Physiotherapy practice

There are a number of important safety considerations in relation to diabetic patients and exercise (338).

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 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 BGLs 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 to 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.

During periods of acute illness/exacerbation or courses of corticosteroids, BGLs and insulin requirements may be altered such that patients may require more careful monitoring (338).

PRACTICE POINTS

- **People with CFRD can be encouraged to perform moderate aerobic exercise for at least 150 minutes per week**
- **Insulin injection sites should be away from areas used during the chosen form of exercise.**
- **Fast acting carbohydrate snacks should be immediately accessible during and after exercise**
- **Consider monitoring BGLs before and after strenuous activity.**

7 PHYSIOTHERAPY FOR PREGNANCY, LABOUR AND THE POST-NATAL PERIOD

The improvement in health, quality of life and longevity in CF has increased the desire and possibility of adults with CF 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 (339-343). Women with CF can have successful pregnancies following lung transplantation but the risks of organ rejection and death are high (344).

Physiological changes during pregnancy

The pregnancy 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 (345). 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 does the 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 gestation. Blood volume increases by approximately 40%, with a peak at 30 weeks gestation, secondary to new placental circulation. General vasodilatation occurs. This results in increased cardiac work during pregnancy (346). 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.

Pre-pregnancy planning

It is widely recognised that a planned pregnancy is likely to result in fewer problems than an unplanned pregnancy. The multidisciplinary 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 (347).

All women with CF are advised to approach pregnancy with a regular ACT routine. An optimal ACT routine suitable for pregnancy should be discussed. 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 ACTs, inhalation therapy and exercise (348). Frequent contact with the multidisciplinary CF team and the obstetric team should be encouraged during pregnancy and the postnatal period (349).

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 (79). 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:

- ACBT
- AD
- PEP therapy
- Oscillating PEP
- Effective huffing from different lung volumes avoiding dynamic airway 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 – 7%
- Inhaled mannitol
- 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 ACTs to maintain a neutral lumbar spine for prevention and/or minimisation of urinary incontinence during treatment (see Appendix 5). 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.

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.

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 gestation. 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.

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.

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 (346). 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 (348).

Physiotherapy post-Caesarean section in CF

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

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.

These physiotherapy considerations and the following recommendations concur with those detailed in the European guidelines for the management of pregnancy in women with cystic fibrosis (350).

PRACTICE POINTS

- **Postural drainage in head down tilted positions should not be used during pregnancy.**
- **Exercise should be modified during pregnancy according to usual pregnancy guidelines.**
- **During labour, appropriate pain relief, oxygen therapy, inhalational therapy and ACT should be provided as required.**
- **Following delivery, adequate pain relief, oxygen therapy, appropriate inhalation therapy, ACT and early mobilisation should be considered.**
- **Encourage frequent contact with the multidisciplinary CF team and the obstetric team during pregnancy and the postnatal period.**

8 PHYSIOTHERAPY MANAGEMENT OF CONTINENCE

Urinary incontinence is the involuntary leakage of urine. The two types of urinary incontinence are stress incontinence and urge incontinence. The reported prevalence of urinary incontinence in girls and women with CF ranges from 22% to 74% (351-357) in comparison with 13% in healthy women aged 18-24 years (358) . There is limited literature in adult males with CF, with the prevalence reported to be from 8-15%, compared to 7.5% in healthy men (357, 359, 360).

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 ACT, 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 (361). Age has been reported to have a strong positive correlation with the severity of stress urinary incontinence symptoms (356). Studies reporting on the incidence of stress urinary incontinence in people with CF also report increased anxiety, depression and a negative impact on quality of life (360, 362).

It has 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 (363). Care should be taken when teaching pelvic floor exercises as evidence suggests 40% of women with incontinence incorrectly perform a pelvic floor contraction with verbal education alone (364). It is not appropriate in the paediatric setting to use invasive assessment procedures; however data presented in abstract form indicate that adolescent females have correctly and successfully learnt pelvic floor exercises using Real Time Ultrasound (365) without reported embarrassment. Positive outcomes have also been demonstrated with surgical correction of severe stress urinary incontinence in women with CF (366).

Physiotherapy practice

Patients are often 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 issue and learn strategies to prevent and / or resolve the problem. All physiotherapists working in CF should include screening for incontinence as part of routine care for both male and female patients.

Female patients should be taught to perform 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 and will help in the prevention of leakage during all activities that apply force to the pelvic floor. Where available, real time abdominal ultrasound can be used to ensure correct technique without invasive procedures. Patients should also be taught optimal positioning in upright sitting for ACT in positions that maintain a neutral lumbar spine and optimise pelvic floor function (367) with the adding of perineal support in those with urinary incontinence. 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.

Pelvic floor exercises should be prescribed routinely for women with incontinence. Protocols for pelvic floor training, including handouts can be found through the APA or Continence Association of Australia at http://www.continence.org.au/resources.php. Treatment protocols are less well described for men, who may

require direct referral to a physiotherapist with expertise in continence.

Female 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 and may require referral to a gynaecologist or urologist.

RECOMMENDATIONS

19. **Women with CF and symptoms of stress urinary incontinence should be taught rehabilitative strength and endurance exercises to provide better control of the pelvic floor (C).**
20. **Men and women with CF should be screened for symptoms of stress urinary incontinence (C)**
21. **Airway clearance should take place in postures that maintain a neutral lumbar spine, to optimize pelvic floor function (C).**

PRACTICE POINTS

- **From puberty onwards, consider teaching females with CF pelvic floor exercises as a way of preparing the pelvic floor to overcome the downward pressure during activities such as exercise, forced expirations and coughing.**
- **In patients who continue to have difficulties with bladder or bowel control despite prescription of rehabilitative exercises, consider referral to a qualified continence physiotherapist.**

9 PHYSIOTHERAPY MANAGEMENT OF THE NEWLY DIAGNOSED PATIENT

The newly diagnosed infant

Most children born in Australia are screened at birth for CF through a heel prick blood test performed usually between 48 and 72 hours of age. Regardless of symptoms, all infants and their families should meet with the CF multi-disciplinary team soon after diagnosis, either as an inpatient or outpatient (368, 369). Physiotherapy intervention should begin immediately unless specifically delayed for a short period at the discretion of the CF team (eg post bowel resection for meconium ileus, high levels of family anxiety).

The role of physiotherapy in airway clearance, exercise and active play should be explained, demonstrated and practiced at initial education sessions, regardless of symptoms (162, 370). Educational materials should be provided for the family. The rationale for ACTs should be explained with relation to:

Pathophysiology – Even in asymptomatic infants there is evidence of inflammation, infection and structural change in the airways (371, 372). Treatment of early changes may preserve lung function and optimise long-term outcomes (373, 374).

Theory of airway clearance techniques - By improving mucociliary clearance, the development of chronic lung disease may be delayed (36, 373).

Physiotherapy practice

To aid adherence, airway clearance for the newborn should fit in with the family's routine (1, 36, 375). General consensus amongst Australian physiotherapists working with CF children suggests treatment of an asymptomatic infant should consist of five modified PD positions performed 1-2 times daily as appropriate. These positions should not include traditional gravity-assisted postural drainage in the infant due to the risk of GOR (68, 72, 75). In each position percussion or thoracic compressions should be performed for 3-5 minutes. Vibrations are not generally used with an infant. Total treatment time should be a maximum of 25 minutes per session. Other techniques such as infant PEP, assisted autogenic drainage (36), play and age-appropriate daily physical activity (376) can be introduced, dependent on the individual needs of the infant and family.

Generally treatment should be encouraged before or at least one hour after feeds (36, 375) 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 may be encouraged from early on. If the child has a respiratory exacerbation then treatment should be increased to 2-4 times daily as appropriate and able. Airway clearance therapy may need to be modified as the results of investigations become available (eg CT scans, CXRs and sputum cultures).

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 (377) and include changes in fever, cough frequency and/or sound, mood, stools, reflux patterns, work of breathing or breathing patterns, appetite or weight loss.

The use of music/singing, regular routines, toys and pacifiers can be demonstrated and encouraged to assist with adherence to treatment (378). Positions and methods with which to handle, distract and settle the child during ACTs can be introduced as appropriate, particularly with first-time parents. The importance of exercise and normal activity participation should be regularly discussed. Normal developmental play and prone lying should be encouraged as the first steps towards an active physical life style and routine (36).

Ongoing education and engagement of the patient/carers relating to appropriate dosage and order of physiotherapy including ACT, adjunctive inhalation therapy and regular exercise should be provided.

The newly diagnosed adult

Adults with a new diagnosis of CF usually have milder disease than those diagnosed in infancy (162). 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 (162). 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 (373). 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 (373).

Education about CF and its management should consider the implications of the disease on established lifestyles (373). 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 (36). 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 a 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 may be appropriate stand-alone ACTs (102). However, it is still important that these patients are given information about other ACTs 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 ACTs and exercise regimens and educated about the role of nebulized drugs in their treatment.

RECOMMENDATIONS

22. **Treatment for newly diagnosed infants may include:**
    a. Percussion for 3-5 minutes in each of 5 modified postural drainage positions (B)
    b. Daily age-appropriate physical play (C)

23. **Physiotherapy treatment for the newly diagnosed child and adult should include regular physical exercise (B); other forms of airway clearance therapy should be added as required (C).**

PRACTICE POINT

- **Education by the physiotherapist begins at diagnosis**

10 TRANSITION FROM PAEDIATRIC TO ADULT CARE – THE PHYSIOTHERAPY ROLE

Transition can be defined as 'the purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centred to adult- orientated health care systems' (379). It is widely accepted that young adults with CF should receive their health care in adult settings (380, 381). However, transition can be a stressful period for patients and families (382). Areas of most concern include potential exposure to infection; leaving a well-known physician; and meeting a new care team (383-385).

There is a lack of evidence in the literature evaluating existing CF transition programs, particularly in Australia (386). The Cystic Fibrosis Standards of Care Australia (2008) (349) lists six standards for transition, based on expert opinion:

Transition from Paediatric to Adult Care

Standard 1 Transition from paediatric to adult care involves a process of close cooperation between paediatric and adult specialist care teams.

Standard 2 All CF Centres should have a transition programme incorporating active education on adult issues, e.g. fertility, and the process should engage the young person with CF and their family in a positive way.

Standard 3 The concept of transition should be raised soon after diagnosis with more active discussions commencing around secondary school entry (12 years) and the process finishing with transfer to adult care around school leaving age (18 years).

Standard 4 Paediatric and adult specialist care teams should meet regularly to discuss individuals in transition.

Standard 5 The adult co-ordinator should meet individuals during the year before transfer, and the adolescent should have the opportunity to visit the adult CF Centre at this time.

Standard 6 A comprehensive summary of medical and social issues should be available to the adult team well in advance of transfer. The local CF Association can be involved to help facilitate the process.

There is no consensus regarding the best model of transition for patients with CF in Australia. The goal of each centre should be to facilitate a structured transition process for the patient, by following the standards of care. A key feature of effective transition includes early preparation and facilitating self-management skills of the young person with CF (386-388).

Whilst there are no direct references to physiotherapy in the current literature evaluating transition programs, 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 (389). It may be beneficial for the young person with CF to meet the physiotherapist from the adult centre prior to transfer. Infection control policies for physiotherapy in the adult setting should be discussed as part of the transition process (383). Physiotherapists in the paediatric centre can assist the transition process by actively promoting self-management in the time leading up to transfer of care (387, 388, 390) 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 engaging both the young patient with CF and their parents in a non-confronting way (388). Cooperation between physiotherapy staff at adult and paediatric centres is essential for successful transition in CF.

PRACTICE POINT

- **During the process of transition, paediatric and adult physiotherapists will need to communicate directly regarding the detailed aspects of each patient's physiotherapy care.**

11 PHYSIOTHERAPY MANAGEMENT FOR END-STAGE DISEASE

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 proven physiological benefits of NIV in CF include unloading of the respiratory muscles resulting in improved respiratory muscle performance, increased alveolar ventilation and improvement in gas exchange (391). Short-term physiological studies have shown reduced respiratory muscle work during NIV in both adults and children with CF, with reported reductions in work of breathing of 20– 60% (392-394). This is associated with a 30% increase in minute ventilation and tidal volume, and reduction in transcutaneous carbon dioxide of 7% (394). 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.

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 (395-401). 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 (400) where it may be useful for palliation of dyspnoea in end-stage disease.

There remains no disease-specific guideline for initiation of NIV during acute respiratory failure in CF. Surveys aiming to establish current practice in centres within Australia and overseas have suggested variability in indications for NIV and method of initiation (402, 403). Many useful principles can be taken from experience in other lung diseases (404). 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 (405), and may have implications for response to NIV in hypercapnic patients. In some patients, electrolyte and volume correction may be required to restore acid-base balance.

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 (406). The levels of humidity delivered during bilevel are lower than the levels reported to cause airway drying in users of CPAP (407). 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 MDIs are available; alternatively, a T-piece connector for nebulisation can be used. The circuit may need to be altered to ensure that the nebuliser is connected between the patient and the exhalation port.

Sleep disordered breathing and chronic respiratory failure

Hypoxia and hypercapnia occur commonly during sleep in moderate to severe CF (408, 409). These alterations in gas exchange are frequently seen during sleep prior to being evident in the daytime (410, 411). Repeated deterioration in gas exchange during sleep may impair ventilatory drive and result in daytime respiratory failure (412). Positive short-term effects of NIV during sleep in CF have been reported (410, 413). 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 (414, 415). Young and colleagues examined outcomes of domiciliary NIV over a 6 week period in a randomised, placebo controlled study (416). Significant improvements in quality of life, chest symptom scores, dyspnoea, nocturnal ventilation and increased exercise performance were reported. The sustained reduction in nocturnal carbon dioxide levels was not reflected in awake hypercapnia however. Recent retrospective studies have reported a stabilization or even reversal of the decline in lung function in patients using NIV with advanced disease (401, 417). These results need to be confirmed in prospective trials.

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.

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 (83), adverse effects on respiratory muscle performance (418), alterations in gas exchange (77, 419) and dyspnoea (23). A single session of NIV 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 (418, 419).

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 inspiratory pressure (IPAP) as tolerated. Coaching will be required so that the patient is able to perform forced expirations, cough and where possible expectorate, without removing the mask. The use of various interfaces such as nasal pillows or nasal masks to assist with ease of expectoration should be explored.

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 (147). 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 (420). 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. Bilevel NIV also improved ventilation, reduced desaturation and increased functional walking performance in children and adolescents with CF (421). These data indicate that NIV may have a role to reduce work of breathing and improve exercise performance in patients with advanced lung disease. More recently, a randomised controlled crossover trial showed that six

weeks of nocturnal NIV significantly improved the MSWT compared to nocturnal oxygen or placebo (416). The mechanism for this improvement is not clear, but warrants further examination.

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.

General considerations for NIV

Whether using NIV to treat acute exacerbations, chronic hypercapia, during physiotherapy or exercise, the ventilator settings should be adjusted to reduce work of breathing. Clinically these settings are determined using a combination of subjective assessments of respiratory comfort and non-invasive clinical monitoring of SpO2, respiratory rate and use of accessory muscles to support ventilation. This clinical assessment has been shown to be as effective in reducing work of breathing as using physiological outcomes (monitoring of transoesophageal and transdiaphragmatic pressures) in young CF patients (422).

High flow nasal prongs are a useful adjunct to the treatment of people with CF in acute respiratory failure on NIV. In some patients these can be used during periods off NIV for eating, nebulisation, ACT and socialising. They may also be useful during the process of weaning from continuous NIV.

RECOMMENDATIONS

24. **Non-invasive ventilation should be considered in all patients with acute respiratory failure who are listed for transplantation (C).**
25. **In patients with symptomatic nocturnal ventilatory failure, a trial of nocturnal NIV may be undertaken (B).**
26. **NIV is a useful adjunct to airway clearance in patients with severe disease in whom dyspnoea and fatigue limits effective airway clearance (B).**
27. **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 (B).**
28. **Heated passover humidification should be incorporated into the circuit for all applications of NIV in CF (C).**

PRACTICE POINT

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

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 end-stage lung disease. 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.

There are many systemic features of CF which have the potential to impact on lung transplant suitability and outcomes, including skeletal muscle weakness (195) and poor bone health (155). Physiotherapy management has a key role in optimising wellbeing prior to transplantation and restoring the best possible level of function after transplantation.

Transplant assessment

The assessment of potential recipients is performed by an experienced multidisciplinary team at a transplant centre with input from the CF 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, which is a good predictor of waiting list survival (167) and post-transplantation outcome (423). Musculoskeletal abnormalities such as reduced muscle mass, structural/postural thoracic kyphosis 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 may 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.

Preparation for transplantation

Time on the waiting list can vary from weeks to years, as organs are matched to recipients on numerous factors including size, clinical need, blood group and tissue typing. 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, in order to optimise physical fitness and strength. A recent large, retrospective study which included 70 people with CF (424) showed that 6-minute walk distance was well maintained from the time of listing to the time of lung transplantation in those who undertook thrice weekly supervised endurance and resistance exercise training. Those with a greater 6-minute walk distance prior to transplantation had a shorter hospital stay in the post-transplant period.

Exercise prescription principles in the pre-transplant period should be consistent with those for other individuals with CF (Chapter 4). 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.

Post-operative period

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 airway clearance and early mobilisation. Lung transplant patients often have a poor ability to perceive the presence of secretions and this may persist in the long term, due to poor cough reflexes from denervation post transplant (425). 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. On discharge, supervised rehabilitation usually continues as an outpatient at the transplant centre for up to three months.

Rehabilitation post transplant

Exercise rehabilitation is an established therapy for lung transplant recipients (426). Although studies in CF are uncontrolled, three months of post transplant rehabilitation has been associated with improvements in functional exercise capacity, strength and quality of life in both adults (427) and children (428). A recent randomised controlled trial of three months of rehabilitation in lung transplantation recipients with other respiratory disorders, performed immediately following hospital discharge, showed significant improvements in daily physical activity, quadriceps force and 6-minute walk distance at one year following transplantation (429).

Patients attend a formal outpatient rehabilitation program comprising of exercise training and education at the transplant centre. Primary goals include:

- Improve physical condition (strength, endurance, posture)
- Promote independence in maintaining and monitoring 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

The content of post transplant rehabilitation programs generally includes aerobic and resistance exercise, performed at least three times per week in an outpatient setting (426). Although most rehabilitation takes place in a group setting, patients with resistant organisms may need isolation from other immune suppressed patients with individual sessions during rehabilitation.

By approximately 12 weeks, most patients have achieved a good level of fitness and function (426) 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.

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
- Acute or chronic graft dysfunction
- Musculoskeletal morbidities (osteoporosis, pathological fracture, myopathy)
- Sternal instability
- Diaphragm dysfunction
- 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.

RECOMMENDATIONS

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

30. **Patients with CF who have undergone lung transplantation should participate in a formal, supervised rehabilitation program post-operatively (B).**

PRACTICE POINTS

- **To ensure comprehensive assessment of patients with CF prior to lung transplantation, consider the need for direct communication between the CF physiotherapist and the transplant physiotherapist, in addition to communication with other members of the multidisciplinary team.**
- **Physiotherapy management early following lung transplantation follows principles similar to the management of other thoracic surgery patients.**

Cystic Fibrosis and the Intensive Care Unit

Intensive Care for Reversible CF Complications

In some centres, people with CF who have severe but reversible conditions such as haemoptysis, pneumothorax, antibiotic desensitisation and distal intestinal obstruction syndrome are managed in the intensive care unit (ICU). Although there are limited data describing outcomes following ICU admission in CF, several studies have reported ICU survival of more than 80% for patients admitted to the ICU with reversible complications (430, 431). In those patients requiring mechanical ventilation for reversible conditions, longer intubation time has been associated with worse outcome (430).

Intensive Care for Respiratory Failure

The admission of CF patients to the intensive care unit for the management of acute on chronic respiratory failure remains controversial. There have been mixed results for survival following intubation for respiratory failure in patients with end stage lung disease. Efrati et al (431) reported 17 out of 18 adult patients dying before discharge, however Hayes and Mansour (432) report 10 out of 10 adults surviving to 6 months without lung transplantation. A retrospective analysis of 34 intubations reported 59% survival to discharge of 22 patients requiring intubation as a result of haemoptysis/pneumothorax and 33% of 12 patients requiring intubation for respiratory exacerbation (433). Interestingly, studies have reported 100% survival in children requiring intubation under the age of 18 months (434, 435) and 78% survival in children under five years of age (436).

Due to the known benefits of NIV for acute on chronic respiratory failure in CF (395-401), it is widely accepted that patients should not be considered for invasive mechanical ventilation unless they have failed a trial of NIV.

Extra-corporeal Membrane Oxygenation (ECMO)

Extracorporeal membraneous oxygenation (ECMO) is increasingly being used as a bridge to lung transplantation. The circuit for veno-venous ECMO, used to bypass the lungs and provide respiratory support, is displayed in Figure 1. Although there is very limited evidence for its use in CF (437), it may have advantages over mechanical ventilation as it reduces the need for sedation and paralysis, it allows the patient

to participate in physiotherapy and allows the patient to eat and drink. Three case series have reported a total of nine individuals with CF who were safely and effectively bridged to transplantation with veno-venous ECMO (437-439). Active rehabilitation during the ECMO period included airway clearance, range of motion, early assisted mobilisation including standing and walking, and strength and endurance exercises. Some authors have suggested that the key to success is the early application of ECMO after the need for mechanical ventilation is established (437).

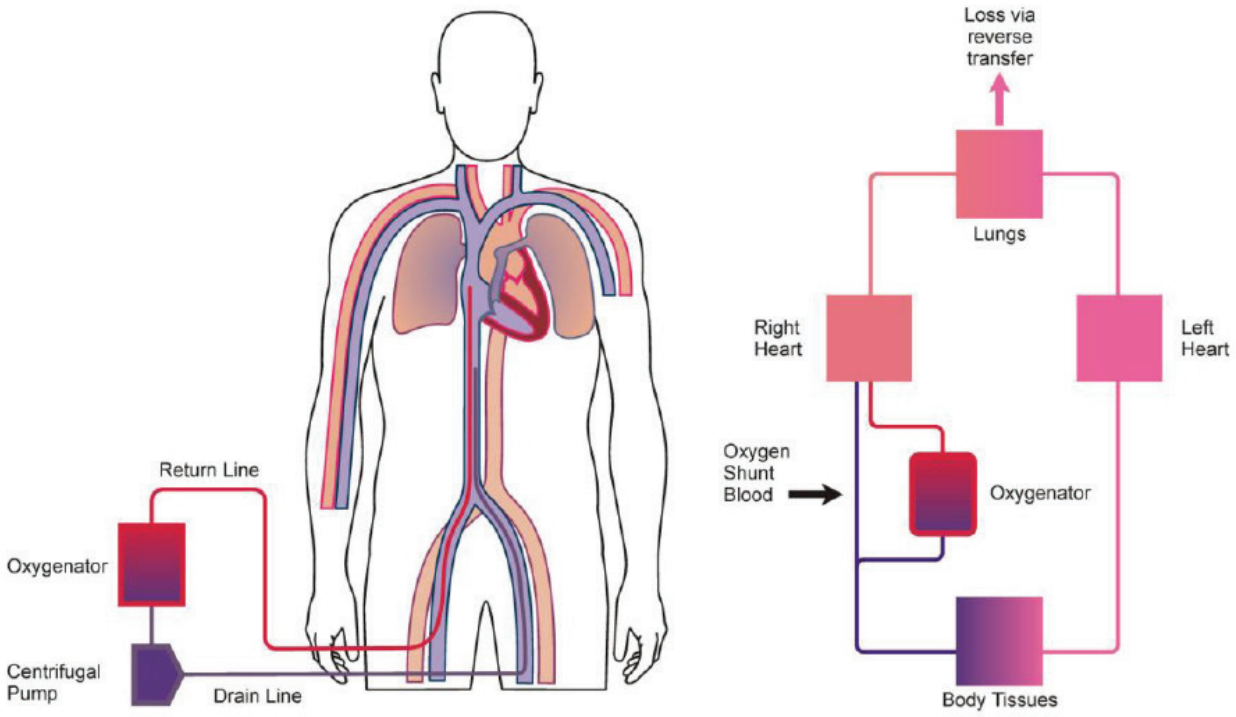

Figure 1. Circuit for veno-venous ECMO.

From the Alfred Health ECMO Guideline. Used with permission.

Physiotherapy for CF in Intensive Care

Physiotherapy management of patients admitted to the ICU should follow the usual principles of individualised assessment and treatment detailed elsewhere in this document. Good communication between the CF and intensive care teams is imperative for establishing physiotherapy treatment goals and optimal patient management.

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. Palliative care is introduced in parallel to active treatment as both therapeutic models help to relieve symptoms (440). The likelihood of lung transplantation will influence decisions regarding when to move from aggressive treatment to support and/or comfort care (441). Ninety percent of patients die of respiratory failure (442) and most patients die during a pulmonary exacerbation and/or viral infection (443).

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 (444).

Increasingly, guidelines recommend that palliative care should be discussed earlier, rather than when patients are in the end stage of their disease (445). 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. Long term, planned palliative care can empower patients and enable them to be active in the decision-making process regarding their end of life care (i.e. Advanced Care Directives, wills, Not For Resuscitation orders).

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 needs
- assistance to the patient, family and carers with planning for the end of life and after
- loss, grief and bereavement support (12).

Interdisciplinary care consists of continuing care from the CF team integrated with the specialist 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 (443). Terminal care should be organised in the place chosen by the patient and their family where possible (440).

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 (446).

Symptoms that cause discomfort in patients with CF include:

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

When to change 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 NIV 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 (447). The majority of patients will receive palliative care/comfort measures alongside these treatments (443, 447).

The impact of lung transplantation on end of life care

For patients who are awaiting lung transplantation, the objective is to keep the patient as well as possible until potential donor organs can be found and, as such, this goal may warrant more invasive interventions such as mechanical ventilation, NIV and enteral feeding (441). Prolonged waiting time and organ scarcity means some patients may not survive to receive a transplant (448) and, as such, end of life care remains an important subject for all CF patients with severe lung disease, including those who are awaiting lung transplantation (449).

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 (8).

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 (83) and may compromise respiratory muscle performance in those with severe disease (418, 419). 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, and education regarding methods of enhancing breathing control to minimise the respiratory work required. A mucolytic should also be considered to keep secretions thin and easy to expectorate. Intubation and ventilation is uncommon in the final stages of the disease, however NIV may also be useful to unload the respiratory muscles, relieve dyspnoea or as an adjunct to airway clearance (440). High flow nasal prongs may also be useful.

Other techniques

Towards the end of life, patients often report significant benefits from alternative techniques such as soft tissue massage (306), positioning for relaxation, trigger point release, music therapy and use of a fan to blow air on the face. 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.

PRACTICE POINTS

- **Physiotherapy treatment at the end of life should be flexible and tailored to each patient's wishes.**
- **Airway clearance for patients with end-stage disease should aim to minimise work of breathing and maximise patient comfort.**
- **Airway clearance may be continued even in the palliative stage if the patient finds it beneficial to relieve symptoms.**
- **Comfort measures such as soft tissue massage and positioning should be considered in the palliative patient**

12 ADHERENCE TO PHYSIOTHERAPY IN CYSTIC FIBROSIS

Physiotherapists frequently encounter adherence challenges in both inpatient and outpatient settings for clients with CF and their families. Adherence to physiotherapy has been reported as low as 53% in some centres (450). This may vary according to the component of treatment - adherence to frequency of ACTs has been reported at 51% whilst adherence to duration of ACT sessions was 64% (451). Adherence for inhaled dornase alfa in children has been reported at 67-84% (452, 453) whilst in adults this varies from 24-82% (454). Exercise therapy is perceived differently from other forms of treatment (450), with greater adherence to exercise than airway clearance techniques. In an Australian study, 17.5% of adults with CF performed 'exercise only' in place of traditional airway clearance techniques (455).

Measuring adherence is inherently difficult. Assessment of adherence by patients, parents and clinicians give consistently higher adherence rates than other measurement methods (456, 457). For example, self-report data of 50% overall adherence to treatment regimens was objectively measured electronically as 27% and by diary as 46%. (451). New technologies may provide opportunities for better assessment of adherence. The development of nebuliser systems that record usage, such as the I-Neb® and Prodose® (not currently available in Australia or New Zealand) have allowed for more accurate assessment of adherence to inhalation therapy. In a 12-month observational study, children using an I-Neb® maintained adherence to inhaled colistin at 60-70% (458), while a separate study showed adults using a Prodose® maintained adherence to inhaled colistin at only 50% (459).

Many barriers to adherence exist, varying from patient-related factors, social and economic, therapeutic, and healthcare related factors (460). Reasons for non-adherence to treatments across all age groups include: boredom of techniques/therapy, desire to be normal, forgetfulness, causes embarrassment, too time consuming, interference with other activities, feeling the treatment is not needed or that it won't work, and also feeling too unwell (455, 461-464). A structured daily routine may improve adherence. In a group of adolescents who provided nebuliser data from the I-neb® over the course of a scholastic year, adherence was significantly better during term-time and on weekdays as compared to school holidays and weekends (465). In order to address non-adherence, an individual's barriers to adherence must first be identified.

Clinical and demographic variables are poor predictors of treatment adherence. Knowledge and adherence are not correlated but more frequent contact with the health care team increases adherence (466). The degree of adherence to treatment is influenced by a person's style of coping and self-perceptions. It has been reported that adherent clients scored higher on optimistic acceptance scale and hopefulness scale, whilst partially adherent clients used distraction as a way of coping and non-adherent clients used avoidance as a coping strategy (467). Therapeutic adherence improves with strong personal beliefs in the effectiveness and necessity of the treatment being undertaken (468) and when treatments have a perceived greater influence on quality of life (462) or immediate symptomatic benefit. Consequences of poor adherence include increased

morbidity and mortality, reduced quality of life and increased health care costs (469-473). 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. Engaging in a partnership approach, to identify and discuss barriers to adherence openly and normalise difficulties opens the way to behavioural change (474).

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. It is important that the patient understands all aspects of the treatment prescribed. One study demonstrated that 33% of non-adherence with airway clearance techniques was due to the patient following what they perceived to be the recommendations from team, concluding that a portion of non-adherence is related to miscommunication (475). Formal coaching and interviewing strategies that encourage collaboration and affirmative interactions between health professional and client may be useful. For example, motivational interviewing is an effective treatment for modifying behaviour in chronic conditions (476), however it has not yet been adequately tested in CF (477).

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. People with CF tend to prefer self-administered ACTs (478), which may promote adherence.

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

PRACTICE POINTS

- **Adherence to prescribed ACTs, inhalation therapy and exercise should be explored openly and non-judgementally on a regular basis.**
- **Management of adherence problems should be client-focussed and individualised accordingly.**
- **Effective communication strategies between the patient and CF team may help resolve some aspects of non-adherence.**

13 INFECTION CONTROL DURING PHYSIOTHERAPY IN CYSTIC FIBROSIS

Respiratory tract infections have a significant impact on morbidity and mortality in CF (479). Good infection control practices are critical to preventing transmission of pathogens. Segregation and cohorting of inpatients and outpatients according to respiratory organisms are now routinely practiced, both nationally and internationally (480, 481).

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)* (482, 483). Because there may be differences in virulence and outcome associated with different clones, even patients with the same organism may need to be managed in separate cohorts (484). Physiotherapists should therefore be familiar with the cohorting requirements of their own centre.

Education of patients and families regarding the importance of infection control and discussion of infection control guidelines increases the knowledge and confidence of patients and families in following these guidelines. Other factors suggested to facilitate compliance with infection control include ready availability of materials to perform hand hygiene (485).

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 practice points 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 these organisms can survive on dry surfaces for a number of days (483, 486, 487). There is also potential for airborne transmission (488). *B. cepacia* has been isolated from the hospital rooms and hands of patients following airway clearance (489-491) and has been isolated from the outside surfaces of sputum cups (489). 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 (492).

Bacterial contamination of home nebulisers of CF patients has been documented and sharing equipment has been associated with transmission of B. cepacia (140, 493, 494). 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 the responsibility for cleaning respiratory equipment lies with patients or families, with the advice and encouragement of physiotherapists and nursing staff. Adherence to nebuliser disinfection guidelines can range from 36-79% (495).

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 one metre of an infected patient (483) although it has been reported that contamination can occur at a distance between 1 and 2 metres, although the probability is low (1.7%) (496). It is therefore recommended that patients with different organisms, or in different cohorts, do not exercise together. When people who are considered suitable for cohorting 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 and New Zealand physiotherapists is that patients with *B. cepacia* and MRSA should exercise on their own in the hospital setting, whilst inpatients with VRE or hVISA should exercise in their own room or outdoors. In many centres exercise equipment is brought into the patient's room to facilitate exercise training.

Outpatient Practice

Exam rooms should be cleaned in between each patient to reduce surface contamination and sinks should be frequently disinfected. Patients and staff should perform frequent and repeated hand hygiene with an alcohol based hand rub throughout outpatient clinic visits (487, 497). Some studies also recommend cohorting of clinic rooms depending on microbiology (487). The introduction of cohorting has been shown to reduce the prevalence of epidemic strains of *Pseudomonas aeruginosa* (498).

PRACTICE POINTS

- **Physiotherapists should be aware of the colonising organisms and cohorting requirements for each of their patients.**
- **Patients should not share airway clearance therapy or inhalational therapy equipment under any circumstances.**
- **Patients should clean their own airway clearance equipment at home and in hospital as advised by the CF team or local infection control department.**
- **Patients who are unsuitable for cohorting should not exercise in the same gym area at the same time.**
- **Patients with B.cepacia and MRSA should exercise on their own in the hospital setting.**
- **Inpatients with multi-resistant organisms (such as VRE or hVISA) should exercise in their own room and outdoors.**
- **Staff should practice strict handwashing between patients and stethoscopes should be wiped with alcohol before applying to patients.**

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 people with CF. There are no controlled trials to guide practice in this area. The following recommendations represent expert clinical opinion and are consistent with the Standards of Care for Cystic Fibrosis in Australia (349) and New Zealand (499).

Physiotherapy treatment for inpatients

Patients should be assessed and physiotherapy treatment started on the day of admission (349). 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, ACTs 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 ACT 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.

Physiotherapy treatment for outpatients

Patients attending the outpatient department of the Cystic Fibrosis Service should have access to a physiotherapist with expertise in CF management 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. One uncontrolled study involving 12 adolescents with CF has shown a reduction in the need for intravenous antibiotics with fortnightly review by a physiotherapist; however controlled data are needed before this intensive practice can be widely recommended (500).

A formal annual review by the CF team, including physiotherapy review, has been advocated for people with CF (349, 499). However this does not occur in all settings due to resource constraints (164). Regardless of whether such a formal review occurs, each patient should complete the following reviews with their physiotherapist at least once per year:

- 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
- have 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.

PRACTICE POINTS

- **Inpatients with CF should be assessed by a physiotherapist within 24 hours of hospital admission and treatment commenced at the earliest opportunity.**
- **The physiotherapy treatment plan for inpatients with CF should specifically address airway clearance therapy, inhalation therapy and physical exercise.**
- **Outpatients with CF should be reviewed by a physiotherapist every three to six months.**

15 DIRECTIONS FOR FUTURE RESEARCH

There are a number of areas where insufficient evidence was available to the writing team to make recommendations for physiotherapy practice. Priority areas for research, where additional data are likely to have a clinically important impact on practice were identified by the writing team. Key research questions that should be addressed in robust trials include:

- What is the most effective airway clearance technique for infants with CF?
- What is the impact of physiotherapy techniques (positioning, percussion, vibration) on GOR across the lifespan in CF?

- Is PEP therapy equally effective when delivered using a mouthpiece compared to a mask?
- Is there an advantage to combining inhalation therapy and airway clearance techniques?
- Is physical exercise an effective stand-alone airway clearance technique for people with CF, particularly in those with mild disease?
- What is the role of strength training in children with CF?
- What are the optimal prescriptions for exercise training and physical activity participation for people with CF across the lifespan?
- What is the role of exercise training in management of CFRD?
- Does treatment of musculoskeletal complications impact on long term outcomes in CF?
- Are there long term benefits of nocturnal NIV in people with CF and chronic respiratory failure?

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APPENDICES

Appendix 1

Protocols for airway clearance techniques

Descriptions of the protocols for performance of airway clearance techniques, as described by the International Physiotherapy Group for Cystic Fibrosis, can be found here:

https://www.ecfs.eu/ipg_cf/booklet

Appendix 2

Three-minute step test protocol

Outcome Measures

- Heart rate
- Oxygen saturation
- Perceived level of breathlessness (eg Borg score)

Equipment

- Standard 6 inch (15 cm) step
- Stopwatch
- Metronome
- Pulse oximeter
- Borg scale
- Recording sheet on a clipboard
- 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 saturation and Borg breathlessness rating should be recorded prior to commencing the test.

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 SpO2 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 3

Modified shuttle test protocol

Outcome Measures

- Distance
- Heart rate
- Oxygen saturation
- Perceived level of breathlessness (eg BORG score)

Equipment

- Shuttle CD* and CD player
- Pulse oximeter
- Borg scale
- Recording sheet on a clipboard
- Cones to mark the turn-around points, placed 9 metres apart

Procedure

The modified shuttle test is a 15-level or 25-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.

Patients should be familiarised with the procedure by conducting a practice test.

Measures of resting pulse rate, oxygen saturation and perceived level of breathlessness using the Borg breathlessness scale should be taken prior to commencing the test. If you need to determine levels of desaturation the probe should remain on the patient throughout the test. 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, experience desaturation to less than 80% or fail to maintain the set pace (0.5m away from the cone when the beep sounds on two consecutive shuttles).

The distance covered, pulse rate, oxygen saturation, perceived level of breathlessness using the Borg scale and the reason for stopping the test should also be recorded at the completion of the test.

- MST-15 is available from Dr Sally Singh, Dept of Respiratory Medicine, Glenfield Hospital NHS Trust, Groby Road, Leicester LE3 9QP, UK
- MST-25 is available from Mark Elkins, mark.elkins@sydney.edu.au

Appendix 4

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 5

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 (367).

   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 6

Conflict of Interest Statements

Jenny Bishop	Nothing to declare
Ryan Black	Conference support, Novartis, 2013
Summar Bowen	Nothing to declare
Brenda Button	Pharmaxis Allied Health Advisory Committee; Novartis Allied Health Advisory Committee; Vertex Allied Health Advisory Committee; Conference support, Roche; Conference support, Pharmaxis.
Robyn Cobb	Conference support, Novartis
Narelle Cox	Conference support, Roche.
Rebecca Davis	Nothing to declare
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Julie Depiazzi	Nothing to declare
Ruth Dentice	Nothing to declare
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Tiffany Dwyer	Nothing to declare .
Alison Elliot	Nothing to declare
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Esta-Lee Tannenbaum	Nothing to declare
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Nathan Ward	Conference support, Roche 2007, Pharmaxis 2012
Samantha West	Nothing to declare
Dianne White	Nothing to declare
Christine Wilson	Meeting support, Pharmaxis
Lisa Wilson	Nothing to declare
Jamie Wood	Conference support, Roche 2009, Pharmaxis 2012, Novartis 2013; Abbott Products scholarship 2011; Bronchitol workshop 2012.
Michelle Wood	Travel support for attendance at clinical trials investigator meetings, Vertex (2010 – 2014), PTC (2014), Aradigm (2014). Advisory board consultancy fees, Vertex (2014).

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