QUANTITATIVE EVALUATION OF THE PERFORMANCE OF AUTOGENIC DRAINAGE IN HEALTHY ADOLESCENTS

by

Kimbly M. Morgan

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DEDICATION

I dedicate this project, in fulfilment of the requirements for my Master of Science degree, to….

…my Grandfather, Walter Morgan, who imparted to me the important distinction between knowledge and education,

…my parents, who instilled in me the value of a strong work ethic and who have believed in and supported my every endeavour,

… my bright and beautiful daughter, Kate, may you be inspired to persevere and follow you dreams.

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ABSTRACT

Introduction: Autogenic drainage (AD) is a breathing pattern comprised of 3 phases of tidal volume (V_t) breathing distinguished by low, mid, and high end-expiratory lung volumes (EELV). [1-8] AD increases FVC and clears clinically significant amounts of sputum. [9-11]

Methods: AD was defined by EELV as a percent of functional residual capacity (FRC): ≥30% below FRC Phase 1, ±10% at FRC Phase 2, ≥40% above FRC Phase 3, and V_t ±10% of resting V_t. Thirty-two healthy adolescents were taught AD and assessed using spirometry and plethysmography.

Results: The mean EELV was 26%, 16%, and 53% of FRC for Phases 1,2,3 ($p<.001$). The mean V_t was 87%, 108%, 138% of V_{trest} for Phases 1,2,3 ($p>.05$). All defining criteria were met or were within 1 standard deviation of the defining mean. At least 20% of participants achieved each criterion.

Conclusion: The AD quantitative definition is achievable in a cohort of healthy adolescents.

LIST OF ABBREVIATIONS USED

CF	Cystic Fibrosis
ACTs	Airway Clearance Techniques
EELV	End Expiratory Lung Volume
FRC	Functional Residual Capacity
CFTR	Cystic Fibrosis Transmembrane Conductance Regulator
cAMP	Cyclic Adenosine Monophosphate
ENac	Epithelial Sodium Channels
EPP	Equal Pressure Point
PCL	Periciliary Layer
pHP	Potential of Hydrogen
DNA	Deoxyribonucleic Acid
TLC	Total Lung Capacity
FEV_1	Forced Expiratory Volume in 1 second
FVC	Forced Vital Capacity
FEV_1/FVC	Forced Expiratory Volume in 1 second to Forced Vital Capacity Ratio
$FEF_{25-75\%}$	Forced Expiratory Flow from 25% to 75% of vital capacity
TV	Tidal Volume
RV	Residual Volume
VC	Vital Capacity
IPGCF	International Physiotherapy Group for Cystic Fibrosis
PD&P	Postural Drainage and Percussion
ACBT	Active Cycle of Breathing Techniques
PEP	Positive Expiratory Pressure
OPEP	Oscillating Expiratory Pressure
AD	Autogenic Drainage
ERV	Expiratory Reserve Volume
EPP	Equal Pressure Point

L/min	Litres per minute
mm	Millimetres
V_t	Tidal Volume measured in AD
V_{trest}	Tidal Volume measured in the Preparation Phase of AD
ATS	American Thoracic Society
L	Litres
L/s	Litres per Second
cmH_20	Centimeters of Water Pressure
TMT A	Trail Making Test A
TMT B	Trail Making Test B
ANOVA	Analysis of Variance

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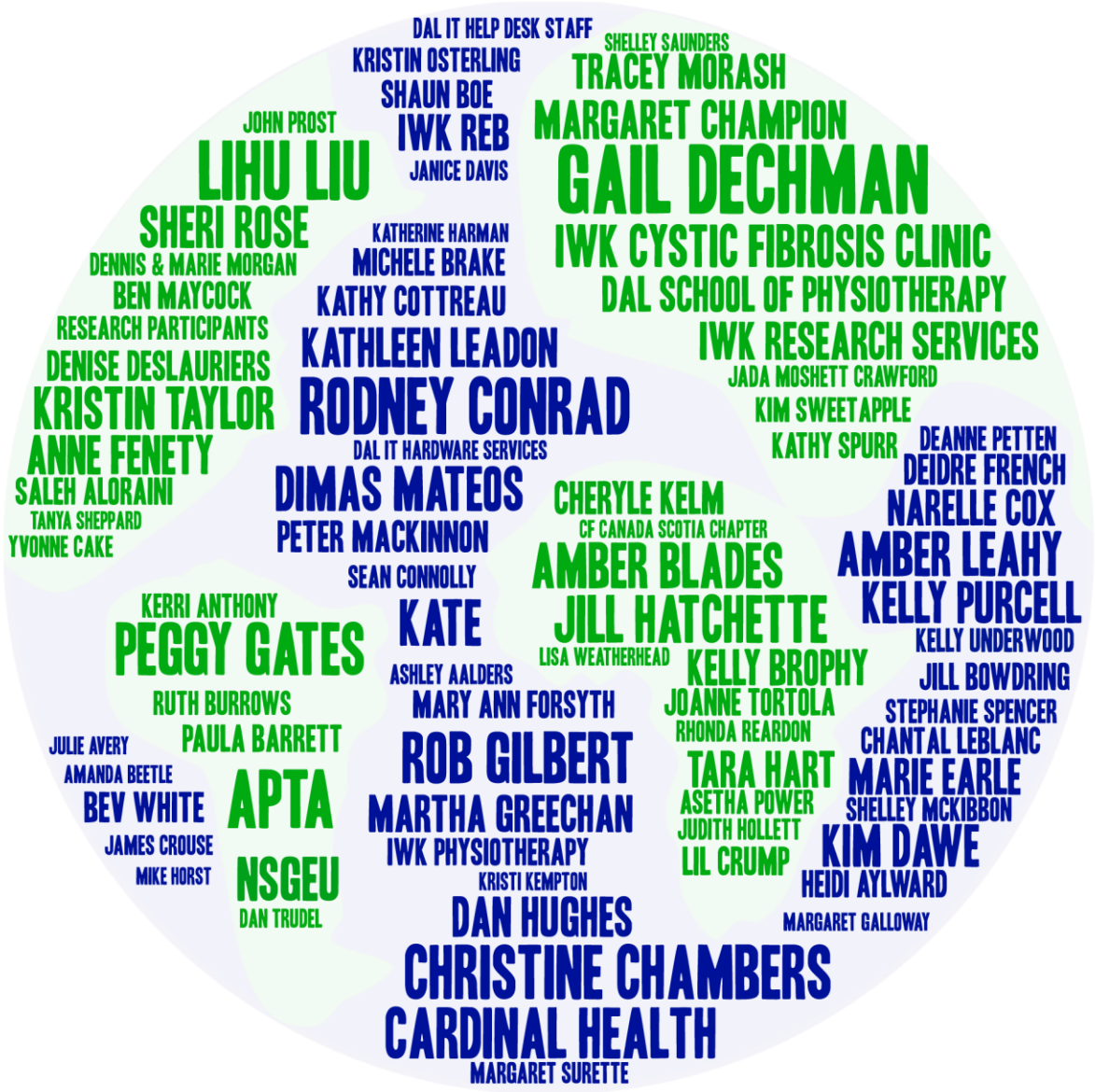

CHAPTER 1 INTRODUCTION

Cystic fibrosis (CF) affects approximately 70,000 people worldwide and is the most common, fatal genetic disease in Canadian children and young adults.[12] This disease primarily impairs the function of the respiratory and digestive systems, but also affects the reproductive system, sweat glands, salivary glands, and biliary tract.[13] There are approximately 4000 Canadians living with CF, 90% of who will die due to respiratory failure at a premature age.[14] Although 60% of Canadians with CF are adults, the median age of the Canadian CF population is 21.4 years.[14] Studies show that children and adolescents with CF have poorer quality of life, take part in less intense physical activity than their peers, and have a higher rate of anxiety and depression.[15-17] These modifiable factors contribute to poor health outcomes in the CF population.[17]

Cystic fibrosis lung disease begins at birth with the dehydration of airway mucus that leads to mucous plugging and a progressive cycle of airway obstruction, infection, and inflammation.[18,19] There is an amplified, persistent inflammatory response to repeated pulmonary infections.[20-22] This increases mucus retention and causes permanent structural lung damage.[23,24] All Canadian provinces have newborn screening for CF, which allows a preventative approach to disease progression.[12] Diagnosis in the newborn period yields a better prognosis due to early initiation of treatment prior to symptoms of poor growth, chronic cough, and increased work of breathing.[12,18,25,26] Cystic Fibrosis disease management is multi-faceted and primarily focused on controlling pulmonary symptoms and preventing pulmonary infections, permanent lung damage, and subsequent loss of pulmonary function.[27-30] Standard respiratory care involves numerous medications and airway clearance sessions that are administered multiple times a day.[29-31] The burden of treatment for CF is acknowledged to be significant.[31,32] In the event of a pulmonary exacerbation, which can occur often, an early, robust response is imperative and involves additional daily interventions.[28,29,33]

Airway clearance is a key treatment aimed at alleviating airway obstruction caused by thick, copious secretions that are retained in the lungs of those with CF.[29] There are a number of standard airway clearance techniques (ACTs), many of which are independently administered once people reach adolescence.[34] One such technique is autogenic drainage (AD), which is a unique breathing pattern designed by Jean Chevaillier in 1967.[8] Autogenic drainage aims to mobilize mucus from the small airways and transport it to the larger airways where it can easily be expectorated.[1] It involves manipulation of one's breathing pattern such that normal size breaths with breath holds are completed at "low, mid and high lung volumes" within one's total lung capacity.[1,5,7] Autogenic Drainage has been shown to be effective in clearing clinically significant amounts of sputum and in increasing FVC.[9,35] It has also been demonstrated that maximum expiratory airflow can be achieved during AD.[36-38] However, it is a complex technique that is challenging to teach and to learn.[39-41] This makes AD time consuming to introduce in the clinic environment.[42] Time and practice are required for one to master AD and incorporate it into a daily airway clearance routine.[6,39,40,43] For these same reasons, it is also challenging to train healthcare professionals to teach and evaluate this technique.

Autogenic drainage has been a preferred ACT in Europe, Australia, Scandinavia, and Canada for many decades but is not commonly used in the USA.[3,4,44,45] Despite its longevity and widespread use, AD has only ever been qualitatively described. The teaching approach and evaluation of the technique have also been qualitative in nature, based on observation of chest wall movement and expectoration of sputum.[5,46] Investigations of the effects of AD on sputum recovery ensured that there was in-depth, quality instruction to the participants on AD technique. However, none of the studies objectively evaluated AD performance following the intensive teaching to determine if the technique was being done properly.[10] Currently there is no standardized, objective method for assessing AD performance.[47] Thus, clinicians cannot determine if patients are performing AD correctly. This greatly impedes the ability to improve or individualize a person's technique and evaluate various methods for teaching it. These factors discourage

clinicians from teaching AD. Researchers are equally disadvantaged, as they cannot verify the technique they are testing.

An ideal evaluative tool of AD performance would be widely available, quickly and easily administered in a clinical environment, reliable and valid, standardized, and quantitative. The defining feature of the AD breathing cycle is the end expiratory lung volume (EELV) or the lung volume at which breaths are taken i.e. low, mid, and high.[7] There are two clinical tools that, together, can be used to evaluate this unique lung volume. Spirometry, the measurement of inhaled and exhaled volumes as a function of time, can determine the volume of a breath.[48] Plethysmography is commonly used to assess the volume of gas remaining in the lungs following a normal, passive exhalation.[49] This yields the functional residual capacity (FRC).[49] Spirometry can be used to determine the EELV and plethysmography can relate this volume to the lung volume at which one normally breathes i.e. FRC. Collectively, these are valid tools to assess the distinct AD breathing pattern.[48] Plethysmography is commonly used in clinical practice to assess lung volume.[49] Spirometry is the gold standard assessment of pulmonary function.[48,50,51] These evaluations are standards of CF care, used in all accredited CF centres worldwide to monitor CF disease progression.[52-54] Therefore, these tools are widely available and suitable for the assessment of AD.

The purpose of this study is to quantitatively define the AD breathing pattern, develop a method for the quantitative assessment of AD, and apply it to AD performance in a healthy group of adolescents. The following literature review provides information on the merits of AD and the challenges of using it with the CF population. This will provide a rationale for these initial steps in determining a method to quantify AD.

CHAPTER 2 LITERATURE REVIEW

2.1 Cystic Fibrosis

Cystic fibrosis is caused by a mutation in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene.[55] There are over 2,000 mutations in the gene, but the most common is the delta F508 mutation which is found in approximately 90% of the 4100 Canadians who have CF.[55,56] The defective gene results in an abnormal CFTR protein that is expressed in the epithelial cells of the exocrine glands in the body.[57] The dysfunctional CFTR protein poorly regulates ion transport causing the majority of these glands to produce abnormally thick mucus. This impairs the function of all the exocrine glands, however the most devastating effects occur in the pulmonary system.[12,25,55,57]

The CFTR protein is primarily a cyclic adenosine monophosphate (cAMP)-regulated chloride channel that normally conducts chloride out of the epithelial cell and signals the secretion of bicarbonate into the airway lumen.[55] It also controls sodium absorption into the cell via signalling of epithelial sodium channels (ENac).[25,55] When CFTR function is impaired, chloride and bicarbonate are retained in the airway epithelial cells and sodium is excessively absorbed. This creates an osmotic gradient that favours movement of water into the epithelial cell and an ionic imbalance that lowers the pH of the airway surface liquid.[58] This results in thick, acidic airway mucus covering the airway epithelium.[55,59] The altered airway surface liquid impairs mucociliary clearance and compromises anti-microbial activity in the airway lumen.[55,59,60]

The airway surface liquid, generally referred to as “mucus”, is comprised of two gel layers the periciliary layer and the mucus layer.[59] The periciliary layer (PCL) bathes the cilia on the epithelial surface and contains membrane-tethered mucins that generate a greater osmotic pressure than that of the mucus layer.[59] This creates a fluid-filled environment that maintains lubrication of the cilia and allows them to move freely and uniformly.[59] The mucus layer blankets the top of the beating cilia providing a protective barrier that is propelled towards the oropharynx as it traps

inhaled particles and microorganisms.[58,61,62] This mucociliary escalator is a primary airway defence mechanism.[61,62] Normally, the mucus layer is 98% water with a solid content of 1% salt and 1% secreted mucin.[59] In CF, the dehydrated mucus layer has a minimum solid content of 6.5%, most of which is secreted mucins that increase in number when infection occurs.[60,63] This creates a greater osmotic pressure in the mucus layer that draws water from the PCL and causes the cilia to collapse. Once this occurs, the mucins in each layer bind tightly to each other and the airway wall causing mucus retention and adherence to the apical surface of the epithelial cells in the lumens of the small airways.[55,59,62-64]

The impairment of the mucociliary escalator allows pathogens, inhaled from the environment, to remain in the distal airways where they are able to thrive due to the viscous mucus, lower pH, and CFTR-related dysregulation of the innate immune system.[18,20,25,28,55,59,65] The lower pH inhibits anti-microbial activity of the airway surface liquid by impairing the activation and migration of molecules and cells involved in the capture and killing of microbes.[20,59,60] Antimicrobial peptides, such as lysozymes and lactoferrin, are inactive so pathogens remain viable. Recent findings reveal that individuals with CF have an increased number of macrophages but decreased macrophage-mediated bacterial killing.[21,66] There is a paucity of lymphocytes and eosinophils and a reduction of phagocytosis and intracellular bacterial killing.[66,67] Mucin macromolecules are poorly formed and unable to bind to pathogens that would normally then be cleared by the mucociliary escalator.[25,55,68] This compromises the airway defence system allowing infection to occur and recur.[28]

There are a number of bacteria and fungi that commonly infect the lungs of people with CF. *Staphylococcus aureus*, *Hemophilus influenza*, *Stenotrophomonas maltophilia*, *Achromobacter xylosoxidans*, *Burkholderia cepacia complex*, and *Aspergillis fumigatus* are among the most common.[25,28,45,65,69] Respiratory viruses play a significant role in respiratory exacerbations and can damage the epithelial barrier allowing other opportunistic pathogens to invade the epithelial layer.[25] *Pseudomonas aeruginosa* is one such pathogen and is regarded as the primary organism that influences disease progression.[70] It is associated with an accelerated

loss of pulmonary function and decreased survival. [19,65,70,71] *Pseudomonas aeruginosa* is usually acquired in the first few years of life. Although it can be eradicated, it often recurs and persists in the airway lumen and infects the epithelium forming a biofilm. [18,25,65] These mucoid strains of *Pseudomonas aerguinosa* thrive in oxygen-deprived environments and the obstructed airways create an optimal medium for this to occur. [20,59] These strains are inherently resistant to host defenses and, like other CF pathogens, stimulate and sustain airway inflammation. [18,20,28,55,59]

The presence of pathogens signals neutrophils to migrate from the capillaries to the site of infection. [20,21,55,60] Tenacious mucus impedes the movement of neutrophils within the airways so they are unable to capture and kill pathogens. [60] The continued presence of these pathogens, particularly *Pseudomonas aeruginosa*, signals the inflammatory response to remain active, thus neutrophils keep migrating to the infected airways but are unable to carry out their role. [20,21,25] Once the neutrophils degenerate there is an excessive amount of cellular debris released into the airway, including oxidants, neutrophil elastase, and deoxyribonucleic acid (DNA). [20,21] The elastase activates other proteases, degrades antimicrobial peptides, impairs the release of antimicrobial proteins, prevents the removal of apoptotic neutrophils, and inhibits multiple signals that terminate the inflammatory process. [20,21,25] This increases the viscosity and volume of the mucus and enhances mucus stasis while summoning additional inflammatory mediators. The ongoing inflammatory response is further stimulated and new infections are facilitated. [20,21,65] The cycle of airway obstruction, infection, and inflammation is inherent to CF disease, however inflammation is the pivotal component of disease progression. It is responsible for permanent structural lung damage that results in loss of lung function.[24,65]

2.2 Structural Consequences of CF Lung Disease

The lung is comprised of a conducting zone and a respiratory zone (Figure 1). The conducting zone includes airways from the trachea to the terminal bronchioles and functions as conduit to and from the alveoli. The respiratory zone includes the alveolated region where gas exchange occurs. [72]

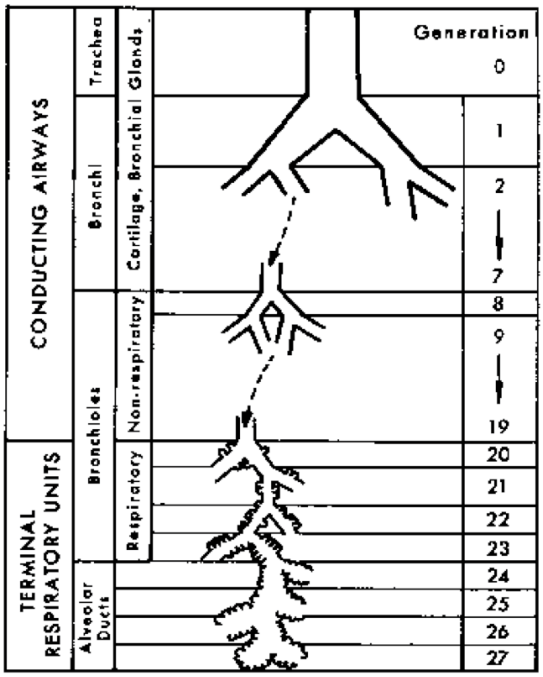

Figure 1: Subdivisions of the conducting and respiratory zones.[73]

In CF lung disease, the smaller airways in the conducting zone are initially and progressively affected, followed by the larger airways, and eventually the alveoli in the respiratory zone.[24] There are multiple structural changes that are reflective of CF disease progression. The airway walls lose cartilage content due to the destructive effects of neutrophil elastase. This inflammatory by-product degrades the connective tissue, elastin, collagen, and fibronectin that provide stability and support to the airway walls.[20,21,74] This predisposes the airways to collapse. Damage to the connections between the airway wall and the lung parenchyma lead to a loss of mechanical tethering, which enhances the tendency for airways to collapse.[23,25,75] The changes also compromise the airways' ability to rebound from inward and outward forces placed on the airway. This loss of elastic recoil results in airway dilation where mucus collects. Collectively these changes result in bronchiectasis that is common in CF.[25]

Studies show that there is extensive airway remodeling that is specific to CF, although the exact cause has not yet been identified.[75] The cross-sectional area of the CF airway wall is increased by hyperplasia of smooth muscle, mucus glands, and

epithelial cells.[23,74-76] An abnormally high loss of epithelial cells is believed to increase smooth muscle tone and shortening.[75] The altered airway dimensions and smooth muscle content contribute to increased bronchial responsiveness found in approximately 50% of people with cystic fibrosis.[19,23,25] Airflow in the conducting zone is compromised by luminal narrowing and airway collapse associated with architectural changes and the loss of structural integrity.[24,72,77]

2.3 Impaired Pulmonary Mechanics & Function

Expiratory flow limitation is the primary, functional impairment of CF lung disease.[25] It is commonly quantified using spirometry, which involves a maximal forced expiratory manoeuvre from total lung capacity (TLC).[51,72] The volume of air expired in one second (FEV_1) is measured and expressed as a ratio with the forced vital capacity (FVC).[72,77] An FEV_1 that is less than 80% percent predicted with an FEV1/FVC ratio that is less than 0.7 or 70% indicates there is airway obstruction.[51,72] The severity of airway obstruction is categorized as mild when FEV_1 is >70%; moderate when FEV_1 is 60-69%; moderately severe when FEV_1 is 50-59%; severe when FEV_1 is 35-49%; and very severe when FEV_1 is <35%.[51] The forced expiratory flow from 25% to 75% of vital capacity (FEF_{25-75}) is used as an indicator of airflow in the small airways.[24,51] This is often the first component of spirometry to decline, while FEV_1 remains normal until lung disease progresses to involve the larger airways.[24,51]

Airflow in and out of the lung results from a pressure difference between the alveoli and atmosphere via the mouth.[72,77] This gradient directly influences how fast air moves throughout the lung, however the airway radius is the primary determinant of the rate of airflow.[77] According to Poiseuille's Law and its derivatives, a unit decrease in the airway radius causes a sixteen-fold increase in airway resistance and an associated exponential decrease in airflow.[77] As discussed above, in CF disease there are multiple pathologic changes that narrow the airway lumen and increase the resistance to airflow.[78] This decreases the rate of airflow and makes it difficult to breathe. The muscles of respiration are required to increase their activation to generate a sufficient driving pressure, i.e. a pressure change that

creates a gradient for airflow.[72,77] In healthy lungs expiration is passive, but in CF disease expiration becomes active in order to overcome airway resistance and maintain ventilation of the lung.[72] With disease progression, the total work of breathing increases for both the inspiratory and expiratory phases of the breathing cycle.[78]

Early in the disease, airway obstruction is most obvious during a forced exhalation. However, this obstruction becomes more apparent during tidal volume (TV) breathing (normal size breaths) as lung disease becomes more severe and airway collapse occurs. During a forced exhalation, in healthy and diseased lungs, the pressure surrounding the lung (pleural pressure) is significantly increased. At high expiratory flow rates this pleural pressure can exceed the pressure in the airway (intrabronchial pressure) causing a choke point in the airway. In a normal lung, this usually occurs at volumes below 20% of total lung capacity.[77] In CF, these choke points can occur at any lung volume, and at relatively lower flow rates. Airway collapse in diseased lung regions often accompanies these choke points because the damaged airways are unable to remain distended.[72,77] When CF lung disease progresses to moderate and severe stages, premature airway closure can occur in the exhalation phase of TV breathing due to the extensive structural damage in the airway walls and lung parenchyma.[13,72] Typically, this results in tidal breathing at a higher lung volume. This increase in functional residual capacity (FRC) is an adaptation to maintain ventilation by breathing at a lung volume that has optimal structural support. This occurs involuntarily when air becomes trapped in the lung due to mucus plugging and airway collapse. The change in FRC can become permanent once residual volume (RV), the amount of air remaining in the lung after an active and complete exhalation, increases.[13,72,77]

As CF lung disease progresses, FEV_1 declines, the RV/TLC ratio increases, and vital capacity (VC) eventually decreases. These values reflect increasing airway obstruction, air trapping, and eventually, with severe disease, the development of restrictive lung disease.[13,25,51,78] These changes impair the ability to effectively and forcefully move air in and out of the lungs. The inability to force air out of the lungs at or near TLC, indicated by a decline in FEV_1, compromises one's ability to cough

and clear retained mucus. Aside from the mucociliary escalator, cough is the only other innate airway defence mechanism that clears mucus from the lungs. Both mechanisms are essential for effective lung defence.[61,62] Once the lungs become compromised by infection, the resulting inflammatory response progressively destroys the structural support system of the lung. This effectively abolishes all lung defences and promotes disease progression. Eventually, the respiratory system is no longer able to maintain ventilation and meet the body's requirements for gas exchange thereby leading to respiratory failure.[25]

2.4 Treatment

The primary aim of CF treatment is to preserve lung function and slow the progression of lung disease by intervening early and preventing permanent lung damage.[25,27,28,74,79] The progression of CF lung disease is clinically defined by a decline in FEV_1, thus maintaining FEV_1 is important in clinical care.[51] This measure becomes predictive of ensuing respiratory failure and death once it is below 30% of the normative value.[80] The progressive loss of pulmonary function in people with CF is highly variable, but on average there is an annual loss of 2% of the FEV_1 value.[25,70] Studies show that permanent structural changes occur in the airways due to the CF disease while FEV_1 remains stable.[74] Thus, there is an inherent clinical assumption that the disease process is always ongoing and therefore treatment must also be ongoing.[28,29,74] The impairment of pulmonary mechanics makes it extremely challenging to clear the airway mucus and deliver inhaled therapies to the diseased lung regions. Consequently, the prevention and treatment of CF lung disease requires an intensive daily routine.[29,31,71,79]

The main pulmonary therapies comprising standard CF care include antibiotics, inhaled medications, and airway clearance all of which aim to mitigate the effects of the cyclical mucous plugging, infection, and inflammation.[29,39,79] Oral, inhaled, and intravenous antibiotics are used to eradicate and control intermittent and chronic pulmonary infections.[28,79] Other inhaled medications target specific properties of the mucus or airway in order to enhance mobilization of secretions, retained in the peripheral airways, and improve clinical outcomes. Dornase alfa is a

mucolytic that degrades the DNA content of CF mucus and has been shown to improve lung function and reduce the number of pulmonary exacerbations. [79] Hypertonic saline is a hydrator that increases the volume of the airway surface liquid. [81] It has been shown to reduce pulmonary exacerbations and improve lung function. [82] Salbutamol is a bronchodilator used to decrease smooth muscle tone and alleviate bronchoconstriction that can impede airflow and mucus movement in the airways.[31,83]

The administration of the majority of inhaled medications is timed with the use of ACTs in order to enhance the effects of these medications and/or airway clearance. [26,29,79,83-85] Guidelines for CF care recommend daily use of ACTs in order to compensate for the impairment of the mucociliary escalator and cough. [26,29,79,86,87] These techniques are physical means of removing retained mucus from the lung via the external or internal manipulation of airflow. [29] There are a number of ACTs recognized by the International Physiotherapy Group for Cystic Fibrosis (IPGCF). [34] Individuals with CF tend to use multiple techniques as no one technique is always appropriate, especially considering the need for airway clearance across the lifespan. [34,41] Airway clearance techniques are effective in improving mucus clearance in the short-term. [88] In theory, ACTs facilitate secretion clearance, diminish bacterial load and remove inflammatory by-products, which decreases infection and inflammation thereby reducing lung damage and preventing CF disease progression. [26,41] The removal of the mucus helps restore airflow through the airways and promote homogeneous ventilation of the lungs. [34]

The following airway clearance techniques are recognised by the IPCGF and are used by Canadians with CF.[34,56]

Postural Drainage and Percussion (PD&P)

Postural drainage and percussion involves patient positioning that aligns the main bronchiole of each lung segment with gravity while a percussive force is manually applied to the chest wall with a cupped hand. There are 6-12 positions with 3-10 minutes of percussion per position. The aim is to mobilize and drain mucus from the periphery of the lung. This was the original ACT used as the primary technique until the 1980s. [34]

Active Cycle of Breathing Techniques (ACBT)

Active cycle of breathing techniques is a combination of different breathing patterns that vary lung volume and expiratory flow. The components include TV breathing at FRC; large, sustained TLC breaths with exhalation to RV; and repeated, forced exhalations.[34] These components are combined in a cycle. ACBT is equivalent to other forms of airway clearance in removing mucus.[89]

Positive Expiratory Pressure (PEP)

Positive expiratory pressure, generated via exhalation through a one-way valve against resistance, recruits closed or obstructed lung regions using pressure between 10-20 cmH_2O. This increased pressure uses collateral ventilation to loosen and move mucus towards the larger airways where it can be expectorated. Huffing is used to enable expectoration.[34] PEP has been shown to reduce pulmonary exacerbations and is superior to high frequency chest wall oscillation airway clearance device based on this outcome.[90] Approximately 70% of the Canadian CF population uses PEP as an ACT.[91]

Oscillating Positive Expiratory Pressure (OPEP)

This is PEP with oscillation of the expiratory airflow, which creates vibration in the airways that loosens mucus and alters its rheology.[92] The positive pressure directs air through the collateral ventilation and helps support the airways.[34] Oscillating PEP is equivocal to other forms of airway clearance based on sputum expectoration.[93]

Autogenic Drainage (AD)

Autogenic drainage is a breathing pattern that requires an individual to alter the depth of their ventilation.[6] The individual uses TV breaths, with inspiratory pauses and controlled inspiratory and expiratory effort throughout the vital capacity of the lungs. The cycle starts in the expiratory reserve volume (ERV) and moves through FRC into the inspiratory reserve volume (IRV) in three defined stages. It aims to

create airflow throughout the lungs' full capacity and move mucus towards the larger airways where it can be expectorated.[1,5,7,35,94] Autogenic drainage is effective in clearing mucus and has been shown to increase FVC in the short-term.[9,10,95]

Autogenic drainage allows independence with airway clearance and does not require equipment.[4] This alleviates some of the burden associated with pulmonary therapies. The AD technique is unique because it involves the manipulation of airflow within the lung that is tailored to the individuals' lung disease and airway stability.[7,94] It is the only ACT that can be adapted in this way and therefore has great potential to be an integral component in the management of CF.

2.5 Autogenic Drainage

Autogenic drainage (AD) was introduced in the late 1960s by Jean Chevaillier, as a breathing pattern comprised of 3 stages each with a specific purpose.[1,5,7,8] The aim is to mobilize mucus from the small, peripheral airways to the large, central airways.[5,7] This must be done using the highest possible airflow throughout the bronchial tree while avoiding bronchospasm and/or airway collapse.[1,5,7] The AD breathing pattern is often depicted on a volume-time graph (Figure 2).

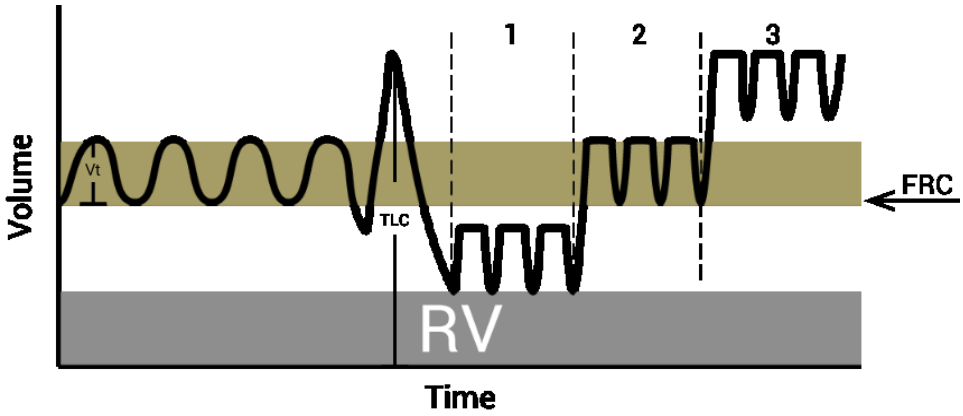

Figure 2: Autogenic Drainage Graph with phases 1,2,3; residual volume (RV), tidal volume (Vt), Functional Residual Capacity (FRC), and total lung capacity (TLC) indicated.

According to Chevaillier, the first stage "unsticks" the peripheral mucus using very low lung volume breathing at RV or well within the ERV. The second stage "collects"

the mucus in the medium sized airways using low to mid-lung volume breathing at or below functional residual capacity. The third stage "evacuates" the mucus to the large, central airways where it can be expectorated using high lung volume breathing in the inspiratory reserve volume. [1,5-7] The individual is expected to generate tidal volume breaths with a slow inspiration, followed by a 2-3 second pause with an open glottis, and a sigh-like exhalation. [3,8,43]

There have been multiple investigations of the effects of AD and the evidence to date suggests that AD is effective in clearing clinically significant amounts of mucus from the airways of people with CF. [10] Autogenic drainage has been shown to significantly improve oxygen saturation and yield as much sputum as postural drainage and percussion. [46] A study using scintigraphy demonstrated that AD can improve the ventilation of central and peripheral airways and mobilize mucus faster than ACBT. [96] It has also been shown to immediately improve specific airway resistance and forced vital capacity. [9,10,36,95] However, most of these studies were short-term investigations with small sample sizes. In addition, the studies used variations of the AD technique and compared it to at least one other ACT making the body of evidence very heterogeneous and difficult to assess. [3,9,10,46,92,95,97-103]

Although AD has been shown to effectively clear airway mucus, there is resistance to using it clinically as it is complex and time consuming, requiring concentration and body awareness by the patient. [42,47,104] This makes AD challenging to teach and difficult to learn. [5,42,104,105] A trained professional is required to guide the patient using tactile and auditory cuing in a one-on-one session. [5,7,8,43,104] The fidelity of AD technique is evaluated by observing the patient's chest wall movement and estimating the amount of mucus that is expectorated. [5,46] These are indirect measures of AD. To date, AD has not been quantitatively verified. Thus, the model of the AD breathing pattern remains theoretical.

2.6 Physiologic Rationale for Autogenic Drainage

Chevaillier developed AD based on his observations of children with obstructive lung disease and the effect of each child's breathing pattern on the mobilization of their retained secretions. [5] He noted that when these children

laughed, thereby exhaling deeply, or were sleeping and breathing in a relaxed manner the secretions were audible during exhalation.[5,6,8] He also noted this occurred when these children, many of whom tended to breathe at an elevated FRC, exhaled into their ERV.[6] Chevaillier's concept of AD was also influenced by theories on pulmonary mechanics that emerged around the time of his observations.[7,106,107] Chevaillier referred to AD as a "correlation between the inspiratory volume, the expiratory force, the mechanical properties of the bronchial tubes, the degree of obstruction, the compression phenomena, and the frictional resistance".[7] According to Chevaillier, when these components are "correlated" the highest possible airflow throughout the bronchial tree can be achieved and used for airway clearance.[5,7,8]

The AD breathing pattern is created by altering inspiratory and expiratory volumes and expiratory effort to influence the flow of air within the airways.[7] Air flows through the airways following a gradient from high to low pressure between the alveoli and mouth.[72,77] Alveolar pressure is determined by the elastic recoil of the lung and the pleural pressure. Lung elastic recoil is the inward force of the lung tissue created by the elastic components of the airway, the lung parenchyma, and the connections between them. Pleural pressure surrounds and acts on the lung tissue inwardly and outwardly depending on the action of inspiratory and expiratory muscles on the chest wall.[72,77,108] Since atmospheric pressure is constant, alveolar pressure determines the driving pressure and resultant airflow. Alveolar pressure is greatest at high lung volumes where the lung elastic recoil and pleural pressure are both acting inwardly on the lung.[77] Thus, inspiratory lung volume is a major determinant of expiratory airflow.

The breath holds in the AD breathing pattern are used to enhance the volume of inspired air by allowing ample alveolar filling time and take advantage of its influence on airflow. When airway resistance is increased, it takes longer for air to fill the alveoli. This results in an elevated inspiratory time constant, thus air continues to flow into the alveoli after the inspiratory phase has ended.[72] The breath holds augment inspired volume and subsequently expiratory flow. Expiratory airflow is also influenced by expiratory effort.[77,106,107] At the onset of an active or forced exhalation the inspiratory muscles relax, the expiratory muscles

contract, the chest volume decreases, and pressure in the pleural space rises generating an expiratory pressure gradient.[77] Pleural pressure is determined by the balance of forces generated by the inspiratory and expiratory muscles acting on the chest wall and thus is affected by expiratory effort.[77] Pleural pressure is also a key component of the equal pressure point (EPP) phenomenon, which is central to Chevaillier's theory of AD. The concept of the EPP was developed by Mead et al and predicts expiratory airflow limitation based on the relationship between lung recoil (inspired volume) and the resistive pressure drop along the airway (Figure 3).[106]

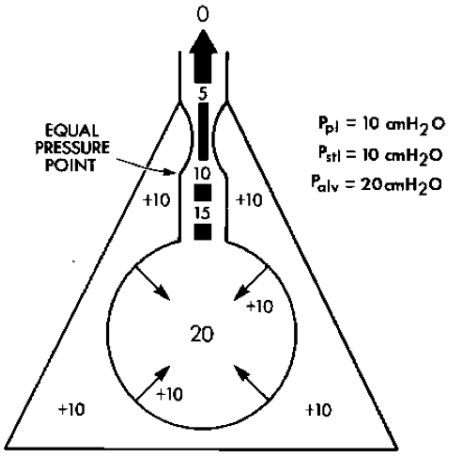

Figure 3: Schematic of the airway and surrounding lung tissue with a depiction of the relationship between pleural pressure (P_{pl}), elastic recoil (P_{stl}), and alveolar pressure (P_{alv}). The equal pressure point occurs where the intrabronchial pressure and pleural pressure are equal.[73]

As air flows through the airways during a forced exhalation, a pressure drop occurs due to frictional resistance. This results in a point where the intrabronchial pressure becomes equal to the pleural pressure.[77,106] Beyond the EPP, that is downstream or towards the trachea, a site of flow limitation is created when the airway becomes compressed by the dominant, inward force of the pleural pressure.[106] According to the Bernoulli effect, this airway compression creates a point of gas acceleration, assuming the airways are compressed but not collapsed.[77] The Bernoulli principle states that an increase in velocity will occur at a point of narrowing in order to maintain flow at the expense of pressure.[77] Chevaillier theorized that the EPP and

subsequent acceleration of air could shear mucus from the airway walls and transport it downstream.[5,7]

In order to use EPPs for airway clearance, Chevaillier proposed that one must manipulate the inspired and expired volumes as well as the expiratory effort since they determine pleural pressure and thus the position of the EPP. At a low lung volume the lung elastic recoil and the alveolar pressure are low. Thus, the driving pressure and flow rates are small placing the EPP in the lung periphery. At high lung volumes elastic recoil and pleural pressure are high thereby generating a steep pressure gradient to drive airflow.[77,106] In this case, the intrabronchial and pleural pressures equalize much farther downstream and the EPP occurs in the larger airways. According to Macklem, the EPP can be localised to the small, peripheral airways when lung volume is below FRC, and positioned at the segmental or lobar bronchi when lung volume is above FRC.[107] This corresponds to the first and third phases of Chevaillier's AD breathing pattern.

The effective mechanism of the AD breathing pattern is attributed to airway caliber changes.[5] Chevaillier's theory focuses on accelerating airflow by affecting airway caliber however this rationale can be challenged when applied to low lung volume breathing. In healthy lungs, breathing at low lung volumes results in airway closure, hence it most likely occurs in CF lungs as the airways are inherently unstable due to weakness associated with chronic inflammation and infection.[72,108] However, active exhalation at low lung volumes may still mobilize mucus from the peripheral airways. Schöni described the initial "unsticking phase" of AD to be in the range of closing volume, the lung volume at which airway closure begins to occur.[5,7,108] Schöni suggested that secretions are mobilized from the peripheral lung regions by compression of peripheral alveolar ducts.[5] Van der Schans described this clearing of secretions as "milking" the airways.[109] Macklem equated this phenomenon to "squeezing toothpaste out of a tube."[107]

Chevaillier's application of airflow acceleration principles is reasonable for AD breathing at mid and high lung volumes where EPPs are occurring in airways that have more structurally supportive components. Cystic fibrosis lung disease is heterogeneous with respect to severity and location. Chevaillier seemed well aware

of these pathological effects when he stated that exhalation must be performed with sufficient force to generate EPPs and induce airflow acceleration without causing bronchospasm and collapse. [5,7,8] Excessive expiratory effort may generate pleural pressures that are higher than those at the EPP and cause airway collapse downstream of the EPP. [77] Thus, it is very important to adjust the expiratory effort to create a pleural pressure that will promote airflow.[7,34]

Maximal expiratory flow does not equate to maximal expiratory effort, [77] hence Chevaillier's description of a "sigh-like" manoeuver for the expiratory phase of AD. This point is illustrated by isovolume-flow curves in Figure 4.

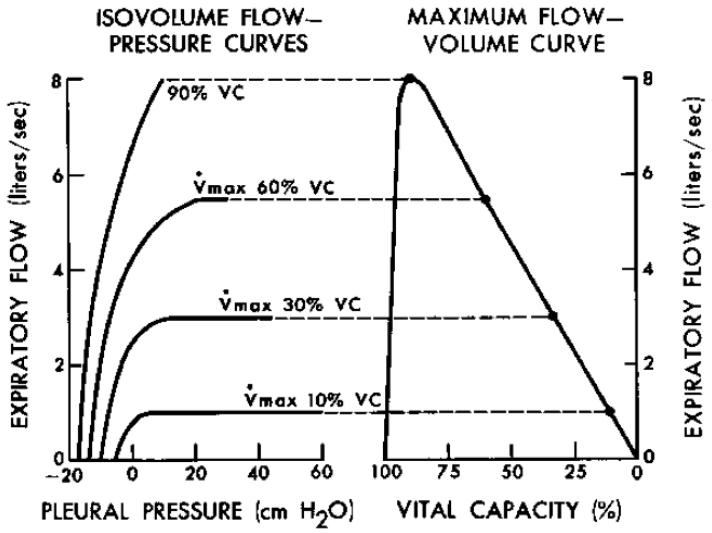

Figure 4: A series of isovolume flow-pressure curves with associated maximum flow-volume curves. Maximal expiratory flows (Vmax) and associated pleural pressure at specific lung volumes expressed as a percentage of vital capacity (VC).[73]

These curves demonstrate the relationship between pleural pressure (expiratory effort) and airflow at various lung volumes. Expiratory effort increases pleural pressure, indicated on the x-axis. The expiratory flow rate peaks in each plot despite increases in pleural pressure. The point at which flow plateaus despite increasing pleural pressure marks the beginning of the effort-independent flow. [77] The maximum flow-volume curve on the right in Figure 4 is a composite of the

individual plots and illustrates effort-independent expiratory airflow through the full lung volume.

Early investigations that compared AD to maximal forced exhalations using superimposed flow-volume loops support the theory that higher expiratory flows can be achieved using AD technique compared to forced expiratory manoeuvres. [5,36,42,94] These flow-volume loops (Appendix A) demonstrate that expiratory flow rates generated by AD can equal or exceed the expiratory flows generated by a maximal forced expiratory manoeuvre. [5,36,42,43] Although these flow-volume loops do not depict every phase of AD, other investigators have provided preliminary evidence of the effect of AD on expiratory airflow at low, mid, and high lung volumes. [37] McIlwaine et al studied 14 patients with CF aged 13-18 years and found mean peak expiratory flow rates of 47.7 ± 17 L/min, 85 ± 28.6L/min, 115 ± 31.7L/min corresponding to the low, mid, and high lung volume stages of AD. [110] These flow rates are within the range (30-60L/min) that Kim and colleagues suggest is necessary to mobilize viscoelastic secretions.[111]

There is a strong physiologic rationale for the mechanism of action of AD. Many variations of the technique have arisen in the literature and in practice (Appendix B) due to the lack of an objective, quantitative definition. [5,8,42,43] Explanations of AD in the published literature differ with respect to TV and the volume at which the breaths occur within the lungs' capacity (the end expiratory lung volume). [40,42,87,104,112-114] Clarifying the definition of AD and providing a method to determine whether the technique is being performed correctly would encourage more clinicians to use the technique and facilitate research regarding its effectiveness. Therefore, the purpose of this thesis is to quantify AD technique and evaluate the performance of AD in a healthy group of adolescents, using a new assessment method.

CHAPTER 3 OBJECTIVES & HYPOTHESIS

The objectives of this study are to:

1) develop a quantitative definition of AD

2) develop a method for evaluating this AD definition,

3) assess the achievability of the AD definition in a healthy group of adolescents.

The hypotheses for this study are:

1) that I will be able to develop a quantitative definition of AD.

2) that the criteria used to define AD are measureable using spirometry and plethysmography.

3) that healthy adolescents can achieve the lung volumes that define AD as measured by this new measurement protocol.

    i) The participants' ability to learn AD will not limit the performance of AD.

    ii) The physiotherapists' ability to teach AD will not limit the participant's performance of AD.

CHAPTER 4 METHODS

4.1 Overview

There were 3 parts to this project that involved the development of: a quantitative definition for the AD breathing pattern, a measurement protocol to evaluate the performance of the AD breathing pattern, and an observational study to test these tools. The quantitative definition of the AD breathing pattern was based on Chevaillier's qualitative description of AD, the descriptions in the scientific literature, pilot data, and analysis of the proportional relationship between normal lung volumes. The definition informed a measurement protocol for the performance of AD using spirometry and plethysmography. An observational study of AD performance was then conducted in a cohort of healthy adolescents at the IWK Health Centre Chest Clinic. The study protocol was approved by the IWK Research Ethics Board #1021114.

4.2 Development of the Quantitative Definition of AD

The defining feature of the AD breathing pattern is the EELV.[7] Chevaillier categorized the lung volumes that corresponded to each phase of AD, however the descriptions were vague. Phase 1 was described as "very low (expiratory reserve volume)", Phase 2 as "low (expiratory reserve volume ± TV)", and phase 3 as "high (± vital capacity)".[5,7] Since that time, other authors have used FRC to identify the phases of AD. During phase 1, TV is "lowered below FRC into the range of ERV but not to RV".[5,43,96] During phase 2 breaths are taken "in the range of FRC" "at mid lung volume".[6,43] During phase 3 breaths are taken at "mid IRV".[5,43]

In this study, pilot data were used to mathematically determine the possible range of EELV associated with each phase of AD, according to the available qualitative descriptions.[5-7,43,94,96] The pilot data were acquired from eight patients with CF aged 7-16 years. Each patient signed a consent form allowing their data to be used, without their identifying information, for research and teaching purposes. The patients had a range of pulmonary function from normal to moderate airway

obstruction, as determined by a standard pulmonary function test, including plethysmography. [48,51] The patients were taught AD and asked to practice the technique daily. They returned for evaluation 2 weeks to 3 months later and performed AD twice on a Sensormedics Spirometer - Body Plethysmograph System (Viasys Healthcare, California, USA). Their breathing pattern was recorded using change in volume over time on the Sensormedics system software.

The graph that best resembled the model AD graph (Figure 2) was selected and printed. Figure 5 is a sample of one patient's graph. The y-axis of each spirometry graph, representing volume, was marked in millimetres (mm). All measurements of volume were determined according to the 1mm scale. The distance from the x-axis to the lowest point of the trough of each sine wave in the spirometry graph was measured with a ruler marked in 1mm gradations. The average distance to the troughs of the initial tidal breaths of the AD breathing pattern was used as the reference point and assumed to represent FRC. All remaining troughs were measured and a mean value was used to represent the EELV for each phase and was expressed as a percentage of the reference point. The estimated EELVs (Table 1) achieved for each phase of AD in the pilot data were quite variable, ranging from 10-55% of FRC in Phase 1, 30-155% of FRC in Phase 2, and 140-233% of FRC in Phase 3.

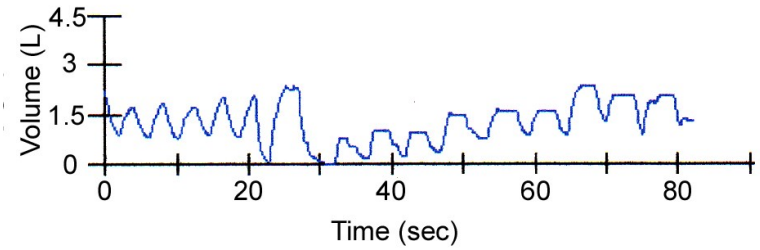

Figure 5: Sample of spirometry during an AD trial.

Table 1: Pilot Data of estimated End Expiratory Lung Volume (EELV) for Phase 1 ($EELV_1$), Phase 2 ($EELV_2$), Phase 3 ($EELV_3$) and estimated Functional Residual Capacity (FRC) during Autogenic Drainage

SUBJECT	PARAMETER	VOLUME (L)	PERCENT of FRC
1	$EELV_1$	0.4	44%
	$EELV_2$	1.4	155%
	$EELV_3$	2.1	233%
	FRC	0.9	
2	$EELV_1$	0.2	20%
	$EELV_2$	1.1	110%
	$EELV_3$	2.2	220%
	FRC	1.0	
3	$EELV_1$	0.2	55%
	$EELV_2$	0.6	66%
	$EELV_3$	1.7	188%
	FRC	0.9	
4	$EELV_1$	0.3	43%
	$EELV_2$	0.7	100%
	$EELV_3$	1.2	171%
	FRC	0.7	
5	$EELV_1$	0.3	37%
	$EELV_2$	0.7	87%
	$EELV_3$	1.2	150%
	FRC	0.8	
6	$EELV_1$	0.3	37%
	$EELV_2$	0.6	75%
	$EELV_3$	1.4	175%
	FRC	0.8	
7	$EELV_1$	0.1	16%
	$EELV_2$	0.4	66%
	EELV3	1.2	200%
	FRC	0.8	
8	$EELV_1$	0.1	10%
	$EELV_2$	0.3	30%
	$EELV_3$	1.4	140%
	FRC	1.0	

The pilot data provided a broad range of volumes that were achievable in each phase of AD. These were used in conjunction with Needham's normative lung volume data for adolescents aged 11-19 years to determine the proportional relationship of TV to FRC, VC, ERV, and IRV.[115] According to Needham's data, TV is approximately 29% of FRC.[115] Therefore, in Phase 1 of AD, if TV was completely below FRC the EELV would be quantitatively defined as approximately 30% of FRC below FRC. This would occupy 60% of ERV. Phase 2 of AD is TV breathing at an EELV equal to FRC. The normal variability of TV is ±10%, which translates to ±3% of FRC in Needham's data.[115,116] Since the published descriptions of Phase 2 along with the pilot data range are very broad, I determined that it was reasonable to expect one to breathe ±10% of FRC at FRC. Phase 3 of AD involves TV breathing above FRC. The criterion for Phase 1 of 30% of FRC could not be applied to Phase 3 as it would overlap the Phase 2 EELV. Therefore, 40% of FRC above FRC (i.e. 140% of FRC) was proposed in order to create a distinct minimum criterion to define the EELV for breathing at a high lung volume. This was the lower range in the pilot data and theoretically probable within the range of IRV, since TV was estimated to be 35% of IRV. The quantities for each phase of AD were examined in the context of vital capacity. According to Needham's data, it is possible to complete 5-7 sequential phases of breathing using EELVs that are equivalent to TV.[115] Since AD technique requires 3 different EELVs of TV breathing that must be distinct from one another, the proposed definitions appeared to be reasonable and theoretically probable in the context of lung volumes. These definitions were supported by the pilot data.

Following review of all available information and data, the EELV was defined and related to FRC for each phase of the AD breathing pattern.[1,5,7] Tidal volume breathing was defined according to the TV achieved in the preparation phase of AD, the 4 initial breaths at FRC (V_{trest}). The following parameters were proposed to quantitatively define each phase of AD:

- Preparation Phase: Initial tidal volume breaths (V_{trest}) at FRC, a minimum of 4 breaths
- Phase 1: change of EELV of greater than or equal to 30% of FRC below FRC

- Phase 2: change of EELV of ±10% of FRC above or below FRC
- Phase 3: change of EELV of greater than or equal to 40% of FRC above FRC
- Average TV in each phase of AD (V_t) is ±10% of the average V_{trest}, measured in the preparation phase.

4.3 Measurement Protocol

4.3.1 Spirometry and Plethysmography

Spirometry measures inhaled and exhaled volumes. A Vmax Vyntus™ SPIRO (CareFusion, Yorba Linda, CA, USA), donated by Cardinal Health, was used to quantify V_t and EELV. Testing was performed in the Chest Clinic at the IWK Health Centre. The spirometer was set to the slow vital capacity setting to measure the change in volume over time. Each participant completed the AD breathing pattern on the spirometer three times and the data was saved in the system's software, SentrySuite®.

Plethysmography was used to measure the volume of gas remaining in the lungs (FRC).[49] A Vmax® Encore system (CareFusion, Yorba Linda, CA, USA) was used to conduct a standard pulmonary function test, including plethysmography, according to American Thoracic Society (ATS) guidelines.[48,50,51] This was completed in the pulmonary function lab at the IWK Health Centre.

4.3.2 Instrumentation

The technical specifications of the Vmax Vyntus™ SPIRO (CareFusion, Yorba Linda, CA, USA) (Appendix C) were reviewed to ensure the measurement variability was not greater than the expected variability in the quantitative definition of AD. The spirometer contained a mass flow sensor with a range of 0.1-16 Litres per second (L/s). It had a volume accuracy of ±3% of the reading or 0.05 Litres (L) whichever was greater, across a range of 0.5-8L. It had a resistance of < 0.51 $cmH_2O/L/s$ at 10 L/s. The volume accuracy of the spirometer was well within 20-30% variability accounted for in the quantitative definition of AD and within the accepted norm for TV variation.[115,116]

The systems exceeded the ATS standards for assessment of pulmonary function.[48,50] The calibration of the equipment was completed daily, according to ATS guidelines,[48,50,51] prior to the start of the first participant.

4.3.3 Testing of Measurement Protocol

The measurement protocol was tested by the principle investigator using self-generated data (Appendix D). I completed one cycle of the AD breathing pattern on the Vmax® Encore system (CareFusion, Yorba Linda, CA, USA), as well as a standard pulmonary function test, including plethysmography. The EELV for each AD phase was measured and extracted from the SentrySuite® software, then expressed as a percent of FRC. The results for AD Phases 1, 2, and 3 were 45% of FRC below FRC, 3% of FRC below FRC, and 52% of FRC above FRC respectively. The variability in the measurement was ±0.06L. This met the EELV criteria for the proposed quantitative definition of AD.

4.4 Observational Study

4.4.1 Recruitment of Participants

Healthy adolescents, aged 12-18 years, were recruited from the Halifax Regional Municipality and surrounding area using advertisements and social media posts (Appendix F). The potential candidate (age 16-18 years) or parent (when the adolescent was age 12 to 15 years) emailed the principle investigator to express interest in participating in the study. The principle investigator replied via email with a brief summary of the study and a screening questionnaire (Appendix G). Exclusion criteria were self-reported and included: smoking, presence of a respiratory condition, a learning disability, an impairment of attention, or inability to follow instructions given in English. Once the potential candidate or parent confirmed they qualified to participate in the study, an appointment was made to attend the study.

4.4.2 Procedures

The study protocol (Figure 6) required one 90-minute visit for each participant. The principle investigator, the physiotherapist, and an independent assessor carried out the protocol. The principle investigator reviewed the protocol, gave the individual (and parent) the opportunity to ask questions, and obtained written consent (participant aged 16-18 years) or parental authorization and participant assent (participant aged 12-15 years).

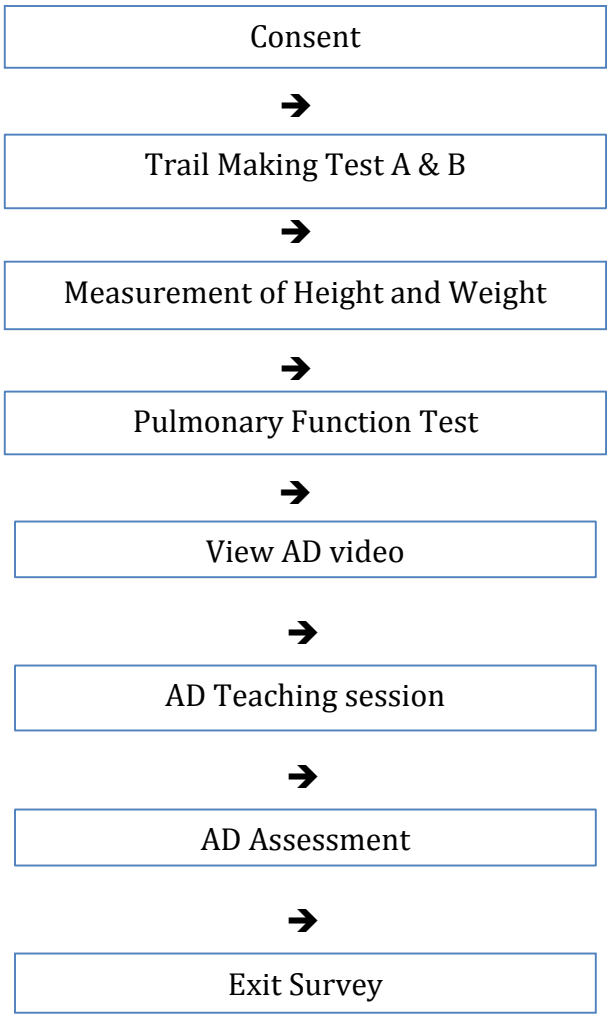

Figure 6: Summary of Procedures

Each participant completed the Trail Making Test A & B (Appendices H and I, respectively), from the Halstead-Reitan Neuropsychology Test Batteries for Children. [117,118] Together, they are a general test of attention that reflects the overall integrity of general brain function. [119] The Trail Making Test A (TMT A) is a test of speeded attention, mental tracking, and visual search while the Trail Making Test B (TMT B) assesses sequencing, mental flexibility, and set shifting. [119] The time for correct completion of the sequential connections between the letters and numbers was recorded and compared to normative values. [117,118,120]

The principle investigator measured the participant's height (in centimeters) and weight (in kilograms) using a mechanical stadiometer and a digital scale, respectively. The participant then completed a standard pulmonary function test, including plethysmography, according to ATS standards. [48,50,51]

The participant was introduced to the assessor who operated the spirometer of AD assessment. Each participant was given a copy of the AD graph as per the teaching protocol (Appendix I) and told, using a standard script, the meaning of the direction of the lines: "an ascending/uphill line means breathe in, a horizontal/flat line means breath hold, a descending/downhill line means breathe out". The participant was instructed to "breathe how the graph is showing you to breathe". S/he kept the graph for reference and proceeded to the AD teaching session.

The participant was introduced to the physiotherapist who would teach AD and viewed a video of an adolescent performing AD. The teaching session was standardized (Appendix I). The physiotherapist explained AD using the reference graph and demonstrated a complete AD cycle. All AD instructions were based on those outlined by the IPGCF, as per Jean Chevaillier. [1] The participant then tried to breathe according to the AD pattern while following concurrent verbal instructions given by the physiotherapist. The participant then practiced the AD cycle 4-5 times during which the physiotherapist provided verbal cuing and coaching on their technique from the physiotherapist during and/or after each cycle. The cues were aimed at helping the participant achieve the lung volumes used to define AD. The participant then donned nose clips and breathed through a spirometer mouthpiece in the final 2 practice cycles in order to habituate to the conditions under which

their AD performance would be assessed. The teaching session did not exceed 30 minutes and the participant performed a maximum of 6 AD cycles.

Following the teaching session, the participant's performance of AD was measured by the assessor using Spirometry. The participant sat against the backrest of a chair with their feet on the floor. The participant donned nose clips, then as per the teaching protocol, placed one hand on their abdomen and one hand on their upper chest for tactile feedback. The assessor held the spirometer head at the participant's mouth and the participant proceeded to breathe into the spirometer according to the AD pattern. The participant was blinded to the spirometer screen so s/he could not see their AD volume-time graph during the assessment.

Following the quantitative assessment of AD, the participant and the physiotherapist each went to a quiet room to complete a questionnaire (Appendix K and L, respectively) about the AD teaching session. The aim of the survey was to gather information about factors that may have influenced the participant's performance. The survey instructions were standardized and neither the participant nor the physiotherapist knew the results of the AD assessment before completing the survey. Participants were given a copy of their signed consent/assent form, a $25 itunes gift card for their contribution to the study, a certificate of participation, and $10 towards parking and transportation expenses.

The pulmonary function tests collected during the study were reviewed by a Pediatric Respirologist to determine if results were normal. [48,50,121-124] This information was included in the analysis of the study results.

4.4.3 Data Extraction

Data were manually extracted from the AD graphs (Figure 6) produced by the Vmax Vyntus™ SPIRO (CareFusion, Yorba Linda, CA, USA) SentrySuite® software. Each EELV was determined using a mouse and cursor to align measurement bars with the peaks and troughs of the sinusoidal waveform. The main measurement bar (bold, black line in Figure 6) was aligned with the trough of the first complete sine wave. The second measurement bar was aligned with the trough of each subsequent sine wave in the 3 phases of the AD breathing pattern to obtain the EELV for each

breath (Figure 7). Tidal volume was measured by aligning the main measurement bar with the peak of the sine wave and the second measurement bar with the trough of each sine wave. Data extraction was performed by the research assistant and confirmed by the principle investigator. The FRC value for each participant was obtained from the pulmonary function report. All data were entered into SPSS by the research assistant and the data set was reviewed by the principle investigator.

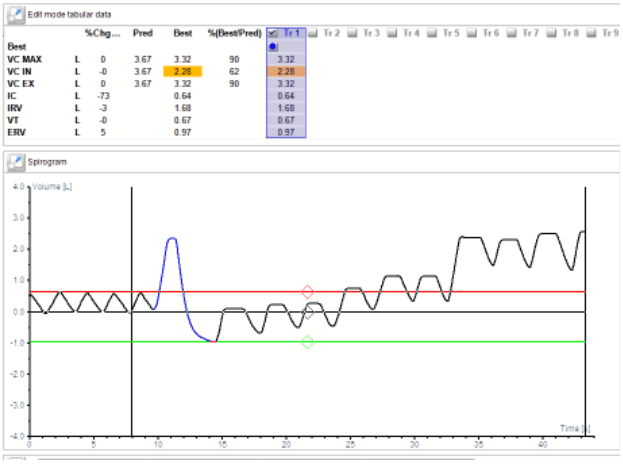

Figure 7: Spirometric volume-time graph representing the AD breathing pattern. The bold, black horizontal line (main measurement bar) and the horizontal line above it (secondary measurement bar) are aligned with the peak and trough, respectively, of the first complete sine wave. All measures were determined using the main measurement bar and a secondary measurement bar, according to the position of the trough of each sine wave.

4.4.4 Data Analysis

Data analysis in this study examined the AD performance of healthy individuals to determine if the definition was achievable. Each spirometry assessment trial (n=96) was included in the data analysis. All calculations and statistical tests were completed using SPSS Statistics software (IBM® SPSS® Statistics, Version 23).

1. a) The spirometry software was used to identify:

I. the V_{trest} for each of the 4 breaths in the preparation phase of AD
II. the EELV of each breath in each of the 3 phases in the AD cycle
III. the V_t of each breath in each of the 3 phases of AD.

b) The following values were calculated for each participant for each Phase of AD:

I. Mean V_{trest}: average of 4 initial breaths
II. Mean V_t: average of the 3 breaths per phase
III. Mean EELV: average of 3 breaths per phase

c) The Mean V_t was normalized by expressing it as a percentage of the trial mean V_{trest} for each participant. The mean EELV was normalized by expressing it as a percentage of FRC for each participant. The mean of the 3 trials for each participant was compared to the a priori quantitative definition and the participant success rate was calculated.

d) The grand means of the normalized V_t and EELV for the group were calculated for each AD Phase along with the following descriptive statistics: standard deviation, median, minimum, maximum, skewness, and kurtosis. The grand means were compared to the a priori quantitative definition of AD to determine if the group results met the defining criteria.

2. The defining features of AD are the 3 distinct EELVs with a consistent V_t across the Phases. Parametric testing would permit analyses of the differences in these variables across phases and trials. This would help determine the accuracy and consistency of AD performance by the group during the measurement process. Therefore, normality tests were conducted on the normalized V_t and EELV for each AD Phase. [125-127] Some of the data were not normally distributed. Thus, all of the data were transformed using Log10 to allow parametric testing. [125,128] Normality tests were repeated on the transformed data.[125,126,128]

3. In order to determine if the cohort performed AD according to the definition a one-way repeated measures analysis of variance (ANOVA) with a factor of time (3 levels) was used to determine if the EELV and V_t was significantly different for each Phase. The significance level was set at $p<0.05$. The participant demographics and results of the lung function and Trail Making Tests were tested in the one-way

repeated measures ANOVA when a significant difference was found. One-way repeated measures ANOVAs were performed on the transformed data to compare:

i) The grand mean EELV for all 3 trials for each AD phase.

ii) The grand mean V_t for all 3 trials for each AD phase.

iii) The mean EELV for each AD phase across trials.

iv) The mean V_t for each AD phase across trials.

4. The survey data from the physiotherapist and the participants were compiled and examined to determine if factors in the teaching and learning process influenced AD performance. The percentage of the responses for each component of the likert scale were calculated and summarized. The data was reviewed to determine if there any negative influences identified by the physiotherapist and/or participants.

CHAPTER 5 RESULTS

5.2 Participants

Recruitment for participants occurred from June to September 2016. Thirty-two adolescents were recruited and completed the study protocol during this time. Participant characteristics displayed in Table 2. The mean age of the participants was 14.8 years with all ages from 12 to 18 years represented. Fifty-nine percent of participants were female. The results of the lung function and Trail Making Tests are displayed in Table 3. Lung function was abnormal in 4 participants. The TMT results were outside the normative range for 6 participants on the TMT A and 4 participants on the TMT B.

Table 2: Characteristics of Participants

Age (years)	Number of Participants (% of Total Participants)	Number of participants who were female/male
12	6 (19%)	3/3
13	1 (3%)	1/0
14	8 (25%)	3/5
15	2 (6%)	2/0
16	8 (25%)	4/4
17	5 (16%)	4/1
18	2 (6%)	2/0

Table 3: Pulmonary Function Test and Trail Making Test A & B Results

Tests	Number of Participants with Normal Results	Number of Participants with Abnormal Results
Pulmonary Function Test	28	4
TMT A	26	6
TMT B	28	4

5.2 Lung Volumes

The normalized mean EELV and mean V_t per AD Phase are displayed in Tables 4 and 5, respectively. The AD definition was achieved in Phase 3 EELV and Phase 2 V_t. All means met their respective definition or were within one standard deviation of the defining mean. The percentage of participants that achieved the definition for each component of AD is summarized in Tables 4 and 5. A substantial number of participants were able to achieve the defined lung volumes for each AD phase following an initial AD teaching session. A total of 6 participants achieved the EELV for all AD phases and 1 participant achieved the V_t for all AD phases. None of the participants achieved the definition for EELV and V_t in all phases of AD.

Table 4: Cohort mean EELV normalized to FRC for the AD Phases

AD Phase	Cohort Mean EELV expressed as a percent of FRC (SD)	Definition of EELV	Percentage of Participant Success
1	26% (12%)	≥ 30% of FRC	38%
2	16% (10%)	± 10% of FRC	40%
3	55% (24%)*	≥ 40% of FRC	78%

Participant success in meeting the AD definition is described by percentage of participants. *AD quantitative definition was achieved. AD = autogenic drainage; EELV = end expiratory lung volume; FRC = functional residual capacity; SD = standard deviation.

Table 5: Cohort mean V_t normalized to V_{trest} for the AD Phases

AD Phase	Cohort Mean V_t expressed as a percent of V_{trest} (SD)	Definition of V_t	Percentage of Participant Success
1	87% (29%)	90-110% of V_{trest}	19%
2	108% (35%)*	90-110% of V_{trest}	22%
3	138% (53%)	90-110% of V_{trest}	25%

Participant success in meeting the AD definition is indicated by percentage of participants. *AD quantitative definition was achieved. AD = autogenic drainage; V_t = quantified tidal volume; V_{trest} = quantified tidal volume in preparation phase of AD; SD = standard deviation.

The descriptive statistics and results of the normality tests for the normalized lung volumes are displayed in Table 6. The range of results was broad for EELV and V_t in all AD phases. The standard deviation was substantial for all except EELV in Phases 1 and 2. The data were normally distributed in Phase 1 EELV and Phase 1 V_t only. Therefore, all of the data were transformed using logarithm 10 to permit parametric testing.[125,129]

Table 6: Descriptive statistics for normalized mean EELV and mean V_t for the AD Phases

Lung Volume	Mean	Standard Deviation	Median	Minimum	Maximum	Skewness	Kurtosis	Test of Normality p-value
EELV Phase 1	26%	12%	26%	6%	45%	.064	-1.010	p=.153
EELV Phase 2	16%	10%	13%	4%	47%	1.598	2.493	p=.000*
EELV Phase 3	55%	24%	24%	16%	142%	1.623	4.722	p=.003*
V_t Phase 1	87%	29%	81%	38%	148%	.326	-.567	p=.524
V_t Phase 2	108%	35%	99%	59%	192%	.913	.122	p=.021*
V_t Phase 3	138%	53%	130%	63%	338%	1.664	5.129	p=.002*

The p-values for each test of normality are listed. *Data deviated from a normal distribution. AD = autogenic drainage; EELV = end expiratory lung volume; V_t = quantified tidal volume.

The transformed data and normality test results are displayed in Table 7. All data were normally distributed, except for $EELV_{Log10}$ Phase 1, which was approaching normality.[127,128]

Table 7: Descriptive statistics for Log_{10} transformed lung volume data

Lung Volume	Mean	Standard Deviation	Median	Minimum	Maximum	Skewness	Kurtosis	Test of Normality p-value
$EELV_{Log10}$ Phase 1	-.6493	.24988	-.5926	-.1.19	-.34	-.764	-.396	p=.013*
$EELV_{Log10}$ Phase 2	-.8761	.26318	-.8966	-1.40	-.33	.174	-.244	p=.843
$EELV_{Log10}$ Phase 3	-.2961	.18202	-.3054	-.80	.15	-.251	1.402	p=.761
$V_{t\ Log10}$ Phase 1	.0027	.13807	-.0718	-.20	.30	.610	-.303	p=.164
$V_{t\ Log10}$ Phase 2	.0358	.13977	.0212	-.29	.34	-.185	.249	p=.979
$V_{t\ Log10}$ Phase 3	.0243	.15489	-.0050	-.28	.35	.174	-.748	p=.701

Log_{10} of normalized mean EELV and mean V_t. The p-values for each test of normality are listed. *Data deviated from a normal distribution. EELV = end expiratory lung volume; V_t = quantified tidal volume; Log_{10} = Base 10 logarithm.

The transformed EELV and V_t for all trials were compared by phase using a repeated measures ANOVA i.e. Phase 1 compared to Phase 2 compared to Phase 3 for each lung volume. The results are displayed in Table 8. There was a statistically significant difference in the EELV across the AD Phases (p=.000). Pairwise comparisons revealed there was a statistically significant difference between EELV Phase 1 and 2 (p=.007), Phase 2 and 3 (p=.000), and Phase 1 and 3 (p=.000). A factor analysis revealed there was no influence on EELV across phases by the following factors: age {F(1, 25) = .575, p>0.05}, sex {F(1, 30) = .512, p>0.05}, lung function {F(1, 30) = .343, p>0.05}, TMT A {F(1, 30) = .366, p>0.05}, TMT B {F(1, 30) = .107, p> 0.05}. There was no significant difference in the V_t for AD Phases 1,2, or 3 (p=.137).

Table 8: Results of the one-way Repeated Measures ANOVA comparing EELV and V_t for AD Phases 1,2, 3 by phase

Lung Volume	Source of Variation	df	Sums of Squares	Mean Square	F-statistic	p-value
$EELV_{Log10}$	Group	1.479	5.469	3.698	43.758	.000*
	Error	45.847	3.874	.085	-	-
V_{tLog10}	Group	2	.018	.009	2.056	.137
	Error	62	.273	.004	-	-

***Denotes a statistically significant difference. df = degrees of freedom; EELV = end expiratory lung volume; V_t = quantified tidal volume; Log_{10} = Base 10 logarithm.**

A one-way repeated measures ANOVA was used to compare the EELV for each AD Phase across the 3 trials i.e. Phase 1 EELV of Trial 1 compared to Trial 2 compared to Trial 3. The results are displayed in Table 9. There was a statistically significant difference in Phase 1 EELV ($p<.05$). Pairwise comparisons revealed there was a statistically significant difference between Trials 1 and 2 ($p<.05$). There was no statistically significant difference between Trials 2 and 3 ($p>.05$) and Trials 1 and 3 ($p>.05$).

A one-way repeated measures ANOVA was used to compare the V_t for each AD phase across the 3 trials i.e. V_t Phase 1 Trial 1 compared to Trial 2 compared to Trial 3. There was a significant difference in the V_t Phase 3 across trials. Pairwise comparisons revealed that Trial 1 was significantly different from Trial 2 ($p<.008$). There was no significant difference between Trials 2 and 3 ($p>.05$) and Trials 1 and 3 ($p>.05$).

Table 9: Results of one-way Repeated Measures ANOVA comparing EELV and V_t for AD Phases 1,2, 3 by trial

Lung Volume	Source of Variation	df	Sums of Squares	Mean Square	F-statistic	p-value
$EELV_{Log10}$ Phase 1	Group	2	.163	.082	3.429	.039*
	Error	60	1.427	.024	-	-
$EELV_{Log10}$ Phase 2	Group	2	.274	.137	1.696	.192
	Error	62	5.006	.081	-	-
$EELV_{Log10}$ Phase 3	Group	2	.080	.040	2.177	.122
	Error	62	1.137	.018	-	-
V_{tLog10} Phase 1	Group	2	.013	.007	.806	.451
	Error	62	.510	.008	-	-
V_{tLog10} Phase 2	Group	2	.010	.005	1.015	.368
	Error	62	.305	.005	-	-
V_{tLog10} Phase 3	Group	2	.045	.022	3.418	.039*
	Error	62	.405	.007	-	-

***Denotes a statistically significant difference. df = degrees of freedom; EELV = change in end expiratory lung volume; V_t = quantified tidal volume; Log_{10} = Base 10 logarithm; AD = autogenic drainage.**

5.3 Teaching and Learning

The physiotherapist who conducted the AD teaching session and all participants completed exit surveys at the end of the appointment. There were a total of 64 surveys completed. The results of the exit survey completed by the physiotherapist are displayed in Figures 3,4, and 5. The majority of participants were described as attentive. Approximately half of the participants were able to verbally describe the AD breathing pattern adequately. One participant was unable to follow instructions given by the physiotherapist. Most participants incorporated the physiotherapist's feedback and demonstrated observable changes in their chest wall movement during AD. At least 28% of the participants seemed to be able to perform AD properly and the physiotherapist did not have any concerns about the methodology used for AD instruction.

The average length of the AD teaching session was 15 minutes and 44 seconds (Figure 9). Fifty percent of the participants completed the session in 15 minutes. The majority of participants (n=30) completed 5 cycles of AD in total prior

to being assessed. Only 1 participant felt they were not ready for the AD assessment. No participant requested to end the AD teaching session nor did any request additional practice. The most common reasons for ending the AD teaching session were because the teacher felt that the participant was doing AD properly and/or no further progress could be made at that time (Figure 5). The physiotherapist determined culmination for almost all teaching sessions (n=30).

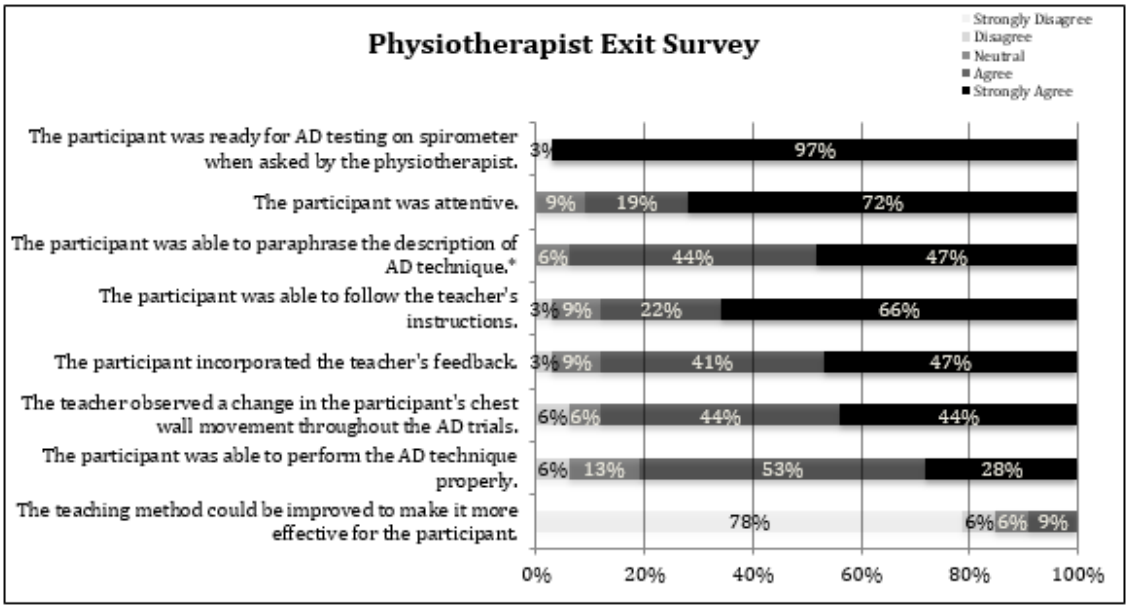

Figure 8: Survey results of the AD teaching session completed by the physiotherapist. *One data point missing in this survey question. AD = Autogenic drainage

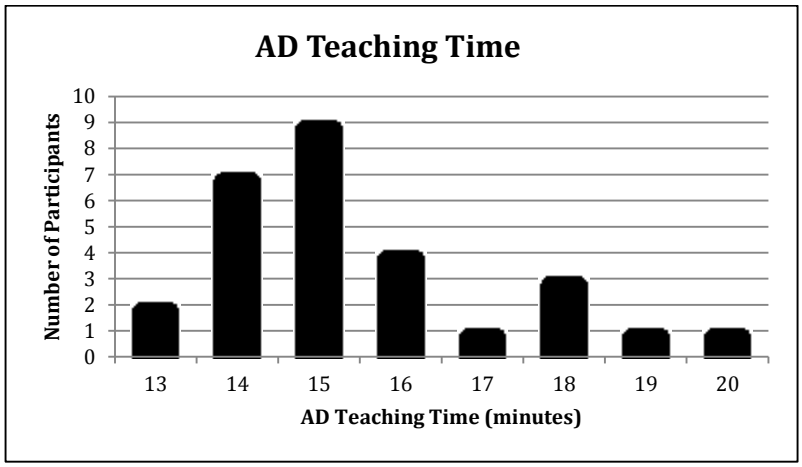

Figure 9: Length of the AD teaching session. AD = Autogenic drainage

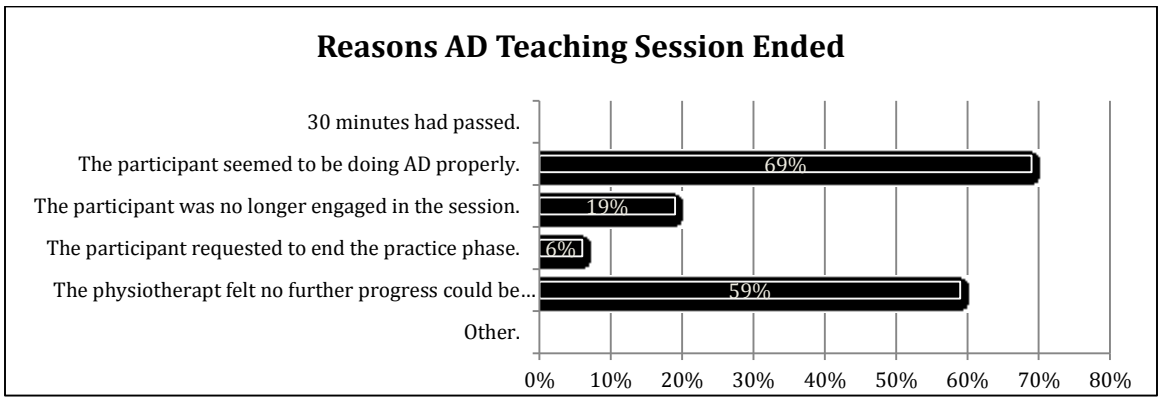

Figure 10: Physiotherapist reported reasons for ending AD teaching session. The physiotherapist selected one or more options from a list of potential reasons to end the teaching session. The "other" option was never selected. AD = Autogenic drainage

The results of the participant exit survey are displayed in Figure 6. Similar to the teacher's perspective, the participants indicated that the AD teaching method was satisfactory. They had adequate time to learn AD and the number of AD practice cycles was found to be helpful, not excessive. Participants did not find it difficult to control their breathing. The physiotherapist's demonstration, explanation, and feedback instructions were beneficial. None of the participants identified problems with the AD teaching session.

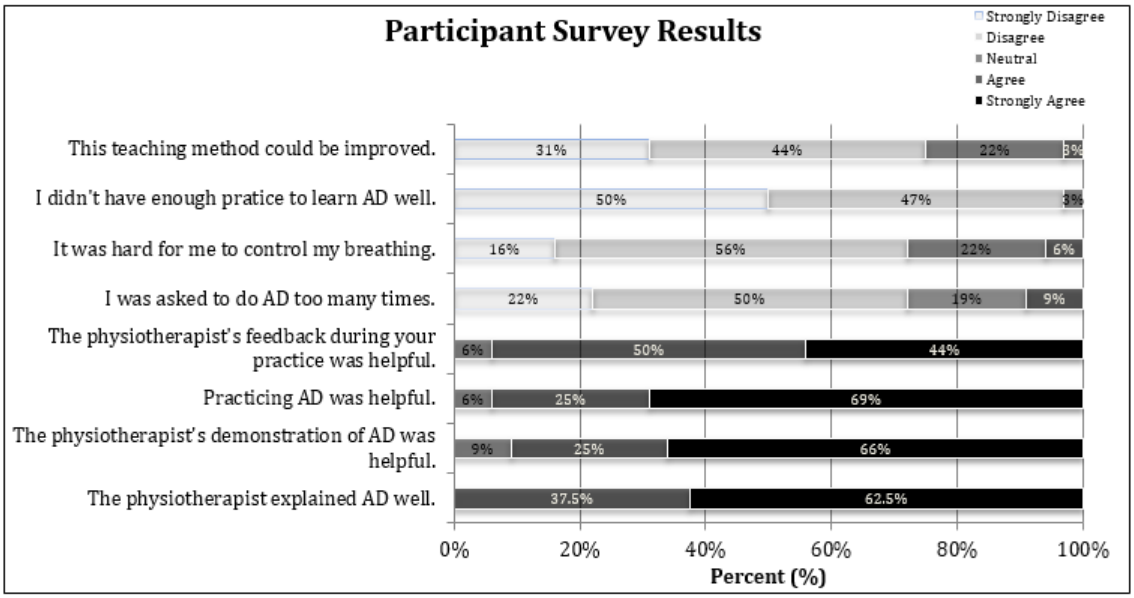

Figure 11: Survey results of the AD teaching session completed by the participants. AD = autogenic drainage

CHAPTER 6 DISCUSSION

The aim of this research was to establish an objective, quantitative method to evaluate AD that could be used to inform clinical practice as well as research on the effects of AD. This study was successful in creating a measurable definition of AD and developing an objective protocol to measure it. The results of this study show that the defining criteria of the definition are achievable however not all healthy adolescents in the cohort could achieve all defining criteria following an introductory teaching session. While proficiency, defined by consistently achieving all 6 criteria, was not the goal of this study additional practice and coaching would undoubtedly improve performance to this level.

6.1 AD Definition

This study offers the first quantitative definition of AD, a technique developed by Chevaillier in 1967. [8] Theoretically, AD is rooted in physiologic principles but the lung volumes purported to characterize AD have never been verified. The quantitative definition of AD developed in this research established measureable criteria representing the key lung volumes described for the AD technique: EELV and V_t. Healthy adolescents had significant success meeting the definition of EELV and V_t. Based on motor learning theory and associated research, there is potential to improve the accuracy and consistency of AD performance.

6.1.1 AD Defining Criterion: EELV

The results of this study demonstrated that a cohort of healthy adolescents could manipulate their EELVs to achieve the distinct phases that are the hallmark of AD. This is the first verification of lung volume manipulation in the performance of AD. At least 40% of the participants were able to achieve the defined EELV for a given AD phase and 20% of the cohort met the definition for all 3 phases. The group mean for Phase 3 met the definition, however the group means for Phases 1 and 2 were close to the definition and had low variability. These results are exceptional given the complexity of AD, the short duration of the introductory teaching session

and the lack of participants' experience in altering their voluntary breathing pattern from the norm.

The control of breathing and the feedback mechanisms that inform the voluntary control of breathing are poorly understood and remain largely unexplored. [130-135] However, the pulmonary mechanics of AD and the current understanding of motor learning provide some insight into the results from this study. Phase 1 of AD occurs at a low EELV where the outward recoil force of the chest wall is high. This would tend to promote breathing at a higher EELV. The group mean was only 4% above the defining range and it is likely that the recoil forces dominated over sensory input to achieve this result. According to Road, the proprioceptive information from the intercostal muscles is predominant in the perception of lung volume. [134] These muscles have a high concentration of muscle spindles and golgi tendon organs, compared to the diaphragm, and provide maximal feedback at RV and TLC, the end ranges of lung volume. [134,135] The costovertebral joints, although slowly adapting, may also provide helpful information about joint position that corresponds to lung volume. Phase 1 AD requires lowering EELV towards RV and would therefore yield a large amount of proprioceptive input. However, it appears that this input was not integrated into the sensorimotor system well enough to influence motor performance and generate the target EELV. This is typical early in the first stage of motor learning, the cognitive stage. [136,137] Participants may also have been unaware of the position of their EELV as breathing TV in ERV is unlike any usual pattern of breathing. Waurick investigated breath depth magnitude production in adults and concluded that breath depth sensation is likely related to proprioception however subjects experienced in singing or playing a wind instrument achieved accurate results compared to those who were untrained. Studies on motor learning of upper limb movements determined that proprioception is not generalizable outside the experienced range of motion. [138,139] Hence, the lack of experience in breathing at a low EELV may have resulted in a lack of awareness of valuable sensory input that could improve performance. [140-142]

The group mean for EELV Phase 2 was 16% of FRC below FRC and the defining criteria was 10%. This was surprising as TV typically revolves around FRC.

At FRC the recoil of the lung and chest wall are equal, however AD requires active exhalation and this may have biased EELV to be below FRC. There is less proprioceptive input at FRC due to the length and tension of the intercostal muscles at mid-EELV.[134] Breathing at FRC is usually involuntary and the participants were likely not attuned to the sensory input that may inform lung volume manipulation for AD in this range.[108,134,140,143] This is supported by Bernardi's deduction that a lack of attention to sensory information can affect the integration of proprioceptive input in the motor cortex.[140] Phase 3 EELV met the definition, which was likely due to the participants' experience in breathing in this range. There is a large amount of proprioceptive input available in this volume range and Phase 3 of AD would feel familiar compared to Phase 1, as the EELV is similar to the end-inspiration volume during exercise.[72,144] Therefore, participants would have previously experienced generating sufficient muscle force to overcome the recoil forces of the lungs and chest wall in the IRV and perhaps were more aware of relevant sensory information. The findings of Andrew at el support this notion that previous motor experience with respect to muscle force generation is valuable and not generalizable outside the experienced range of motion.[139]

It has been established that there are multiple sources of internal sensory input for breathing that originate in the circulatory system, lungs, airways, respiratory muscles, joints, and skin.[132,134] The teaching method cued learners to use AD-specific sensory information including visual input from the AD graph, proprioceptive from the chest wall components, tactile from the hands on the chest wall, and verbal from the coaching by the physiotherapist. Research suggests that proprioception is key to developing accurate movement.[135,138,143] In AD, the desired movement is that of the chest wall and diaphragm to manipulate lung volume. The abundance of sensory information available to influence AD performance and the lack of opportunity to identify and integrate it in an introductory session may have been a reason for the lack of cohort success in meeting the EELV definitions for Phase 1 and 2.

According to the Fitts and Posner theory of motor learning, there are 3 stages: cognitive, associative, and autonomous. The nature of the introductory AD

session placed participants at the very beginning of the cognitive stage. This stage occurs over days or weeks and is comprised of the learner understanding the motor task and developing successful strategies to complete it through trial and error. [137,141] It is characterized by inconsistent performance, which relates to the learner perceiving and processing sensory information that is relevant to the motor task. [136,137] Through trial and error, relevant sensory input is identified and used to improve motor performance. [136,137,141,145] It is important to note that normal breathing is automatically regulated and does not require attention to sensory information, [146] but AD breathing seems to mandate increased awareness and integration of proprioceptive input. The participants' performance was likely related to how well they integrated this input into their sensorimotor system. [140] It is likely that those who were attentive to proprioceptive information achieved some success in performing AD, as studies have shown that simply attending to proprioceptive input can improve performance. [140]

Fitts and Posner have shown that progressive improvement in the accuracy of motor tasks occurs with subsequent training sessions that include feedback. [137] While there are no studies available on motor learning with respect to breathing, studies on targeted upper limb movements have revealed that somatosensory input is integral to the early stages of motor learning, and that motor and somatosensory function improve with feedback and practice including repeated active movement. [138,142,143,147,148] These changes are accompanied by increased connectivity in the motor and somatosensory regions of the brain. [147,148] Wong has demonstrated that substantial gains can be made in proprioceptive acuity during motor learning of an upper limb movement. [138,143] Hence, AD performance could potentially be improved with practice that involves repetition of AD and incorporates proprioceptive feedback. Therefore, the results of this study and the predicted ability to improve AD performance verify that the EELV criteria are indeed achievable.

6.1.2 AD Defining Criterion: V_t

The definition required V_t to remain consistent across AD Phases. The group was successful in doing so as there was no significant difference across the AD Phases ($p>0.05$). Twenty percent of the cohort was able to achieve the defining V_t for a given AD Phase and one participant was able to achieve the V_t criteria for all phases. The group means met the definition of Phase 2, as expected at FRC, and were close to the definition of Phase 1. These results support the achievability of the V_t defining criteria. The theories and evidence of motor learning that apply to EELV are also applicable to V_t and pulmonary mechanics offer some explanation of the V_t results.

The group mean for Phase 1 was very close to the definition. Given the difficulty of breathing at a low lung volume, it was expected that the criteria for Phase 1 would be challenging to achieve. It is likely that inexperience and a lack of integration of proprioceptive input influenced this result. Based on the intensity of feedback from the intercostal muscles, there would be relatively less proprioceptive input at end-inspiration in ERV compared to end-expiration which may have been the reason for the underestimation of V_t. Participants may have also overcompensated for an anticipated large V_t that was predisposed by the large outward recoil force of the chest wall at a low lung volume. Since participants were unfamiliar with breathing V_t at a low EELV they would not have developed their sensorimotor system to facilitate accurate performance.

The mean V_t for Phase 3 was very large and since participants were able to maintain a high EELV it appears they overestimated their inspired volume, which has been shown to occur when attempting to inspire a pre-determined volume in IRV.[133,135] The IRV is relatively large compared to ERV with higher recoil forces and proprioceptive input.[134] Participants may have been influenced by their previous experience of exercise-induced inspiration in this volume range, which is increased and typically followed by an increased expiratory volume.[72,144] Hence, they were unaccustomed to processing sensorimotor information relevant to inspired volume that would help maintain V_t within the defined volume.

The variability of the V_t data was very high for all AD Phases. This reflects the inconsistency in performance that is characteristic of the cognitive stage of learning. It also attests to the additional challenge to the sensorimotor system whereby the magnitude of V_t must be determined simultaneously to EELV. The accepted V_t variability of ±10% was stated by Ruppel, however it is important to note that he did not state the population from which this variability was generated and it was based on TV breathing at rest, i.e. FRC. .[116] The conditions of this AD study were dissimilar as the automaticity of breathing was overridden and EELV was manipulated concurrently with V_t.[108] Folinsbee found that the variability of TV increased when the EELV was varied between RV and FRC, which is similar to Phases 1 and 2 of AD.[133] Needham's data of adolescent lung volumes from which the proposed AD definition was derived, found higher variability in the TV of adolescents.[115] Needham expressed variability as a coefficient of variation (C.V. = SD expressed as percent of the mean result) yielding a C.V. of 28% for resting TV, which is similar to the variability of the V_t data in this AD study: Phase 1 C.V 33%; Phase 2 C.V. 32%; Phase 3 C.V. 39%. Katz-Salamon et al have shown that the just noticeable difference (JND) in TV, i.e. the perceivable change, is 25-29% of resting TV.[132] The JND in V_t is accounted for in the definition as the V_{trest} in the AD preparation stage was elevated compared to Needham's normative data for resting TV. Additionally, Katz-Salamon's data pertained to baseline perception of inspired volume and did not reflect a JND following training of lung volume manipulation and proprioception, which would be more applicable to AD. The principles of motor learning apply to V_t and the prediction that performance can be improved holds.

The results of this study prove that the defining criteria for both V_t and EELV are achievable by a healthy cohort of adolescents. Proficiency with AD was not achieved and was not the goal of this study. This supports longstanding clinical observations that proficiency with AD is never immediate and maintain Bernardi's claim that complex motor tasks cannot be mastered in a single training session.[8,140] However, there exists high potential for learning AD given the abundant sensory information, particularly proprioception, available to inform motor output. The current evidence for improving motor performance of an upper limb movement

indicates that proprioceptive acuity can be developed and neural connectivity enhanced in the somatosensory and motor systems. It is possible that these developments can be made in the movements of the thorax to enhance the performance of AD. Participants were successful in this study in achieving the defining criteria with only a short window of opportunity for motor learning. It is expected that with practice and feedback, all defining criteria for AD can be met by the majority of learners. This gives further credence to the achievability of the AD quantitative definition.

6.2 The Measurement Protocol

The measurement protocol used to assess the performance of AD in this study is novel but spirometry and plethysmography are longstanding, gold standard assessments for lung volumes. Measurement of lung volume change over time was conducted according to ATS standards and the study protocol procedures were consistent across participants. The standard measurement variability of the instruments was much less than the variability of the results of this study and therefore had a negligible contribution in this regard. The volume range of the spirometer was broad and exceeded the TLC of the participants. The software recording time was increased in order to capture a complete AD cycle. Therefore, the data should not have been negatively influenced by the instruments or measurement process.

The participants' age, gender, lung function, and TMT results did not affect the group mean EELVs ($p>0.05$) nor did the teaching process. There were no confounding factors identified that would give cause to question the validity of the outcome data. Participants were consistent with AD performance after 2 assessment trials in the measurement protocol. The results of this study indicated that EELV Phase 1 and V_t Phase 3 were significantly different between the first and second trial but there was no significant differences between Trials 2 and 3. Thus, it is advisable to do 2 separate trials of AD to achieve a consistent result and use the second trial for the evaluation of AD performance.

The quantitative definition of AD in this study is achievable and measurable using this novel protocol. The teaching and measurement components of the study protocol are clinically and scientifically feasible given the short duration of the teaching (15 minutes) and assessment sessions (10 minutes) along with the availability of spirometry and plethysmography in CF centres. The data extraction process could be expedited by devising software that calculates the specific V_t and EELV for each phase of AD and normalizes it using the methods in this study. This would facilitate completing the teaching and measurement protocol with results and feedback provided to a patient or research participant in timely manner during a single visit. Clinically, the AD technique can now be quantified and clinicians can objectively determine if patients are performing the technique according to this definition. This research forms a foundation of knowledge that will readily increase the understanding and application of AD technique.

6.4 Limitations of this Study

This study investigated healthy individuals but the AD technique is for people who have mucus retention due to CF lung disease. Mucus may offer valuable sensory input that helps one manipulate their lung volume within a determined range. It certainly is considered clinically important for the AD technique. This study may have ben limited by this factor. We also don't know how people with and without CF compare in their ability to control their breathing. It is possible that people with CF may be better than people without CF because they are accustomed to performing pulmonary function tests that require them to manipulate their lung volumes and airflow. On the contrary, the degree of lung disease may influence this ability whereby people with mild lung disease are capable of breathing control and lung volume manipulation while those with moderate to severe disease are not.

Breath holds are part of the AD technique but are not a defining feature and therefore were not included in the definition or the measurement. There is no precedent in the available AD literature for the length of the breath holds. The breath holds were taught to the participants in this study but were not emphasized in the feedback from the physiotherapist. Breath holds are clinically important as

they increase the filling time of the lung and promote ventilation homogeneity in people with lung disease.[72] They are easily distinguished in the spirometry volume-time graph by the flattened peaks of each sine wave i.e. zero change in volume over time. This visual information may be helpful in the clinical realm however this study cannot offer guidance in this regard.

This cohort of adolescents was an intentionally biased sample of highly motivated individuals who volunteered to participate in this study. They had no known limitations on their ability to learn and therefore their performance might have been better than that of the general population. The limitations of this study are rooted in the characteristics of the cohort, which are not fully representative of the CF population in which AD is used. Therefore, the conclusions from this study are limited to adolescents who do not have CF.

CHAPTER 7 CONCLUSION

The results of this study have determined that the defining EELV and Vt criteria are achievable in a healthy cohort of adolescents following an introductory AD session. These criteria are measurable using plethysmography and spirometry and the teaching and measurement protocol can be feasibly implemented in the clinical and research environment. Proficiency with AD, defined by meeting all 6 criteria, may be possible with practice and feedback. This research sets the stage for investigations on the effects of AD in people with CF and offers a method to enhance teaching of AD in the clinical setting.

This study has been foundational in defining and measuring the AD breathing pattern. This research has increased the understanding of AD and has determined a quantitative definition and measurement protocol by which to assess AD. Having developed a working definition of AD in a healthy population, the next logical step would be to determine how closely this definition matches performance of AD in people with CF deemed proficient in the technique. The V_t and EELV components should be investigated to determine the volumes at which they optimize clinical effects. Using this measurement protocol we are now able to verify that AD is being performed uniformly across participants in studies that investigate AD. It was not the purpose of this study to determine if participants learned AD i.e. retained the ability to do AD. Future studies should employ this quantitative definition and measurement protocol to evaluate the teaching and learning of AD.

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Appendix A: Flow volume loops of Autogenic Drainage breathing

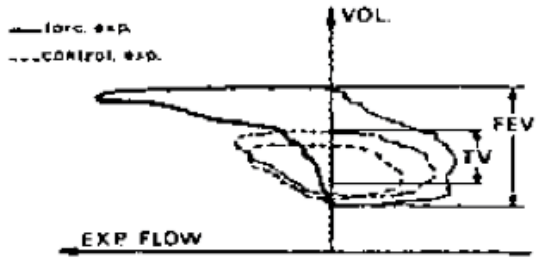


Figure 1: Flow-volume loop from 2 breaths during autogenic drainage ("control exp." Delineated by the perforated line) superimposed on a flow-volume loop from a forced expiratory ("force. Exp" delineated by the sold line) manoeuvre (FEV_1). Vol =volume; exp flow = expiratory flow; TV = tidal volume[94] Values to the right of the vertical axis represent the inspiratory phase and values to the left of the vertical axis represent the expiratory phase. The expiratory phases of the AD breaths have higher sustained expiratory flow whereas the FEV_1 manoeuvre peaks at a high expiratory flow but quickly diminishes.

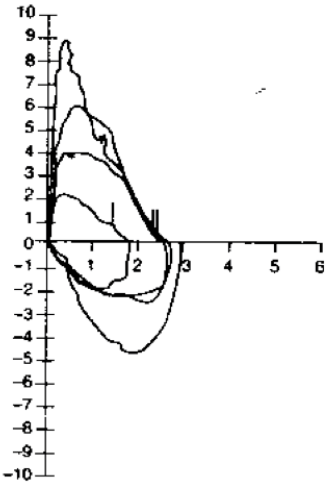


Figure 2: Flow-volume loops resulting during a forced expiratory manoeuvre and 3 breaths of autogenic drainage, one from each phase.[42] Volume is represented on the x-axis and flow on the y-axis. On the y-axis, negative values reflect the inspiratory phase and positive values reflect the expiratory phase.

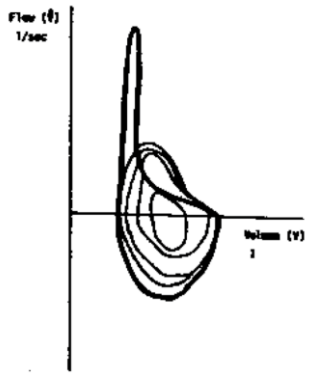


Figure 3: Flow-volume curves from a forced expiratory manoeuvre and multiple breaths during AD.[5] Volume (V) is represented on the x-axis and flow (l/sec = Litres/second) is represented on the y-axis. Higher lung volume is expressed to the vertical axis and lower lung volume further along the x-axis.

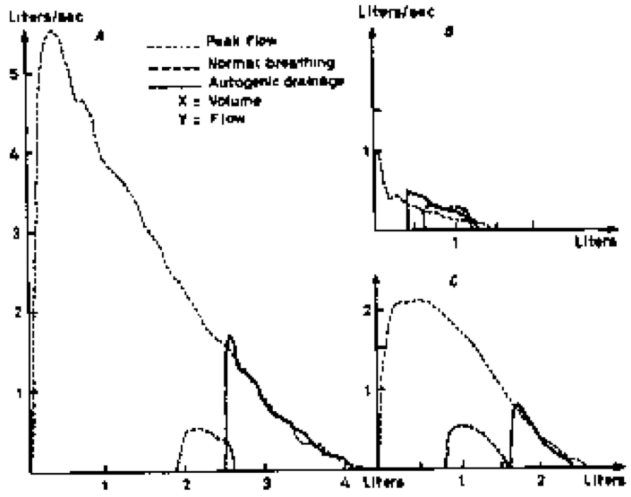


Figure 4: Expiratory flow-volume curves of A) a 16 year-old boy with bronchorrhea, B) a 12 year-old boy with asthma C) an 8 year-old boy with cystic fibrosis.[36] The x-axis represents volume in litres and the y-axis represents flow in litres/second.

Appendix B: Autogenic Drainage graphs from published literature

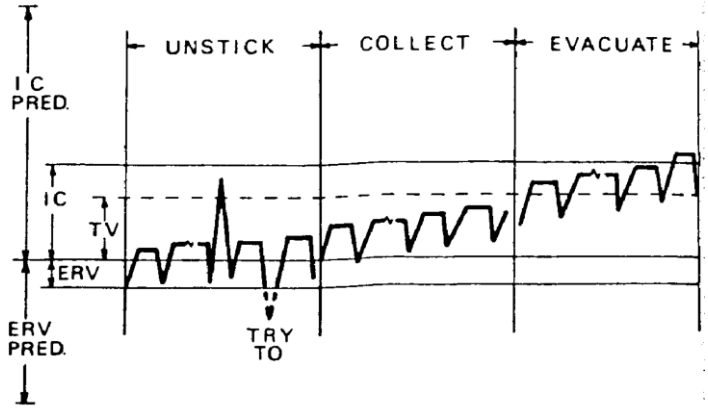


Figure 1: Autogenic Drainage as depicted in Chevaillier 1987.[94]

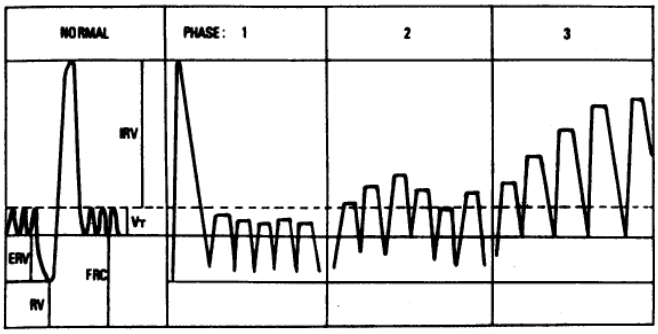


Figure 2: Autogenic drainage as depicted in Schöni 1989.[5]

Figure 3: Autogenic drainage in the IPGCF Physiotherapy for people with CF 2009. Authored by Jean Chevaillier.[1]

Appendix C: Technical Specifications for the Vmax Vyntus™ SPIRO and Vmax® Encore Systems

Vmax Vyntus™ SPIRO

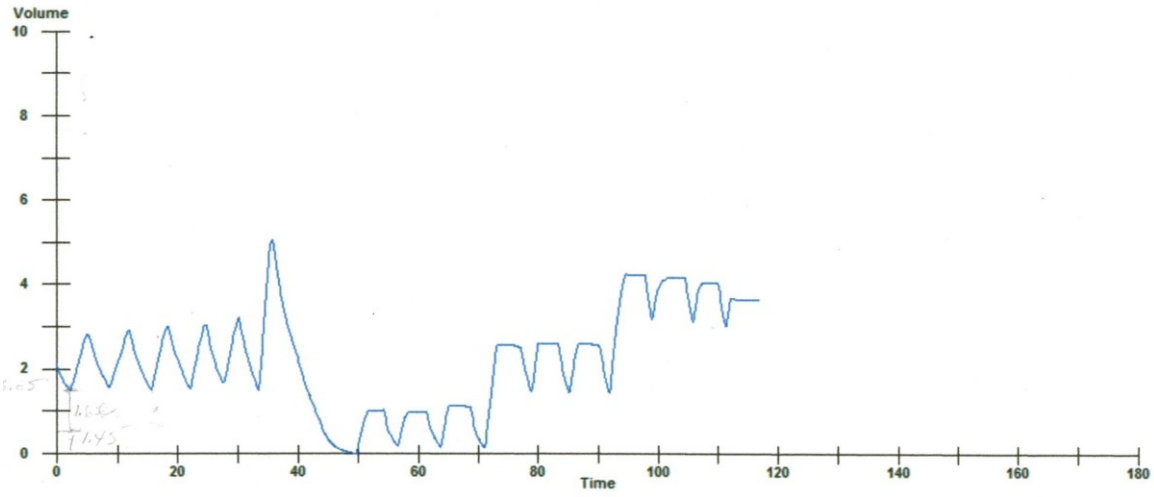
Flow
Type: High-quality pneumotach
Range: 0.1–±16 L/s
Resolution: 1 mL/s
Accuracy: 0.1–14 L/s: ±5% of reading or 0.2 L/s, whichever is greater
Resistance: < 0.51 cm H_2O/L/s at 10 L/s

Volume
Type: Digital integration
Range: ±8 L
Resolution: 1 mL
Accuracy: 0.5–8 L: ±3% of reading or 0.05 L, whichever is greater
Ambient conditions
Altitude: 6,400' (2,000 m)
Temperature: 10–34 °C (50–93.2 °F)
Humidity: 20–80% RH, non-condensing
Pressure: 600–795 mmHg
Power supply Main voltage: 5 VDC via USB

Vmax® Encore System

Flow/Volume
Type: Mas flow sensor
Range: 0-16LPS
Resolution: .003 LPS from .20 – 16 LPS
Flow accuracy: ±3% of reading or 0.25LPS, whichever is greater, across range of .2 to 12 LPS
Volume accuracy: ±3% of reading or 0.05L, whichever is greater
Resistance: <1.5 cmH_2O/LPS at 12 LPS

Appendix D: Testing of Measurement Protocol - Data



	Ref	Best	% Ref	1	2
FVC	3.73	4.87	131	4.87	
FEV1	3.12	3.62	116	3.62	
FEF25-75%	3.55	2.75	77	2.75	
PEF	6.67	8.83	132	8.83	
FET100%		9.63		9.63	
FVL ECode		111000		_000	
TLC	5.68	6.53	115		6.37
VC	3.73	5.05	135	5.05	4.95
IC		3.48		3.48	3.32
Vtg		3.18			3.18
FRC PL	3.07	3.05	99		3.05
ERV		1.60		1.56	1.63
RV	1.88	1.48	79		1.42
RV/TLC	32	23			22
Raw	1.23				
Vtg (Raw)					
Raw f					
Raw ECode					

Reference EELV at FRC: 1.56L (Spirometry)
True FRC: 3.05L (Plethysmography)

EELV Phase 1
$EELV_1$ = |1.56 – 0.18|
= 1.38L

$EELV_1$ /FRC = 1.38L/3.05L
= 45%

EELV Phase 2
$EELV_2$ = |1.56 – 1.46|
= 0.10L

$EELV_2$ /FRC = 0.10L/3.05L
= 3%

EELV Phase 3
$EELV_3$ = |1.56 – 3.14|
= 1.58L

$EELV_3$ /FRC = 1.58L/3.05L
= 52%

Appendix E: Recruitment Advertisements and Social Media Posts

IWK Health Centre

Dear Parent,

Is your child between the ages of 12 and 18 years old?

We are looking for healthy teenagers between the ages 12 and 18 years to take part in a study at the IWK Health Centre about breathing. We are using a new method to measure a breathing pattern called autogenic drainage. This breathing pattern is used by teens and adults with cystic fibrosis to help keep their lungs healthy.

This study involves visiting the IWK for about 90 minutes, at a time that is convenient for you.

Your child will receive a $25 iTunes gift card and certificate of participation, and parents will receive $10 towards parking and transportation costs.

Please call Kimbly Morgan at 902-470-7512 or email kimbly.morgan@iwk.nshealth.ca to see if your child is eligible!

Teens helping teens!

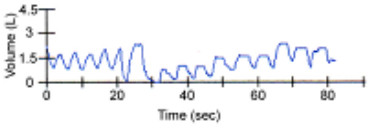
We are looking for HEALTHY volunteer teenagers to participate in our research study on autogenic drainage.

You as a research volunteer would participate in the following:

- Attend one 90 min session at the IWK
- Learn and practice a unique breathing exercise used in Cystic Fibrosis (CF)
- Find out how well you can perform this exercise
- Fill out a survey on the process

So – What's in it for you?!

- Learn about breathing!
- Feel great about participating in research and helping other teens



- A certificate of recognition – add this volunteer experience to your resume!
- Receive a $25 iTunes gift card and reimbursement for parking

We can accommodate your schedule to book these appointments, and you can feel good knowing you have helped us make a difference for kids and teens with Cystic Fibrosis (CF).

IWK Health Centre
June 2 ·

To better understand how breathing exercises could benefit children and teens with Cystic Fibrosis (CF), we need the help of healthy teens (ages 12 to 18) without a history of asthma or other breathing related concerns. We would appreciate you volunteering your time to help us out!

To find out more about this research opportunity, please contact:
Kimbly Morgan, Kimbly.morgan@iwk.nshealth.ca, (902) 470-7512

Like Comment Share

35 Chronological

120 shares

View 4 more comments

Kimbly Morgan We're very excited to be started this phase of the study! There's been a lot of planning and prep and now the science is happening!!! Come one, come all!
Like · Reply · 1 · June 3 at 9:33am

Kimbly Morgan Many thanks to all the teens who have come out to participate in this research study!! We are half way to our goal of 30 participants! There's still time to be a part of research for CF!! If you are interested in participating just email kimbly.morgan@iwk.nshealth.ca
Like · Reply · 1 · July 22 at 3:54pm

Write a comment...

IWK Health Centre
August 26 ·

Only a few more healthy teen volunteers needed!

To better understand how breathing exercises could benefit children and teens with Cystic Fibrosis (CF), we need the help of healthy teens (ages 12 to 18) without a history of asthma or other breathing related concerns. We would appreciate you volunteering your time to help us out!

To find out more about this research opportunity, please contact:
Kimbly Morgan, Kimbly.morgan@iwk.nshealth.ca, (902) 470-7512

Like Comment Share

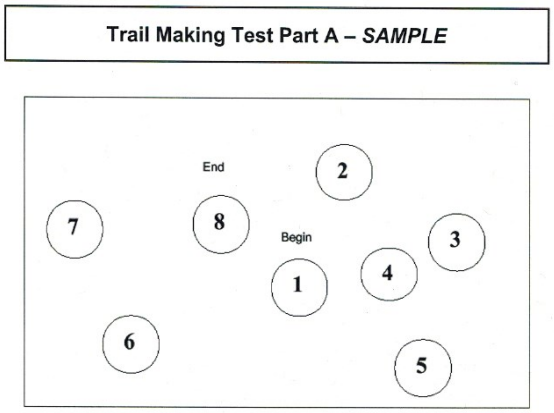
Appendix F: Screening questionnaire for participants

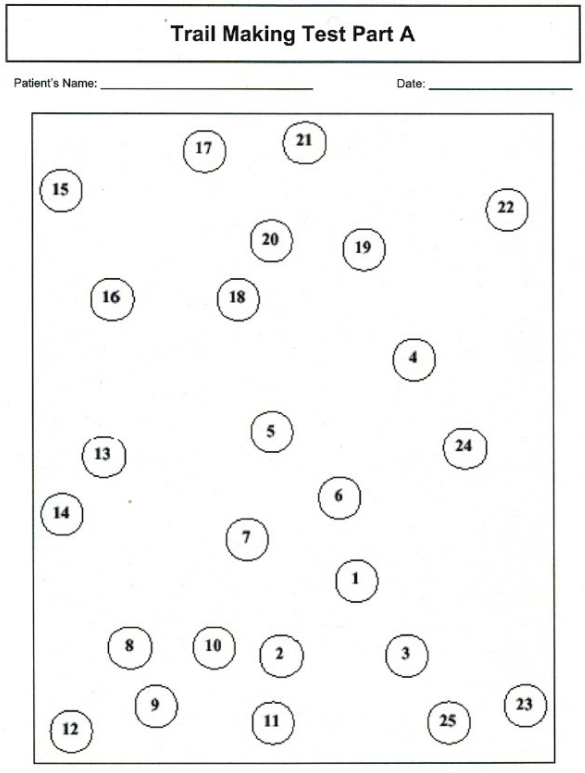
The following questions will be asked of the participant in order to screen for eligibility:

1. Are you able to follow instructions given in English?
2. Has a doctor ever told you that you have a breathing problem such as asthma?
3. Has a doctor ever told you that your rib cage is unusually shaped?
4. Do you use or have ever been prescribed "puffers" or inhaled medications for a breathing problem?
5. Do you ever wheeze or experience bouts of coughing or shortness of breath?
6. Can you do all the activities you want to do without your breathing limiting you?
7. Do you have breathing issues that disturb your sleep?
8. Do you smoke cigarettes or substances?
9. Do you have a learning disability?
10. Do you have an attention deficit disorder?

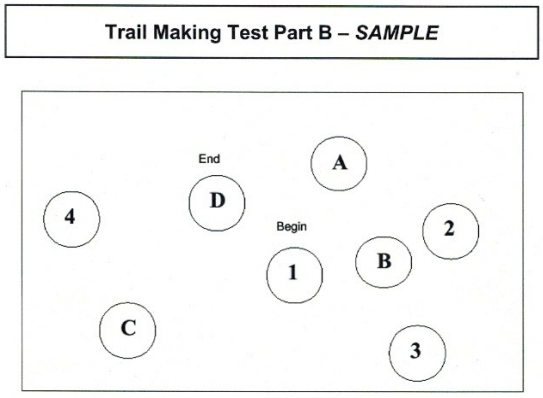
If the individual answered yes to one or more of these questions s/he was ineligible to participate in the study.

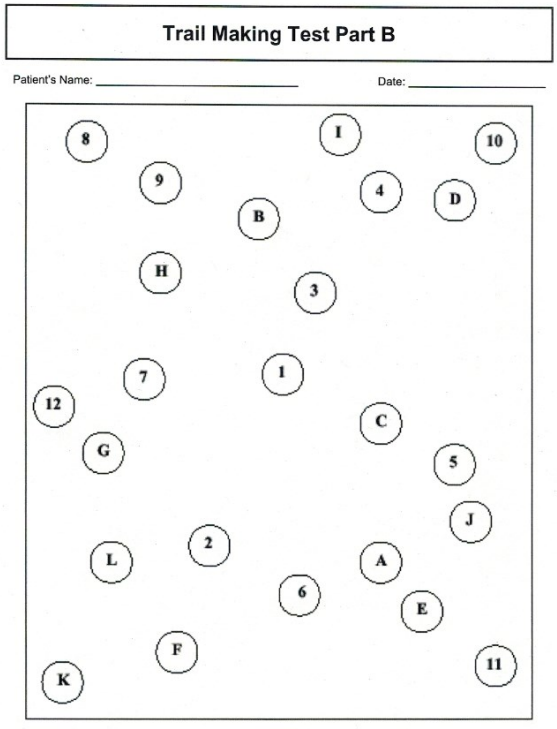
Appendix G: Trail Making Test A





Appendix H: Trail Making Test B





Appendix I: Autogenic Drainage Teaching Session

1. Baseline AD trial on Spirometer
    i. Teacher to introduce participant to the assessor and explain AD graph (Figure 1).
    ii. Participant is given a copy of the AD graph to use for the teaching and evaluation session.

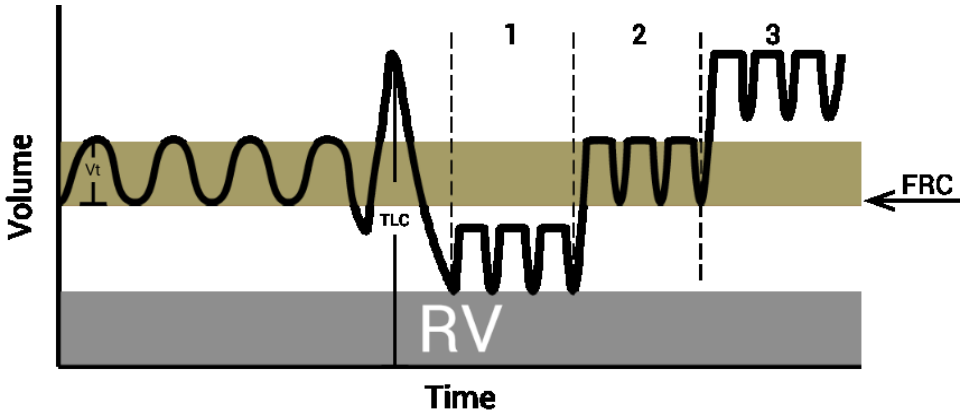


Figure 1: Autogenic Drainage Graph with phases 1,2,3; residual volume (RV), tidal volume (Vt), Functional Residual Capacity (FRC), and total lung capacity (TLC) indicated.

iii. Script: *Here is a picture of the breathing pattern you will learn today. [Trace the graph with your finger as you explain the picture]. When the line is going up it means breathe in. When the line is going down it means breathe out. When the line is straight it means hold your breath. These are normal size breaths [Trace first 4 breaths of the graph]. The longer the line the larger the breath. Here [Indicate shaded FRC] is where you normally breathe in your lung when you are at rest. Here [Indicate Phase 1 AD - low lung volume] you are breathing with your lungs very empty of air. Here [Indicate Phase 2 AD - shaded FRC] you are breathing where you normally breathe at rest. Here [Indicate Phase 3 AD - high lung volume] you are breathing with your lungs very full of*

air. Now we want you to breathe into the spirometer the way this graph is showing you how to breathe.

2. Participant views the AD video (AD video 2521.avi)
3. Teacher explains AD:
    i. Script: *The autogenic drainage breathing pattern consists of normal size breaths breathed at a low, medium, and high levels in your lungs. [Reference the graph as you explain the breathing pattern]. The breathing patterns starts with normal size breaths. Then you take in the largest breath you can possibly take and sigh it out for as long as you possibly can. Once you have emptied as much air from your lungs as you can, you take a normal size breath in and hold it for a count of 3, then exhale with a sigh. Take another normal size breath in, hold for a count of 3 and exhale with a sigh. Take another normal size breath in, hold for a count of 3 and exhale with a sigh. Then you fill up your lungs with more air and breathe normal size breaths with breath holds at that level. Once you have done 3 breaths at this level you fill up your lungs with even more air and breathe 3 normal size breaths with breath holds at that level. The pattern ends with an inhalation. Do you have any questions?* [Answer questions, if any]. *Now I will demonstrate the autogenic drainage breathing pattern for you.*
4. Teacher to demo AD sitting in a chair with one hand on upper chest and one hand on abdomen.
5. Teacher asks the participant if s/he has any questions.

    Participant to try AD with teacher concurrently instructing technique using the AD script. Participant able to view AD graph if s/he chooses.

    (Practice trial 1)

    AD Script:

    Now I'm going to coach you through the AD breathing pattern.

    Sit up straight with your back against the chair and your feet flat on the floor. Place one of your hands on your upper chest and your other hand on your belly. Feel how much your hands are moving with each breath you take.

Relax your breathing and breathe normal size breaths through your mouth. [Pause instruction to allow 4 tidal volume breaths] *Now we're going to do 4 breaths, that's 1, that's 2, that's 3, that's 4.*

Now take a deep breath in, in, in then sigh it out for as long as you possibly can. Out, out, out, out. Keep going.

Once you have breathed out for as long as you can, take a normal size breath in and hold 2,3, sigh it out. Keep breathing low in your lungs.

Take another breath in, hold 2,3, sigh it out.

Breath in, hold 2,3, sigh it out.

Fill up your lungs a little more now, this should feel like normal size breaths. Hold 2,3, sigh it out.

Breath in, hold 2,3, sigh it out.

Breath in, hold 2,3, sigh it out.

Fill up your lungs with even more air. Breathing with very full lungs now.

Hold 2,3, sigh it out.

Breath in, hold 2,3, sigh it out.

Breath in, hold 2,3, sigh it out.

Breath in.

Now you've done 1 cycle of autogenic drainage!

Do you have any questions? [Answer questions, if any]

6. Participant to try AD on their own without concurrent verbal coaching.

   (Practice trial 2). Teacher observes and assesses breathing pattern according to the following criteria:

   a) Observes chest wall movement

   i. During tidal volume breathing looking for consistent amount of movement

   ii. During phase transition looking for increased chest wall movement on inhalation

   b) Monitors signs of discomfort/breathlessness

   i. Eyes are wide and apprehensive

ii. Excessively large breath taken between AD phase 1 and 2

iii. Increased respiratory rate

c) Notes breath holds for each tidal volume breath in Phase 1, 2, 3

d) Listens and observes for length of inspiration and expiration.

Teaching session addresses the following, in order of priority:

i. Tidal volume breaths

ii. Low, mid, and high lung volume breathing

iii. Breath holds

7. Teacher gives verbal feedback referencing the AD graph and participant's breathing pattern. Teacher tells participant what s/he is doing well and what needs to improve/change.
8. Participant to try AD on their own without concurrent verbal coaching.
   (Practice trial 3). Teacher observes and assesses breathing pattern.
9. Teacher gives verbal feedback referencing the AD graph and participant's breathing pattern. Teacher tells participant what s/he is doing well and what needs to improve/change.
10. If participant appears to be doing the correct AD pattern, teacher offers spirometer mouthpiece for one cycle. Participant to try AD with concurrent verbal coaching as needed.
    (Practice trial 4). Teacher observes and assesses breathing pattern.
11. Teacher gives verbal feedback referencing the AD graph and participant's breathing pattern. Teacher tells participant what s/he is doing well and what needs to improve/change.
12. If participant appears to the doing the correct AD pattern, offer nose clips in addition to spirometer mouthpiece for one trial. Participant to try AD with concurrent verbal coaching as needed.
    (Practice trial 5). Teacher observes and assesses breathing pattern.
13. Ask if participant is ready for testing.

    i. If no, do another practice trial with nose clips and mouthpiece.

    (Practice trial 6). Teacher observes and assesses breathing pattern.

    ii. If yes, ask participant to verbally describe the AD breathing pattern.

Appendix J: Participant Survey

Script: Here is a survey that you need to fill out before you leave. We'd like your honest opinion. We need to know if there are things we could change. If we haven't done a good job, we need to know so we can make things better.

1. The physiotherapist explained AD well.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

2. The physiotherapist's demonstration of AD was helpful.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

3. Practicing AD was helpful.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

4. The physiotherapist's feedback during your practice was helpful.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

5. I was asked to do AD too many times.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

6. It was hard for me to control my breathing.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

7. I didn't have enough practice to learn AD well.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

8. This teaching method could be improved. (Please comment below)

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

Comments:

Appendix K: Teacher Survey

Length of teaching session: _____ minutes

Total number of AD cycles completed: _____

1. When asked, the participant was ready for AD testing on spirometer.

   Yes / No

2. The participant was attentive.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

COMMENT: _____

3. The participant was able to paraphrase the description of autogenic drainage technique.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

COMMENT: _____

4. The participant was able to follow the teacher's instructions.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

COMMENT: _____

5. The participant incorporated the teacher's feedback.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

COMMENT: _____

6. The teacher observed a change in the participant's chest wall movement.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

COMMENT: _____

7. The participant was able to perform the AD technique properly.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

COMMENT: _____

8. The teaching method could be improved to make the session more effective for the participant.

1 – Strongly Disagree 2 – Disagree 3 – Neutral 4 – Agree 5 – Strongly Agree

COMMENT: _____

9. Practice time was:

Inadequate Perfect Excessive

COMMENT:_____

10. The practice phase ended because:
    a. 30 minutes had passed
    b. the participant seemed to be doing AD properly
    c. the participant was no longer engaged in the session
    d. the participant requested to end the practice phase
    e. the teacher felt no further progress could be made
    f. other_____
       _____

Additional Comments:

Appendix L: Copyright Agreement letter for Figures 1,3,4

Permission requested to use:

Book title: The Normal Lung

Book ISBN: 0-7216-6613-2

Book Author: John F. Murray

Book Year: 1986

Book Pages: 4, 100, 102 (Figures 1-3, 4-12, 4-14)

Book Chapter numbers: 1 and 4

Book Chapter title: Chapter 1 prenatal Growth and Development of the Lung and Chapter 4 Ventilation

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