

The effect of COPD on Laryngopharyngeal Sensitivity and Swallow Function

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ABSTRACT

The relationship between COPD and laryngopharyngeal sensitivity has not been previously determined. Limited research into the relationship between COPD and swallow function suggests that patients with COPD are at increased risk of aspiration. One possible mechanism for this is a reduction in laryngopharyngeal sensitivity (LPS). Reduced laryngopharyngeal sensitivity (LPS) has been associated with an increased risk of aspiration in pathologies such as stroke, however impaired LPS has not been examined with respect to aspiration risk in COPD. The Aims of this study were to investigate the effect of COPD on laryngopharyngeal sensation using Laryngopharyngeal Sensory Discrimination Testing (LPSDT) and to determine whether a relationship between LPS and swallow function in patients with proven COPD exists. Method: 20 patients with proven COPD and 11 control subjects underwent LPSDT utilising an air-pulse stimulator (Pentax AP4000) via a nasendoscope (Pentax FNL10AP). The threshold of laryngopharyngeal sensation was measured by the air pressure required to elicit the laryngeal adductor reflex (LAR). A number of further examinations were also completed for COPD subjects. These included respiratory function testing, self-reporting questionnaire on swallowing ability (SSQ), bedside clinical examination of swallowing (MASA) and endoscopic assessment of swallowing (EAS). Results: subjects with COPD had a significantly higher LAR threshold when compared to their normal healthy counterparts ($p < 0.001$). Positive correlations were identified for the relationships between MASA score and EAS results for presence of laryngeal penetration / aspiration ($p < 0.04$), vallecular residue ($p < 0.01$) and piriform residue ($p < 0.01$). Conclusion: Patients with COPD have significantly reduced mechanosensitivity in the laryngopharynx. Patients with COPD also have impaired swallow function characterised primarily by pharyngeal stasis. These changes may place patients with COPD at increased risk of aspiration.

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TABLE OF CONTENTS

CHAPTER 1	Introduction	9
CHAPTER 2	Background - The Normal Swallow	13
	2.1 Swallowing and Dysphagia	13
	Oral phase	17
	Pharyngeal Phase	20
	Oesophageal Phase	23
	2.2 Effect of Age on Normal Swallowing	25
	Bolus Volume	25
	Duration of Swallow	26
	2.3 Laryngeal Physiology	27
	2.4 Sensory Receptors of the Larynx	30
CHAPTER 3	Swallowing & Chronic Obstructive Pulmonary Disease (COPD)	34
	3.1 Chronic Obstructive Pulmonary Disease (COPD)	34
	3.2 Relationship between Respiration and Swallowing	36
	3.3 Cough and Dysphagia	40
	3.4 COPD and Dysphagia	44

Preface to Chapters 4 & 5 (including Ethics Approval and Consent)	52
CHAPTER 4	The effect of COPD on Laryngopharyngeal Sensitivity (LPS)
	53
4.1	Study Aims
	53
4.2	Methodology
	53
4.3	Results
	61
4.4	Discussion
	64
4.5	Study Limitations
	67
4.6	Conclusion
	69
CHAPTER 5	Impaired Laryngopharyngeal Sensitivity in Patients with COPD: the relationship to swallow function
	70
5.1	Aims
	70
5.2	Methodology
	70
5.3	Results
	75
5.4	Discussion
	82

	5.5	Study Limitations	88
	5.6	Conclusion	89
CHAPTER 6		Summary	90
APPENDIX A		Ethics Approval	91
APPENDIX B		Participant Information Form	92
APPENDIX C		Participant Consent Form	94
APPENDIX D		Sydney Swallowing Questionnaire (SSQ)	95
APPENDIX E		Mann Assessment of Swallowing Ability (MASA)	99
APPENDIX F		Endoscopic Assessment of Swallowing (EAS)	100
REFERENCE LIST		101
BIBLIOGRAPHY		111

LIST OF TABLES

Chapter 2	Table 2.1	8-Point Aspiration-Penetration Scale16
Chapter 4	Table 4.1	FEV ₁ values for case subjects56
	Table 4.2	Case subject descriptive data61
	Table 4.3	LAR data for cases & controls63
Chapter 5	Table 5.1	Case subject descriptive data76
	Table 5.2	SSQ data summary77
	Table 5.3	EAS data summary for vallecular and piriform residue79
	Table 5.4	EAS data summary for laryngeal penetration / aspiration79
	Table 5.5	Relationship between EAS and MASA80

LIST OF FIGURES

Chapter 2	Figure 2.1	Oral, pharyngeal and laryngeal anatomy - lateral view14
	Figure 2.2	Laryngeal anatomy – superior view28
Chapter 4	Figure 4.1	LPSDT results63
Chapter 5	Figure 5.1	Correlation between laryngeal penetration / aspiration (on EAS) and MASA81
	Figure 5.2	Correlation between vallecular residue (on EAS) and MASA81
	Figure 5.3	Correlation between piriform residue (on EAS) and MASA81

CHAPTER ONE: INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of death in Australian males and the sixth leading cause in Australian females^[1]: over 500,000 Australians are estimated to have moderate-severe disease^[2], and the burden of COPD is likely to increase along with our aging population. Hospitalisation rates of COPD patients increase with age, with the main function of hospitalisation being to provide supportive care and monitor drug therapy. The increasing demands upon the health system calls for further research within this population, so that we can manage these patients more effectively and efficiently.

COPD patients commonly exhibit signs of malnourishment. Studies have indicated that 24% of COPD outpatients^[3], and 47% of COPD inpatients had a bodyweight <90% of their ideal weight^[4]. Dysphagia is often a major cause of this malnutrition^[1]. Other causes may include the development of cachexia as a result of metabolic changes and multiple periods of fasting as a prelude to procedures or investigations^[5].

To date there has been relatively little research conducted on the prevalence of dysphagia and other swallowing disorders in patients with COPD. Prevalence of dysphagia in COPD varies considerably between studies, ranging between 17%^[6] and 85%^[7]. Preliminary findings suggest that COPD may result in a reduced strength of swallow^[8, 9], and an increased prevalence of pulmonary aspiration^[9]. When combined with an impaired ability to use expired air to clear the larynx and protect the airway, a weak swallow may contribute to an increased risk of aspiration of pharyngeal contents, and therefore aspiration pneumonia.

Reid (1998)^[9] conducted a study that evaluated the swallow function of patients with COPD using Modified Barium Swallow examination. She found that these COPD patients presented with a number of dysphagic features including a delay in onset of the

pharyngeal phase, piecemeal deglutition on liquid boluses and greater pharyngeal transit duration. Interestingly, Reid's study (1998) also found that COPD patients were unable to accurately describe their swallowing difficulties when results from a self-reporting questionnaire were compared to Modified Barium Swallow results.

Shaker and colleagues^[10] analysed the relationship between respiration and swallowing, looking at the effects of age, tachypnoea (rapid respiratory rate), bolus volume and COPD. Their findings indicated that there is a significant difference in the coordination between deglutition and phases of continuous respiration in those with COPD compared with young healthy subjects. As swallowing and respiration are exclusive functions (i.e. respiration should cease when the swallow reflex is triggered), it is possible that when pulmonary function is compromised (as in COPD), the relationship between respiration and deglutition may be adversely affected.

Laryngopharyngeal sensory deficits in patients who have suffered a stroke have been reported to be predictive of aspiration pneumonia (AP)^[11-13]. More importantly, a laryngopharyngeal sensory deficit without clinical evidence of dysphagia, i.e. a silent sensory deficit, may be extremely hazardous, as it is likely to escape detection and predispose the patient to silent aspiration^[12]. Conventional clinical techniques used to assess laryngopharyngeal sensory deficits such as the gag reflex are of questionable value. The gag reflex test measures activity of the ninth (glossopharyngeal) cranial nerve, as opposed to the superior laryngeal nerve branch of the tenth (vagus) cranial nerve, which innervates the hypopharynx and larynx. Research has found that the gag reflex test was not found to be a useful predictor of laryngopharyngeal sensation (LPS) or AP^[14].

Preliminary studies have found that a new technique assessing LPS, Fiberoptic Endoscopic Evaluation of Swallowing with Sensory Testing (FEESST) is safe, reproducible and is able to identify patients with laryngopharyngeal sensory deficits and

those at risk of pulmonary aspiration^[15]. In this technique, LPS integrity is defined by the threshold at which the laryngeal adductor reflex (LAR) is triggered in response to air pulse stimuli. The LAR is the transient adduction of the true vocal cords in response to a mechanical stimulus. This reflex is designed to protect the lower airway from foreign material or noxious stimuli, such as food, fluid, hot air and gases. Preliminary LPS data on normal subjects has been reported^[16], as has data for patients with stroke^[12] and known gastro-oesophageal reflux^[17].

A range of abnormalities in swallowing function has been reported in patients with COPD who have frequent exacerbations^[9]. The basis for this swallowing dysfunction (dysphagia) is uncertain. One proposed hypothesis is that a sensory deficit exists but simple tests such as the gag response are not accurate in determining LPS. It is not known whether LPS measured with other techniques is abnormal in COPD. It is also not known whether impaired LPS in COPD patients predicts the presence of swallowing disorders or pulmonary aspiration. A simple reproducible test of LPS such as FEESST, that may potentially predict which COPD patients are at highest risk of swallowing disorders and aspiration, would be clinically useful and allow preventative measures to be initiated.

This thesis presents data on the relationship between chronic obstructive pulmonary disease (COPD) and laryngopharyngeal sensitivity (LPS) and swallowing function.

The aims of this study are as follows:

1. To determine the prevalence of LPS impairment (as measured by the LAR threshold) in patients with proven COPD.
2. To determine the relationship between LPS impairment (as measured by the LAR threshold) and COPD severity.
3. To determine the relationship between LPS and swallow function in patients with proven COPD.

4. To determine whether LPS predictive value may be used as a method of evaluating risk of dysphagia, as identified by the Mann Assessment of Swallowing Ability (MASA) and Endoscopic Assessment of Swallowing in patients with COPD.

CHAPTER TWO: BACKGROUND – THE NORMAL SWALLOW

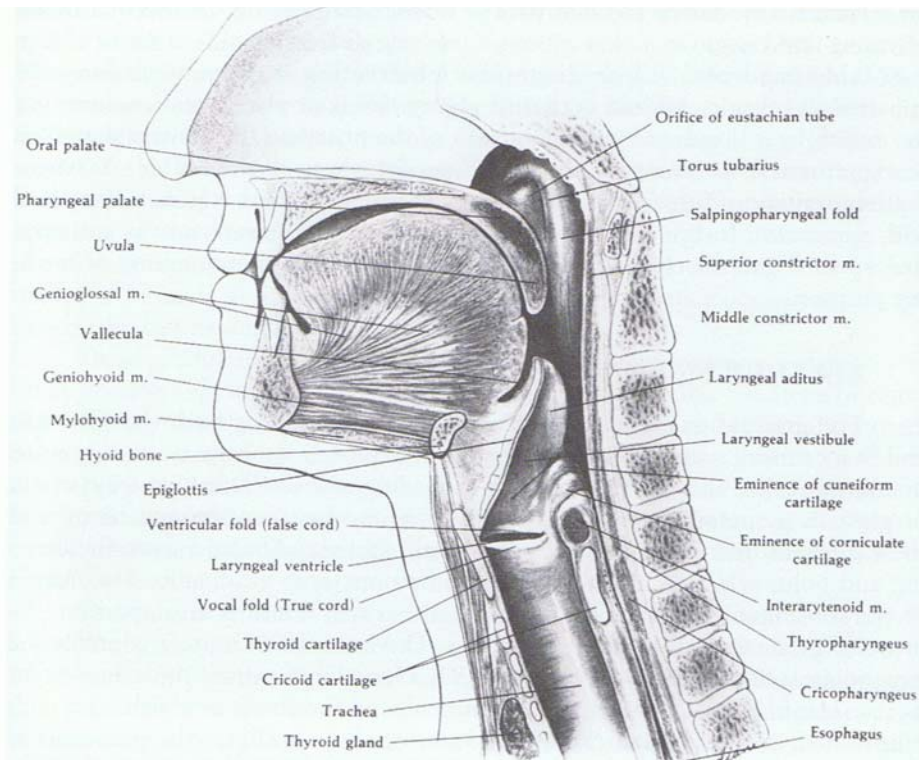
2.1 SWALLOWING AND DYSPHAGIA

In this chapter each phase of the normal swallow process will be discussed, noting dysphagic symptoms that may occur at each stage.

Swallowing is the process by which an individual ingests a food or fluid substance. It refers to the entire act of deglutition commencing from placement of food or fluid in the mouth to the point where it passes the cricopharyngeal junction and enters the oesophagus. It is important to note that the process of swallowing differs from feeding. There are three phases within the process of swallowing, whereas feeding refers only to food placement in the mouth and the oral preparatory phase of the swallow. The three phases of swallowing are described as follows^[18, 19]:

1. *Oral phase*: manipulation and mastication of the food / fluid followed by transfer of the food / fluid bolus posteriorly from the mouth to the oropharynx.
2. *Pharyngeal Phase*: transport of the bolus from the oropharynx via a closed pressure system that commences at the lips anteriorly and the velopharyngeal port superiorly. The bolus continues the downward path with the assistance of tongue base propulsion and pharyngeal constriction, passing the occluded laryngeal vestibule, and then moving through the relaxed cricopharyngeus muscle and into the upper oesophagus.
3. *Oesophageal Phase*: transportation of the bolus inferiorly via peristaltic contraction through the oesophagus, past the relaxed lower oesophageal sphincter and into the gastric cavity.

Figure 2.1: Oral, pharyngeal & laryngeal anatomy – lateral view



From: Groher, M.E., *Dysphagia: Diagnosis and Management*. 3rd ed. 1997, MA: Butterworth-Heinemann. (page 154)

Dysphagia is difficult to define. It is not usually the primary diagnosis, but more a symptom of the underlying pathology. Kuhlemeier (1994)^[20] describes dysphagia as “not a disease, but rather a symptom of one or more underlying pathologies”.

Dysphagia is defined in Mann & Hankey (2001)^[21] as “a disorder of bolus flow”. It is essential that dysphagia be defined independently of laryngeal penetration and / or aspiration as the diagnosis of dysphagia does not require the demonstration of either of these symptoms. For the purposes of this study, the following definitions from Groher (1992)^[19] and Rosenbek et al (1996)^[22] have been accepted to describe the terms laryngeal penetration and aspiration.

Laryngeal penetration: “the entry of oropharyngeal contents through the larynx distal to the true vocal folds”.

Aspiration: “passage of material into the lungs, often with connotation of accompanying inspiration”.

From Groher (1992)^[19]

Table 2.1: 8 - Point Penetration - Aspiration Scale

Score	Description of Events
1	Material does not enter the airway
2	Material enters the airway, remains above the vocal folds, and is ejected from the airway
3	Material enters the airway, remains above the vocal folds, and is not ejected from the airway
4	Material enters the airway, contacts the vocal folds and is ejected from the airway
5	Material enters the airway, contacts the vocal folds and is not ejected from the airway
6	Material enters the airway, passes below the vocal folds, and is ejected into the larynx or out of the airway
7	Material enters the airway, passes below the vocal folds, and is not ejected from the trachea despite effort
8	Material enters the airway, passes below the vocal folds, and no effort is made to eject

(From Rosenbek et al, 1996^[22])

Dysphagic symptoms may occur during one or more of the oral, pharyngeal and oesophageal phases.

The act of swallowing is a highly complex and integrated process. For the purposes of understanding the locus of these dysphagic symptoms, the mechanics of the swallow process can be broken down into artificial phases as mentioned earlier.

Oral Phase

The oral phase of the swallow consists of bolus entry to the oral cavity and mastication, involving both voluntary and involuntary actions. Once the food substance is placed in the mouth, the temporalis, masseter and medial pterygoid stabilise the mandible, the suprahyoid and infrahyoid muscles position the hyoid bone, and the intrinsic and extrinsic muscles of the tongue assist in transferring the bolus posteriorly in preparation to initiate the swallow^[23].

An essential component of the oral phase is lip closure. This promotes bolus formation and control, reducing the risk of anterior spillage through the lips, so that the food / fluid bolus can be transported to the posterior oral cavity in preparation for initiation of the swallow reflex^[18]. The anterior seal of the lips during the oral phase of the swallow is achieved by employing the orbicularis oris, levator and depressor anguli oris muscles.

Symptoms that indicate oral dysphagia have been described by a number of authors^[18, 23, 24]. Each dysphagic symptom shall be addressed in sequence with reference to phases of the normal swallow.

Anterior spillage or drooling occurs as a result of poor lip closure and / or infrequency of swallowing. Drooling may be exacerbated by reduced sensation in the anterior oral cavity, lips and face, as the individual may not be sensitive to the build up in secretions or spill from the lips^[25]. If drooling is not adequately controlled, halitosis and skin breakdown may occur. An excess of salivary secretions may also manifest this problem^[18].

Difficulty chewing and / or poor bolus preparation may also arise from oral phase factors. Decreased or poor quality dentition, ill-fitting dentures, and poor tone of the masseter, temporalis, medial pterygoid and lateral pterygoid muscles (responsible for

jaw opening and closure), can evidence as inadequately masticated solids^[25, 26]. These difficulties may result in prolonged meal times, selective eating of soft foods and avoidance of hard foods^[25]. Patients with poor ability to masticate often present by using a 'munching' as opposed to 'grinding' action when chewing their food^[18].

A combination of decreased oromusculature tone, poor coordination and susceptibility to fatigue may also result in reduced oral control of bolus^[25, 26]. The intrinsic and extrinsic muscles of the tongue work not only to form the bolus, but also transport the substance around the oral cavity for mastication by the appropriate dentition. The role of the buccal cavity muscles (buccinator and risorius), are to keep the bolus within the appropriate boundaries for mastication and avoid collection of particles in the lateral sulci^[18].

Delayed oral transit occurs as a product of decreased tone and coordination of the tongue^[18]. The individual may have difficulty generating sufficient pressure against the hard palate to push the bolus posteriorly. They may also be unable to coordinate the wave-like motion required for anterior-posterior transfer. Deficit at any stage of the transitional process may result in poor oral transportation and bolus formation, impeding efficient initiation of the swallow reflex. Residue remaining in the oral cavity post swallow may also occur due to deficits in the transitional process^[18].

Difficulty initiating a swallow is often related to a deficit with the ninth cranial nerve: glossopharyngeal^[23, 27]. It may also occur due to salivary deficiency or change in saliva viscosity. Saliva is used to assist in the mastication of food and the formation of a cohesive bolus in preparation for swallow initiation. Lack of saliva reduces the cohesiveness of the bolus and therefore allows the bolus to break apart making swallow initiation more challenging^[18]. Impaired saliva flow also lowers the pH level of the oral cavity, providing an environment susceptible to pathogenic organisms. Lack of saliva

can subsequently place an individual at greater risk of oral, pharyngeal or lung infection^[24].

Stasis (or food / fluid pooling in the anterior and / or lateral sulci) takes place as a consequence of poor buccal tension and insufficient lingual function. Stasis may occur prior to or after the act of swallowing^[25, 28]. Inadequate lingual function may also lead to stasis of food to the tongue / hard palate. This is a frequent symptom in those with salivary deficiency and / or poor lingual and palatal sensation^[24].

Premature spillage of a bolus into the pharynx may result from impaired sensation to or motor control of the posterior tongue. A delayed swallow initiation can be described when the swallow occurs beyond the normative point on the tongue base where the normal swallow is said to be initiated^[25, 28]. Damage affecting the glossopharyngeal cranial nerve, responsible for swallow initiation and tongue base control^[18], may also result in premature spillage.

Piecemeal deglutition is a term used to define the process by which the bolus is segmented into smaller balls prior to the swallow. Piecemeal deglutition on small boluses often occurs due to the inability to manipulate the size of a bolus. In this process, the bolus quantity is reduced to make bolus control easier^[19, 28].

Studies examining COPD and the oral stage of swallowing indicate that this population frequently demonstrates a number of dysphagic characteristics. These include: reduced tone of oral musculature, susceptibility to fatigue^[8, 28], and evidence of oral stasis^[7, 29]. Oral dysphagia in COPD will be described in further detail in Chapter 3.4.

Pharyngeal Phase

The pharyngeal phase of swallowing consists of several discrete constituents. According to Brasseur & Dodds, 1991^[30], and Kahrilas, Logemann, Lin & Ergun, 1992^[31], these constituents are: velopharyngeal closure, glossopalatal opening, laryngeal closure, bolus propulsion, cricopharyngeal opening and pharyngeal clearance.

During the pharyngeal phase of the swallow, respiration is ceased for a brief period so as to allow the bolus to pass through the pharynx via a stripping wave (sequential contraction of the pharyngeal constrictors superiorly to inferiorly) without entering the larynx or trachea^[18, 23]. The precise integration of the pharyngeal constrictor muscles elevate the larynx, allowing the epiglottis to tilt down and direct material toward the oesophagus. Positive subglottic pressure in the upper airway assists the vocal cords to adduct, seal off and protect the airway^[32].

In the normal population, respiration is ceased for a brief moment during the act of swallowing. This period of apnoea commences just prior to initiation of swallowing and ends as the bolus passes through the upper oesophageal sphincter (UES), generally lasting 0.5 – 1.0 seconds in duration^[33-35]. Swallowing normally occurs during the expiratory phase of the respiratory cycle^[36].

The transition between the oral and pharyngeal phases of the swallow takes place as the tongue propels the bolus in a wave-like motion into the posterior oral cavity defined anatomically by the faucial pillars, posterior and lateral pharyngeal walls^[25].

The coordination between airway closure and pharyngeal movement is a complex one and there are several theories regarding the order in which the following movements occur during the pharyngeal stage. For the purposes of this thesis, the theory on

pharyngeal movement by Miller (1999)^[23] will be discussed as it describes the role of the respiratory system in detail.

Miller, 1999^[23], suggests that initially the palatopharyngeus and levator veli palatini assist in sealing off the nasopharynx; the preliminary component of this sequence in which respiration is inhibited. This results in sealing off the oropharynx from the nasopharynx. In conjunction, the larynx elevates and the arytenoids move anteriorly achieving epiglottic and laryngeal closure. The stripping wave is used to move the bolus inferiorly and toward the oesophagus and is accomplished via pharyngeal shortening and contraction of the pharyngeal constrictor muscles.

Symptoms that indicate pharyngeal dysphagia include effortful and delayed swallow initiation. These symptoms may arise as a result of poor base of tongue movement, minimal saliva flow and reduced tongue and / or pharyngeal sensation. This is often seen in neurological conditions where damage has occurred to the glossopharyngeal nerve^[18, 27].

Nasal regurgitation may occur as a result of poor velopharyngeal closure^[18]. As the bolus passes through the oropharynx, the soft palate rises by the function of the levator veli palatini muscle, to meet the posterior pharyngeal wall^[23]. Complete or partial failure to achieve this seal in a coordinated fashion may lead to bolus segmentation and fractions may move superiorly into the nasopharynx^[18, 25].

Another pharyngeal phase impairment is uncoordinated or reduced hyoid and laryngeal excursion. This may lead to insufficient epiglottic closure and has a variety of causes. Decreased tone in muscles of the floor of mouth and pharynx, fatigue, the effects of radiotherapy amongst other medical deficiencies can all produce poor hyoid and laryngeal excursion^[25].

Additionally, poor epiglottic closure manifests as a compromise to airway protection against foreign substances^[18, 24]. Poor epiglottic function may be a result of poor tone in the geniohyoid and mylohyoid (muscles of the floor of mouth); or alternatively, calcification may be present as a result of the effects of radiotherapy^[18]. If calcification is the cause of limited epiglottic movement, laryngeal elevation is also often compromised. Abnormal epiglottic closure may be an important feature to be assessed in the management of swallowing, as it has been suggested to be a predictor of aspiration risk^[18].

Weakness or incoordination of oropharyngeal musculature, incomplete epiglottic inversion and reduced laryngeal elevation, may produce incomplete pharyngeal clearance^[25]. Other elements that can manifest as pharyngeal pooling include: reduced pharyngeal pressure (due to incomplete seal of the nasal and oral cavities from the pharynx), cricopharyngeal dysfunction, cervical osteophytes and other anatomical abnormalities^[23, 25]. Stasis of food / fluid may be apparent in the valleculae, the piriform sinuses and along the pharyngeal walls^[26, 28].

Bolus penetration into the laryngeal vestibule and bronchopulmonary aspiration may also occur due to a number of reasons. Lack of cessation of respiration may cause the individual to inhale pharyngeal contents^[36]. Incomplete epiglottic closure results in an airway that is not sealed off from the pharynx, which can permit a misdirected swallow^[26]. Impaired laryngopharyngeal sensitivity may place an individual at risk for not being able to detect a misdirected swallow^[16], and diminished or lack of airway protection (cough and vocal cord closure) may disable the ability to evacuate foreign matter^[28].

Coelho (1987)^[8] describes the range of deficits observed during the pharyngeal stage of swallowing in patients with COPD. These include slower transit time and reduced coordination of pharyngeal musculature. These symptoms manifest as pharyngeal

stasis in the valleculae and piriform fossae, pooling superior to the cricopharyngeus, penetration of substance into the laryngeal vestibule and aspiration past the level of the vocal cords. Pharyngeal dysphagia in the COPD population will be further discussed in Chapter 3.4.

Oesophageal Phase

The oesophageal phase of swallowing commences with transportation of the bolus through the upper oesophageal sphincter (UES). Peristaltic movement transfers the bolus downward, through the lower oesophageal sphincter (LES) and into the stomach^[24].

The cricopharyngeus, located at the level of the UES, has several functions during the act of swallowing. Initially the cricopharyngeus relaxes during the swallow to allow the bolus to pass through the pharyngo-oesophageal segment without restriction. The cricopharyngeus then contracts once the bolus has passed through the UES in order to prevent retrograde movement of the bolus back toward the pharynx. The UES also prevents air from passing into the oesophagus^[23]. As the bolus reaches the level of the lower oesophagus, the LES relaxes to allow passage of the bolus through to the gastric cavity. The tone of the LES subsequently increases once the bolus has passed through to prevent reflux of gastric contents^[23].

Oesophageal dysphagia may present in many ways. Patients often complain of pain or pressure in the mid to high sternal region during or after meals, particularly on solid or dry food consistencies, and may also report coughing after meals^[18, 23, 28].

Incomplete lower pharyngeal clearance may be attributed to the lack of relaxation of the UES / cricopharyngeus. This can lead to symptoms of coughing after swallowing indicating laryngeal penetration or aspiration due to overflow or less dramatically the

sensation of hypopharyngeal fullness^[24]. Another reason for cough post swallow, but less commonly, is due to the presence of a tracheo-oesophageal fistula^[28, 37]. This is where a tract forms between the oesophagus and pulmonary system resulting in a direct channel for aspiration. Tracheo-oesophageal fistulae are most often seen in surgical cases or oesophageal cancer.

Regurgitation of food / fluid after swallowing may be due to poor cricopharyngeal tone, diverticula in the hypopharynx or upper oesophagus, or gastro-oesophageal reflux disease (GORD)^[28]. GORD presents as a result of transient relaxation of the LES and / or UES, allowing the escape of gastric contents from the stomach. The discomfort associated with retrograde movement of food / fluid is commonly described as 'heartburn'^[38].

Inadequate oesophageal tone and peristaltic movement may result in oesophageal stasis. This presents as a sensation of fullness, pressure and / or pain in the sternal region, worse for solid consistencies and increased quantities of food consumed^[38]. Other structural anomalies that may produce poor oesophageal clearance are oesophageal web, stricture, ring and muscle spasm^[18, 23]. As these oesophageal disorders are not the focus of this study, these symptoms shall not be discussed in further detail.

2.2 EFFECT OF AGE ON NORMAL SWALLOWING

The presence of co-morbidities often increases with age and dysphagia is frequently one of these co-morbidities^[10, 39]. As mentioned earlier, dysphagia is not often the primary diagnosis, but rather a symptom of an underlying pathology, hence the presence of swallowing difficulties may present as one of the symptoms of another disorder. Diseases that may influence the swallowing function in an elderly patient include stroke, dementia, progressive neurological disease, COPD, head and neck cancer, as well as many other conditions^[23, 25]. As swallowing is controlled by a central neurological process, any disease affecting the brain may demonstrate oral and / pharyngeal dysphagia as a symptom^[18].

There are several age related changes that affect swallow function. Studies have suggested that alterations can occur in the oral motor function with increasing age. A majority of these studies suggest atrophy in the muscles of mastication may be a primary cause of dysphagia^[18]. Several other authors further discuss age related changes that may affect swallow function.

Bolus Volume

Shaker et al (1994)^[33] examined the effect of age on the threshold volume triggering pharyngeal swallows in healthy adults. Results of this study indicated that the threshold volume required to stimulate a pharyngeal swallow was significantly greater in the elderly when compared with that of their younger counterparts. This may present as an issue in the management of swallowing in the elderly, as during the interval between the entry of a subthreshold amount of fluid entering the pharynx and the stimulation of a swallow, the substance may be inhaled into the airway.

Duration of Swallow

Sonies et al (1988)^[40] studied the durational aspects of the oral-pharyngeal phase of swallow in normal adults. Her findings suggested that swallow duration was greater in the elderly sample, specifically more pronounced in older women. As age increased in this sample, oral swallows were accompanied by extralingual gestures such as increased time required to move the hyoid anteriorly into position, identified as tongue pumping. It was proposed that subtle neurological changes might be responsible for the increased duration of the swallow displayed by this group.

Similarly, Kendall & Leonard (2001)^[41] found in their analysis of bolus transit and airway protection coordination in older dysphagic patients that bolus transit times were prolonged in the elderly. However they also noted that swallowing coordination mechanisms appeared to remain intact. This author noted that early laryngeal elevation was often apparent in older patients and suggested that this may be present as a strategy to avoid aspiration.

COPD is largely found in the elderly population. Given this, an examination of age related effects on swallow function is important within this paper. This issue shall be discussed further in Chapter 3.4.

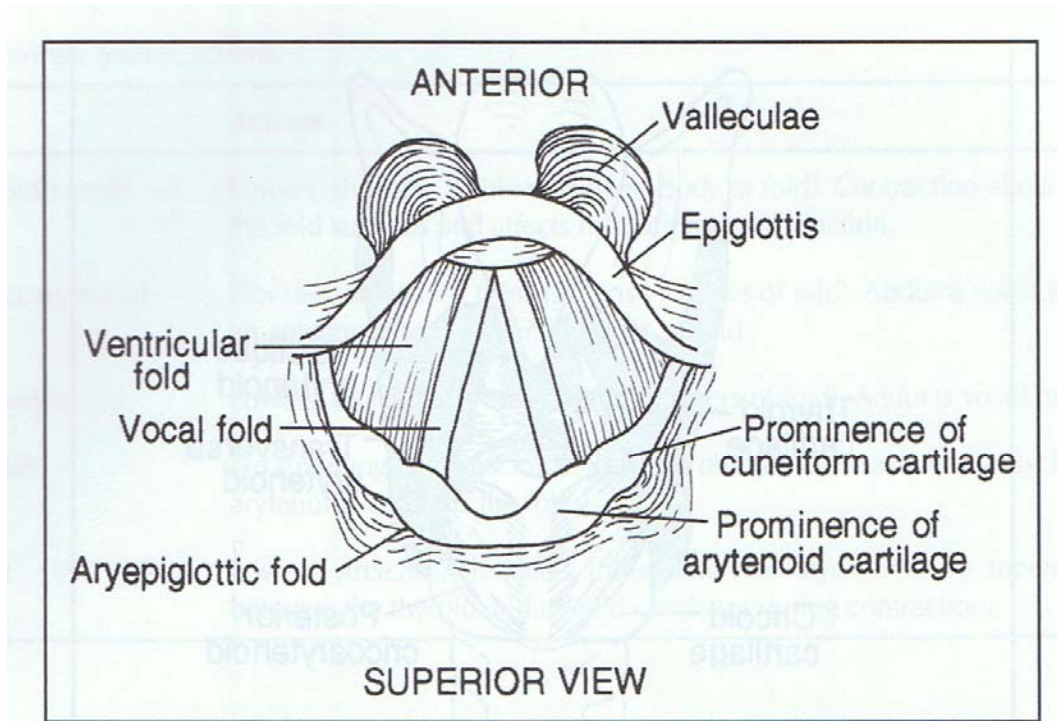
2.3 LARYNGEAL PHYSIOLOGY

The larynx shares three functions: airway protection, respiration and phonation. The larynx protects the airway from aspiration of swallowed material, coordinates and promotes respiration, and also provides controlled phonation for vocal communication.

Unlike in respiration and phonation, the protective function of the larynx is entirely reflexive and involuntary. The glottic closure reflex is a polysynaptic brainstem reflex, which achieves closure of the larynx to protect the airway during deglutition. This response is termed the laryngeal adductor reflex (LAR), the duration of which has been reported to be approximately 25 msec^[18, 42].

Sphincteric closure of the upper airway is achieved through three muscular tiers^[18]. The first occurs at the level of the aryepiglottic folds. Closure is attained by contraction of the superior division of the thyroarytenoid muscle, so that the superior inlet of the larynx is covered. The second tier of protection takes place at the level of the false vocal cords. The thyroarytenoid muscle is also responsible for closure of this tissue containing large majority of fat cells and mucous glands. The third level of protection transpires at the level of the true vocal cords. The inferior division of the thyroarytenoid muscle forms this shelf-like tissue and generates the most forceful closure for protection against aspiration. Sasaki & Weaver (1997)^[42] suggest that the true vocal folds are the most important barrier to prevent material being aspirated. Dua (1997)^[43] disputed this theory and showed that only partial adduction of the vocal cords occurs in 33% of normals during the process of swallowing. This suggests that the breath hold that occurs during swallowing is only obtained via a column of subglottic air^[43].

Figure 2.2: Laryngeal anatomy – superior view



From: Andrews, M.L., *Manual of Voice Treatment: Pediatrics through Geriatrics*. 3rd ed. 2006, New York: Thomson Delmar Learning. (page 19)

Furthermore, unlike animals, humans do not possess a crossed adductor reflex. This means that each side of the laryngeal musculature is controlled by one branch of the superior laryngeal nerve. Therefore it is possible that a unilateral recurrent laryngeal nerve injury may result in failure of ipsilateral vocal fold closure. This may predispose the individual to aspiration^[27]. In clinical practice, symptomatic aspiration may be frequently observed particularly on fluid consistencies, when unilateral vocal cord palsy is present. It is possible however, for aspiration to resolve within a period of time, as patients may learn to compensate for this lack of function even when vocal cord closure does not return.

Many consider glottic closure during swallowing as essential in the protection against aspiration during deglutition. Shaker and several co-authors' examine this relationship in detail. In 1990, Shaker et al^[44] investigated the coordination of deglutitive glottic closure with oropharyngeal swallowing in a sample of healthy subjects. They found that vocal cord adduction is the initial event in the sequence of swallowing. Vocal cord adduction was found to precede movement of the hyoid bone, base of tongue and submental surface myo-electric activity. The authors also determined that glottic closure precedes nasopharyngeal peristalsis. Shaker et al (1990)^[44] postulated that these findings may play an important role in preventing swallow-induced aspiration.

Shaker et al (2002)^[45] continued to examine glottic closure with reference to the pressure exerted by the vocal cords during volitional swallow and other voluntary tasks. They reported that the vocal cords generate closure pressures that vary depending upon the task. These pressures were also found to be significantly greater than those of the intra-tracheal space. The authors suggested that these results may play an integral part of airway protection during swallowing.

2.4 SENSORY RECEPTORS OF THE LARYNX

The trigeminal, vagus and glossopharyngeal cranial nerves provide afferent pathways to innervate the larynx and pharynx^[23]. Unlike the oral cavity, there are many more slow-adapting receptors than mechanoreceptors in the larynx and pharynx. These slow-adapting receptors innervate the epithelium found within the laryngeal and pharyngeal walls, and are most dense upon the laryngeal surface of the epiglottis. They are known as slow-adapting receptors as they discharge continuously throughout the duration of the stimulus^[18].

Not all receptive sites within the oral cavity, pharynx and larynx have the same potential to evoke pharyngeal swallowing^[46]. A stimulus must activate sensory fibres that synapse at specific central neural sites in order to induce or facilitate a pharyngeal swallow^[23]. The most sensitive region for stimuli to evoke pharyngeal swallowing has been suggested to be over the receptive field of the superior laryngeal nerve^[18]. Swallowing can be induced through stimulation of activating fibres of the glossopharyngeal nerve; however the threshold of these fibres is much higher^[18].

There are several criteria to effectively evoke and facilitate pharyngeal swallowing^[23, 46]. The stimulus must excite several receptive fields of a group of sensory fibres. Stimulus presentation will also facilitate initiation: dynamic stimuli that vibrate are much more effective than static stimuli that have constant pressure^[18].

Impaired sensation in the oral, pharyngeal and laryngeal regions may severely damage swallowing function^[47, 48]. Sensation of a bolus is required to trigger initiation of the pharyngeal swallow at a specified threshold and without intact sensation, swallowing may not be initiated. Additionally, if residue is present in the pharynx after the swallow, stasis may not be sensed, resulting in the individual not acknowledging the presence of pooled material and therefore not swallowing again to facilitate clearance. Eisenhuber

et al (2001)^[49] described that impairment in pharyngeal clearance is associated with increased aspiration risk. It is reasonable to postulate that lack of pharyngeal clearance may be related to pharyngeal sensory deficits. Furthermore, should aspiration take place, reflexive coughing may not occur to clear the tracheobronchial tree as the aspirate may not have been recognised^[50, 51].

The evaluation of laryngeal and pharyngeal sensitivity is complex. As stated earlier, laryngopharyngeal sensation can only be assessed through stimulation of the superior laryngeal branch of the vagus nerve. Aviv et al (1993)^[14] developed a technique for determining laryngopharyngeal sensation that involved the use of air pulses to activate cutaneous mechanoreceptors. The methodology involved air pulses delivered to the anterior wall of the piriform sinus while the subject indicated if they had felt the air pulse. He developed this technique further with colleagues (Aviv et al, 1999)^[52], following discovery that mechanical stimulation of the mucosa innervated by the superior laryngeal nerve resulted in the Laryngeal Adductor Reflex (LAR) or the transient adduction of the true vocal cords. During these investigations the stimulation site was altered to the aryepiglottic fold as this yielded a more consistent LAR response. The advantage of this modified technique was that laryngopharyngeal sensation can now be assessed more objectively and intact cognitive functioning is no longer required to ascertain an accurate measure.

In an expansion of his previous work, Aviv et al (1997)^[13] examined LPS testing in combination with Modified Barium Swallow (MBS) as a predictor for aspiration pneumonia after stroke. Results of this study indicated that a combination of MBS and laryngopharyngeal sensory testing may be a more accurate predictor of aspiration pneumonia than MBS alone as the method permitted the assessment of both the motor and sensory components of swallowing.

Aviv and colleagues refined their technique of assessing both the motor and sensory components of swallowing by developing FEESST (Fiberoptic Endoscopic Evaluation of Swallowing with Sensory Testing) in 1998^[15]. This system enabled testing of LPS and swallow function via nasendoscopy within the one procedure.

Setzen et al (2001)^[48] also examined LPS as a predictor of aspiration. They studied 40 patients with dysphagia who underwent endoscopic evaluation of swallowing with sensory testing, and prospectively divided the patients into 2 subject groups. One group included those with severe sensory deficit (determined by absent LAR) and the other group included those with apparently normal sensory function. Each group was administered thin fluid and puree consistencies and were evaluated for presence of aspiration and pharyngeal muscle contraction. These authors found that severe LPS deficits were closely associated with aspiration of thin liquids. They also reported that hypopharyngeal sensory deficits were strongly associated with pharyngeal motor function deficits.

In 2003, Setzen et al^[47] aimed to increase the reliability of LPS predictive value, by combining LPS values with an examination of pharyngeal motor function. They examined the sensory and motor function of 204 consecutive patients who were referred for endoscopic evaluation of swallowing. Pharyngeal motor function was evaluated through determination of presence or absence of pharyngeal muscular contraction during voluntary forceful contraction of the vocal cords (pharyngeal squeeze). Results of the study indicated that laryngopharyngeal sensory function testing, when combined with an assessment of pharyngeal motor function (as defined by pharyngeal squeeze), provided a more accurate indicator of aspiration risk. They also revealed that severe LPS deficits alone are associated with increased aspiration risk, regardless of integrity of pharyngeal motor function.

Perlman et al (2004)^[53] continued the research of Setzen et al (2003)^[47] and investigated the risk of aspiration as determined by FEESST on a pureed food consistency. This author studied the same patient group, divided into 3 categories: normal, moderate and severe sensory deficits. Each category was then further divided into those with normal and impaired pharyngeal squeeze, and subsequently evaluated for aspiration on pureed food boluses. The results indicated a significant difference in the incidence of pureed food aspiration for the normal and moderate sensory loss patients when compared to patients with normal and impaired pharyngeal squeeze.

Interestingly however, in the severe sensory loss group, there was no difference in the frequency of aspiration between those with normal and impaired pharyngeal squeeze. So, in concordance with the work of Setzen et al^[47], Perlman et al^[53] also found that a severe LPS deficit alone is highly predictive of aspiration regardless of pharyngeal motor integrity.

The authors concluded that patients with impaired pharyngeal squeeze at varying levels of sensory loss are at greater risk for aspiration of pureed consistency foods, when compared to those with normal pharyngeal squeeze. They also suggested that aspiration of pureed foods may be more dependent on hypo-pharyngeal muscle tone than laryngopharyngeal sensation.

As described above, the role of sensation may be critical to ensure safe and functional swallowing. Laryngopharyngeal sensation has not been previously examined in the COPD population specifically. The high incidence of co-occurring dysphagia and COPD in patients suggests further information is needed to comprehensively examine the nature and impact of LPS in this patient group.

CHAPTER THREE:

SWALLOWING AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

3.1 CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

The American Thoracic Society (1995)^[54] defines COPD as a disease characterised by progressive development of airflow limitation that is not completely reversible. COPD includes both chronic bronchitis and emphysema. Chronic bronchitis is defined by an increase in mucous production in the lower respiratory tract and presence of a persistent productive cough of more than three months' duration for more than two years^[55]. Emphysema is characterised by dilatation of air spaces, destruction of lung parenchyma distal to the terminal bronchiole, loss of lung elasticity and closure of small airways^[55]. These two diseases nearly always coexist, however their relative extent may vary within individual patients.

There are several risk factors in the development of COPD and many have implications for an individual's swallowing ability. Recognised risk factors for COPD include: cigarette smoking, bronchial hyper-responsiveness, male gender, environmental pollutants, exposure to occupational chemicals, passive smoking, poor diet, increased age (greater than 35 years), acute respiratory infections in infancy and childhood, and genetic predisposition^[56-58]. Similarly, risk factors for dysphagia include increased age, poor airway responsiveness and protection, and malnutrition. Any combination of these risk factors may be related to the development of dysphagia and consequently aspiration pneumonia.

The clinical features of COPD manifest as a timeline of symptoms. Initially there is often a presentation of cough, first in the morning. The cough is frequently productive of sputum containing mucous, which becomes purulent (containing infection) during an exacerbation. Breathlessness on exertion starts subtly, being more prominent on colder

days. As the disease progresses the patient may become persistently breathless on exertion often accompanied by chest tightness and wheeze. For example, the patient may have to rest when climbing one or two flights of stairs^[59]. It is this feature of breathlessness that often terminates a patient's ability to work. In end-stage COPD the patient becomes breathless on minimal exertion such as with activities of daily living^[55]. Accompanying the symptom of increasing breathlessness is increasing fatigue. Much more effort is required to perform simple activities including eating and drinking.

In advanced COPD, the physiological characteristics of disease progression present as a function of interplay between the symptoms of chronic bronchitis and emphysema. The varying degrees of airflow obstruction are caused by a combination of narrowing and distortion in smaller airways and loss of alveolated lung with reduction in the elastic recoil of lung tissue. Increased work of breathing occurs as a result. The irreversible component of airflow limitation results from inflammation, fibrosis and modification of peripheral airways. Airflow limitation leads to non-homogenous ventilation, while the reduction in surface area available for gas exchange is caused by alveolar wall destruction and changes in pulmonary vessels. The deficiency in alveolar wall surface area results in impaired gas exchange and alterations in the physical properties of the lungs that become less elastic. These features are seen in advanced cases of COPD as marked hyperinflation, severe airflow obstruction, trapping of air and poor outcomes on diffusion testing (the ability of gases to cross the alveolar border)^[60].

Moreover, other late manifestations of advanced COPD include hypercapnia (caused by a reduction in ventilatory drive), pulmonary hypertension and cor pulmonae. The latter two features reflect pulmonary vasoconstriction due to reduced alveolar oxygen concentration in poorly ventilated lung segments, evidencing as vascular remodelling^[61].

In addition, the features and symptoms of smoking related lung disease that are described above provide an environment that is susceptible to infection.

3.2 RELATIONSHIP BETWEEN RESPIRATION AND SWALLOWING

Airway protection is critical in maintaining adequate respiratory function. Impaired airway protection places an individual at greater risk of aspiration and subsequently infection^[24, 62]. To date there is limited research available regarding the relationship between Chronic Obstructive Pulmonary Disease (COPD) and dysphagia. Kuhlmeier (1994)^[20] describes respiratory disease as the 3rd most frequent diagnosis associated with dysphagia.

Respiration and swallowing are finely tuned coordinated events that share common pathways; muscle groups and neural coordination. Both systems are controlled by the brainstem nuclei located in the medulla. Langmore & Curtis (1997)^[63] describe that the glottic closure reflex essential to airway protection, is achieved by stimulation of sensory receptors (of the vagus nerve) located in the thorax, which is then relayed to the medullary respiratory centre. This signal is transmitted through a synapse to the recurrent laryngeal nerve causing the posterior cricoarytenoid muscle to shorten and adduct the vocal cords. This method of airway protection is vital for protecting the lungs against foreign bodies or aspirated material.

The mechanisms underlying the high prevalence of reported dysphagia in respiratory disease are unclear. Diseases of the respiratory system effectively alter the respiratory pattern of an individual during swallowing^[10]. This is clinically significant as the respiratory system controls the mechanisms that protect against aspiration, pneumonia and also death. The airways are protected from aspiration during deglutition by a combination of mechanisms. These mechanisms include the upward and anterior movement of the larynx, vocal cord adduction, relocation of the aryepiglottic folds and coordination of respiration with swallowing^[63]. Research indicates that the coordination between these mechanisms is modified in COPD^[10].

The defence mechanisms against aspiration may be described in three tiers. The first line, involving elevation of the larynx, epiglottic inversion and closure of the glottis, helps prevent foreign material entering the airway by effectively sealing it off from the swallow pathway. If aspirated material reaches below the glottis, cough and mucociliary action take over as the second line of defence. If aspirated material reaches the areas of gas exchange (terminal bronchi and alveoli), cellular mechanisms come in as the third line of defence in managing the foreign matter^[28].

Aspiration that is not cleared by these defence mechanisms may result in a variety of complications. Specifically, aspiration of solid particles may cause blockage of small airways and aspiration of fluids may effectively reduce the level of surfactant so that alveolar patency cannot be maintained. Poor alveolar patency results in decreased gas exchange between the lung and circulatory system. Aspirated matter is a source of broncho-pulmonary infection that may be slow to resolve if there is food matter or other retained secretions. Aspiration may induce inflammation in the lung tissue impairing oxygen diffusion and may in turn lead to decreased gas exchange and eventually alveolar collapse: atelectasis. Atelectasis is a predisposing factor to pneumonia due to impaired clearance of secretions^[18].

There is a plethora of information to suggest a key relationship between swallowing and respiration^[10, 34-36, 63-69]. Nilsson et al (1997)^[36], Nishino et al (1985)^[35], and Smith et al (1989)^[66] describe the normal pattern of respiration during swallowing. They note that as swallowing primarily occurs during the expiratory phase of swallowing, this may indicate an important protective role in preventing aspiration^[66].

Breathing patterns are designed so that precise ventilation can be achieved via the lowest possible workload – divergence from this optimal pattern will cause an increase in the work of breathing. Although this may not be of significance in the healthy person,

this factor may have considerable implications for the patient with lung disease and may contribute to dyspnea and fatigue when eating and drinking^[66].

The pattern of respiration may also have significant implications for special populations. Research in normal subjects has shown that during the process of swallowing, breathing becomes increasingly irregular. Resting respiration does not merely cease during eating and drinking, but it is actually substituted by an alternative well-regulated pattern. Nishino et al (1985)^[35] reported that 80% of all normal swallows occur during the expiratory phase of respiration. Normal subjects who try to swallow during inspiration find this most uncomfortable if not impossible. Furthermore, Nishino et al (1985)^[35] comment that the expiration after swallowing may assist in clearing any foreign material in the vicinity of the laryngeal vestibule prior to subsequent inspiration. Interestingly, Nilsson et al (1997)^[36] reported that “misdirected swallows” were more common in subjects with inspiration pre and post swallow, and the duration of apnoea in these subjects is also longer than for those with other respiratory patterns. So, these patients who swallow during the inspiratory phase and have a prolonged period of apnoea during the swallow are at greater risk of dysphagia and potentially developing aspiration pneumonia.

The respiratory pattern during swallowing also alters with age. Leslie et al (2005)^[70] examined 50 healthy volunteers (aged 20-78 years) and established that with increasing age, the period of apnoea during swallowing also increased. Expiration post swallow, multiple swallowing, post swallow respiration reset pattern and resting respiration were found to be independent of age.

Recent research indicated that the coordination between respiration and swallowing mechanisms may be modified in COPD^[10]. During COPD exacerbation, swallowing often takes place during the inspiratory phase^[10]. Following the information discussed

earlier in this section, it seems reasonable to postulate that swallowing during the inspiratory phase of respiration may place the COPD patient at higher risk of aspiration.

In summary, additional strains are placed upon the respiratory system by the presence of COPD during the act of swallowing. This may result in the need for compensatory mechanisms in order to prevent dysphagia and its resultant respiratory complications.

3.3 COUGH AND DYSPHAGIA

Cough is one of the most important defence mechanisms for airway protection and maintenance. Consequently, it is essential to understand the neural control and physiology of the cough when making clinical decisions regarding dysphagia management.

Cough is designed to clear secretions or foreign material from the bronchial tree or larynx^[24]. The act of coughing is under partial voluntary control, however it commonly occurs as an involuntary reflex. The voluntary cough may be described in three phases: inspiration, compression and expiration. The first phase commences with a quick inspiration followed by contraction of the respiratory muscles against a closed glottis. During the second phase, the pharynx shortens and lateral pharyngeal walls squeeze any residue out of the piriform sinuses. While this muscular contraction is taking place, there is a subsequent rise in intrathoracic pressure. The third phase is characterised by rapid opening of the glottis and sharp release of air enables clearance of particles in the path of the airstream, projecting material to the upper airway^[24]. High rates of flow during cough cannot be achieved in severe obstructive respiratory disease, as the airways are narrowed and high intrathoracic pressures cannot be sufficiently generated^[71].

The involuntary cough action occurs through a reflex arc, with sensory receptors located in the respiratory tract. Vagal receptors (rapidly adapting receptors and amyelinated C-fibres), sensitive to mechanical and chemical stimuli, lie in the mucosa of the larynx, trachea and bronchi. Their principal role is to detect and remove unwanted particles by initiating a forced expiration. Minimal inspiration prior to involuntary cough prevents the inhalation of foreign material further down into the bronchial tree. In the lower parts of the respiratory tract, receptors sensitive to chemical stimuli can be located. Should they detect a foreign chemical stimulus such as a toxic gas, the cough reflex arc is

initiated^[71]. More recently, a specific cough receptor has been identified known as TRPV1. Ing (2006)^[72] describes this receptor as a cation-selective channel within the cell membrane, binding with capsaicin and other vanilloids, which may have implications for therapy in the future.

It is important to note that the cough reflex is less sensitive in the elderly^[71, 73], and is lost in conditions of sedation and unconsciousness^[71, 74]. Given that cough after presentation of food / fluid is the single strongest indicator of laryngeal penetration / aspiration^[24], it is reasonable to postulate that the elderly are at greater risk of adverse consequences of aspiration if they do not cough to clear the aspirated material.

Cough is a primary symptom of COPD. Given this, using cough as an indicator for laryngeal penetration and aspiration can be challenging in the COPD population as it is not always clear whether the presentation of cough during a clinical swallow examination is related to the patient's swallow function or the COPD itself.

Addington et al (1998)^[62] designed a method of determining the laryngeal evoked potential of the cough reflex arc by recording from the internal branch of the superior laryngeal nerve. In a study in 1999, Addington et al^[75] expanded upon this method and examined the predictive value of cough in determining aspiration pneumonia risk after stroke. These authors found that an abnormal result on their Reflex Cough Test indicated risk of an unprotected airway and increased incidence of aspiration pneumonia.

Cough may also be related to Gastro Oesophageal Reflux Disease (GORD). There are several acquired risk factors for developing GORD. Among these risk factors is respiratory disease that leads to hyper inflated lungs and a flattened diaphragm. Hyper-inflated lungs are a primary characteristic of COPD^[59], so it would appear that COPD patients may be at increased risk of presenting with co-occurring GORD^[76].

Kadokia et al (1995)^[77] reported on the effect of cigarette smoking on upright GOR events followed by heartburn. The study involved continuous pH recording on 14 cigarette smokers with chronic heartburn. In the initial stage of pH recording, the subjects abstained from smoking for a period of 72 hours. For the secondary stage of recording, the subjects smoked 1 pack of filtered Marlboro cigarettes over a period of 8 hours. Kadokia et al (1995)^[77] reported a significant increase in heartburn episodes during the secondary phase of this study. This research has clinical relevance to the population being studied in this paper, as prolonged cigarette smoking is the main cause of COPD^[78]. It is therefore possible that individuals with COPD as a result of smoking history may be at increased risk of developing GORD.

For the purposes of this study, it is essential to have a comprehensive understanding of the physiology of cough and its relationship with dysphagia. The relationship between cough and dysphagia changes when examining an individual with COPD. The function of cough as a symptom of COPD is to expel excess secretions from the airway. In dysphagia and aspiration, cough is a protective mechanism against foreign material entering the airway^[24, 62]. Therefore when evaluating swallow function of an individual with COPD, it is crucial that the nature of the cough be taken into account to enable accurate diagnosis and management planning.

When the nature of cough during a clinical examination of swallowing is unclear, objective assessments can be useful in providing further information about a patient's swallow function and airway protection. Objective swallowing assessments include videofluoroscopy and endoscopy. Both of these assessments allow visualisation of the pharynx and larynx whilst different food and fluid consistencies are ingested. Videofluoroscopy provides a lateral perspective and endoscopy enables a superior perspective during swallowing, so that penetration of food or fluid material into the

airway may be observed and the presence and integrity of airway response to the penetration can be noted.

Objective swallowing assessments in patients with COPD are frequently utilised, as this population can appear complex on bedside examination due to the frequency of cough presentation. The nature of dysphagia in COPD as defined by objective swallowing assessments will be further discussed in Chapter 8.

3.4 COPD AND DYSPHAGIA

There is a limited amount of literature that has been published on the relationship between COPD and dysphagia. The main focus has been the association between COPD and gastro-oesophageal reflux disease (GORD), and GORD and dysphagia. The objective of this study is to analyse the relationship between COPD and swallowing difficulties.

Coelho (1987)^[8] examined the nature of dysphagia in 14 patients with primary diagnosis of COPD who were referred from the pulmonary unit of a rehabilitation hospital. 13 patients had tracheostomy tubes and 5 were ventilator dependent. Each patient's swallow function was assessed through bedside examination and videofluoroscopy. Results indicated that COPD patients had difficulty during both the oral and pharyngeal phases of the swallow. Oral and pharyngeal transit times were slower when compared to normals, and COPD patients exhibited reduced coordination and strength of the oral and pharyngeal musculature. Considering the link between these features and poor respiratory control during swallowing and reduced airway protection, the overall representation suggests that COPD patients may be at higher risk of developing respiratory complications due to aspiration.

Coelho's study^[8] describes the signs and symptoms of dysphagia in the COPD population from a functional perspective, emphasising the use and importance of therapeutic techniques, such as neck flexion and alternating food / fluid boluses. This research does however present limitations. The majority of the patients studied had tracheostomy tubes. It is well documented that the presence of a tracheostomy tube can alter swallow physiology^[79-84].

Coelho's study^[8] also failed to evaluate laryngeal penetration separate to aspiration, which may hold implications for whether the patient develops pulmonary compromise.

All patients were categorised according to videofluoroscopy result into one of three groups: consistent aspiration, dysphagia with no aspiration and functionally intact swallowing ability. This grouping method may not account for patients who may aspirate intermittently, have laryngeal penetration or aspirate due to fatigue. The small amounts of food / fluid given in this study may also not have been sufficient to examine the effects of fatigue upon swallowing ability. Fatigue is an important issue in respiratory compromised patients as they often become breathless and tired during meals^[55, 66, 85]. Furthermore, their study did not define whether the subjects were in a stable state or during disease exacerbation at the time of assessment. This may have important implications as during disease exacerbation, the COPD patient has poorer outcomes on respiratory function testing. It is possible that this may affect the individual's ability to coordinate respiration and swallowing.

Several questions are raised by the results of Coelho's study^[8]. The mechanics that cause aspiration and dysfunctional swallowing in patients with COPD needs to be investigated. The impact of sensation in the laryngopharynx upon swallow function has not been examined in this population. While videofluoroscopy can provide considerable information on the motor components of swallowing, it does not provide insight into sensory functioning. Deficits in sensation may result in elevated aspiration risk and the inability of a patient to be aware to institute compensatory strategies. The correlation between whether the patient considers they have a deficit in their swallowing ability with an objective assessment of swallowing ability has also not yet been evaluated. It is unclear whether the sample studied by Coelho et al^[8] was aware of their swallowing disorder. The condition of the patient, whether they are stable or in exacerbation also needs to be defined as this may have implications upon the patient's swallowing status.

Clinically, there appears to be a relationship between COPD and GORD. Many patients suffer from both conditions. Mokhlesi et al (2001)^[6] examined the increased prevalence of gastroesophageal reflux disease in COPD and its relationship to dysphagia. The

investigators found that 17% ($p < 0.02$) of the subject population with COPD indicated that they had some degree of difficulty swallowing. However, the impairment of swallowing ability was defined through a self-reporting questionnaire. The use of a self-reporting questionnaire as a measurement tool for this finding remains questionable. Additionally, the issue of sensation was proposed during their discussion of the study, as these investigators suggested that the threshold for detecting reflux events in COPD patients may be lower when compared to age-matched controls.

A further study by Mokhlesi and colleagues in 2002^[29] examined 20 consecutive COPD patients during deglutition. Patients were considered eligible if they were in a stable state with an $FEV_1 \leq 65\%$ of predicted and total lung capacity $\geq 120\%$ of predicted. Videofluoroscopic evaluation was performed on each subject and results compared to 20 age and sex matched historical control subjects. The primary outcome of the study illustrated that COPD patients possess a maximal laryngeal elevation during swallowing that was significantly lower than the control group ($p < 0.001$). The authors also comment that COPD subjects exhibited more frequent use of spontaneous protective swallowing manoeuvres, such as increased duration of airway closure and earlier closure of the larynx relative to opening of the cricopharyngeus, when compared to controls ($p < 0.05$). Mokhlesi et al (2002)^[29] concluded that COPD patients present with altered swallow physiology that may play a protective role in preventing aspiration. They did however comment that these measures may not be useful during disease exacerbation.

Whilst this study was well designed and has highlighted interesting features regarding swallow physiology of the COPD patient, the authors have not addressed how prolonged airway closure may affect the relationship between respiration and swallowing. The authors comment that respiratory rate and oxygen saturation levels remain unchanged during the study, however considering the small quantities administered, one cannot generalise this statement to a COPD patient's respiratory

performance over an average meal. A prolonged period of apnoea during swallowing may result in increased shortness of breath, and as Shaker et al (1992)^[10] has described, tachypnoea itself can alter swallow physiology.

Additionally, the authors did not exclude patients with a history of GORD. Their rationale for the lack of exclusion was that the focus of research was the pharynx as opposed to the oesophagus. It is well documented that GORD is associated with pharyngeal dysphagia, thus presence of GORD may have influenced study results^[38, 86, 87].

Another study, Good-Fratturelli, Curlee & Holle (2000)^[7], investigated the prevalence and nature of dysphagia in VA (Veteran Affairs) patients with a primary diagnosis of COPD referred for videofluoroscopic swallow examination. They described nearly 85% of subjects as evidencing some degree of dysphagia and suggested that the COPD patient's respiratory status should be considered when assessing swallow function. The obvious difference in prevalence rates between the two studies discussed here, does raise several issues with respect to study design, validity and ability to reproduce findings. If the figure Good-Fratturelli et al (2000)^[7] obtained is accurate, then swallow testing should be mandatory in this population, especially if there is also co-morbidity present. However, the fact that these patients were referred for videofluorographic swallow study denotes a source of referral bias as the subjects in this sample were already suspected of having swallowing problems.

The sample analysed is another source of potential bias, as only 84 COPD patients were studied out of the 1,996 COPD patients with known COPD diagnoses at the outpatient facility of the study. The reason for this relatively small sample compared with a much larger population appears to be due to small numbers of referral. This raises the question of whether under-referral may be an issue in this population. Additionally, the subjects' disease status (stable or in exacerbation) was not specified.

With further inspection it may be that broad inclusion criteria, such as past medical history of Cerebral Vascular Accident (CVA), may have contributed to the high percentages of dysphagia diagnoses. It is well documented that CVA is a primary cause of dysphagia^[23, 88]. The failure to exclude such patients would have strongly inflated prevalence results as well as influenced the clinical significance of the study. The investigators also commented that cough may have been an indicator of dysphagia in this population. It is important to note that cough is also a symptom of COPD itself and may not necessarily be related to the patient's swallowing ability^[55].

The relationship between COPD and dysphagia was further analysed by Maclean (1998)^[85]. The author investigated swallow function of patients with COPD during disease exacerbation, then repeated the assessment once patients had stabilised. Swallow function was assessed through a self-reporting questionnaire, a bedside swallow examination, followed by a Modified Barium Swallow.

Maclean's findings^[85] demonstrated that a majority of COPD patients reported a history of difficulties swallowing on the questionnaire, with high percentages indicating decreased strength of cough and coughing whilst eating. Bedside examination demonstrated that increased shortness of breath whilst eating was the most prevalent characteristic between all subjects. Multiple swallows and fatigue were also key phenomena observed. Results from the Modified Barium Swallow assessment indicated that all patients presented with dysphagia regardless of whether they were in acute exacerbation or stable. The most prominent features of swallow dysfunction on Modified Barium Swallow included: poor bolus formation, premature spill, slow oral transit, oral residue, vallecular residue, reduced laryngeal elevation, laryngeal penetration and aspiration during the swallow. Upon comparison of each symptom between initial and repeat assessment, statistically significant decreases in severity scores were observed. However on comparison of overall swallow dysfunction, severity scores for acute exacerbation and stable period were not statistically significant.

Maclean (1998)^[85] raises several interesting features related to swallow function in COPD, and the effect that an acute exacerbation has upon the swallowing mechanism. Also of interest is the patients' insight into swallow function, however the relationship between the questionnaire and Modified Barium Swallow results does not appear to have been examined. The use of severity scores in any disorder remains questionable; severity scores are a perceptual rating and may differ from one examiner to another. Despite evidence of a statistically significant decrease in symptom specific severity scores between acute exacerbation and stable periods of COPD, the reproducibility of these findings is uncertain.

Reid (1998)^[9] conducted another study that examined the role of dysphagia in acute exacerbation of COPD. Fifteen patients with a history of two exacerbations within twelve months or three in two years were studied in conjunction with age matched healthy controls. Each subject underwent a medical and swallowing questionnaire, clinical examination of swallowing and Modified Barium Swallow. The effect of dyspnoea on swallow ability was also evaluated through repeating a portion of the Modified Barium Swallow assessment following a respiratory stressor activity.

Results of this study revealed that the COPD group presented with a number of significant dysphagic features during Modified Barium Swallow examination: piecemeal deglutition on liquid boluses, delay in onset of pharyngeal phase and increased incidence of laryngeal penetration / aspiration. Total swallow duration and pharyngeal transit time was found to be significantly greater in COPD patients for liquid boluses and the pear piece. Oral transit time was also significantly longer for the biscuit consistency in COPD patients.

Interestingly, results from the questionnaire indicated that there was no significant difference in reported swallow difficulties overall between COPD and healthy subjects.

Significant differences were found however, in COPD patients reporting coughing when drinking, needing to eat and drink slowly and the need to cut up food into small pieces. Comparisons were made between the questionnaire answers and results on the Modified Barium Swallow: the author determined that COPD patients' subjective reports of swallowing difficulties were inaccurate in representing their actual swallow ability.

Statistically significant results on bedside examination when comparing COPD to control subjects included hoarse vocal quality, delayed swallow initiation, multiple swallows to clear bolus and coughing after the swallow (for both liquids and solids). Comparison of bedside examination to Modified Barium Swallow results indicated that cough before, during or after the swallow was predictive of aspiration but not for bolus consistency or time of aspiration.

The author acknowledges that age may have contributed to increased incidence of swallow dysfunction in the COPD group: commenting that aspiration only occurred in those greater than 80 years of age. It is well documented that advanced age is related to higher incidence of dysphagia, particularly when co-morbidity is present^[18, 25, 40, 41, 89]. The effect of reduced sensation and impairment of swallow-respiration control is discussed as potential key components in COPD swallow characteristics and it is suggested that this may be an area for further research. Additionally, while COPD patients were recruited on the basis of recent exacerbation, it is unclear whether these COPD patients were examined during an exacerbation. It is also difficult to ascertain the effect of fatigue in this study as limited portions were administered during the Modified Barium Swallow. It is understood however, the need to minimise radiation exposure.

A study from Weinberg, Stein & Williams (1995)^[90] supports the relationship between COPD, GORD and dysphagia. These authors discuss the relationship between COPD, GORD and cricopharyngeal dysfunction. They describe the results from another of their

studies; where they report the overall incidence of cricopharyngeal dysfunction in a sample of COPD patients as 84%. If this figure is compared to previously published data^[91], specifying an 11% cricopharyngeal dysfunction in non-COPD populations, the possible importance of this swallowing feature is highlighted. They further comment that cricopharyngeal dysfunction may contribute to pulmonary exacerbation in patients with severe COPD.

Given the high prevalence of COPD, its significant morbidity and the current evidence of a possible relationship with dysphagia, further investigations are required that define this population in terms of laryngopharyngeal sensation. The ability to detect the risk of developing dysphagia and aspiration through sensitivity testing will have important implications upon the management of those patients with COPD.

The study that will be described over the remaining chapters in this thesis has been designed in order to meet a number of objectives and subsequently further describe the relationship between COPD, laryngopharyngeal sensation and swallow function. Firstly, we aim to determine the frequency of LPS impairment in patients with proven COPD, where LPS impairment is defined by a measure of LAR threshold. Secondly, the presence of a relationship between LPS impairment and severity of COPD will be analysed. Thirdly, we will describe the relationship between LPS and swallow function in patients with proven COPD. Finally, we will ascertain whether LPS predictive value may be utilised as a method to assess risk of dysphagia and aspiration, as established by bedside clinical examination and endoscopic assessment of swallowing function, in patients with proven COPD.

PREFACE TO CHAPTERS 4 & 5

This research is a combination of 2 studies: the first is a prospective controlled study evaluating LPS in COPD patients, and the second is a prospective descriptive study evaluating swallow function in COPD patients. Both studies utilized the same study population. For the purposes of this thesis, these studies will be discussed separately, however cross-referencing will be used between the study methodologies.

ETHICS APPROVAL AND CONSENT

Ethics approval was sought and obtained through the Concord Repatriation General Hospital Ethics Committee (see Appendix A). A Participant Information Form was given to the case subject regarding the aims of the study as well as procedures and information required of them (see Appendix B). Written consent was obtained from all participants prior to further examination (see Appendix C).

CHAPTER FOUR:

STUDY ONE:

THE EFFECT OF COPD ON LARYNGOPHARYNGEAL SENSITIVITY (LPS)

4.1 STUDY AIMS

1. To determine the prevalence of LPS impairment (as measured by the LAR threshold) in patients with proven COPD.
2. To determine the relationship between LPS impairment (as measured by the LAR threshold) and COPD severity.

4.2 METHODOLOGY

LPS was assessed in case subjects during a clinically controlled period of their respiratory condition. The primary physician assessed the stability of the case subject's condition through clinical assessment. All assessments were conducted at The Respiratory Unit, Concord Repatriation General Hospital, under the direct supervision of senior thoracic physicians with experience in managing patients with COPD.

Case Subjects

22 subjects were recruited to participate in the study however 2 withdrew due to their inability to tolerate LPS testing. Therefore the final subject group consisted of a total of 20 patients: 4 women and 16 men, age range of 54–80 years (mean=71.7, SD = 6.8, median=73). Subjects were recruited between August 2001 and June 2003. Both outpatients and inpatients were considered for inclusion. Subjects were recruited through one of two methods. The first method involved consultation of hospital admission lists for patients admitted under the care of respiratory physicians or onto the

respiratory ward. These patients were admitted to hospital for exacerbation of their illness or some other medical / surgical reason. The second method of recruitment consisted of consulting the outpatient lists of visiting Thoracic Physicians for potential subjects. All potential patients' medical records were examined by the Study Speech Pathologist to determine subjects' candidacy for inclusion in the project.

Inclusion Criteria

The prescribed criteria for eligibility to participate within this study included:

1. 40-80 years of age
2. A diagnosis of COPD based on TSANZ criteria
TSANZ criteria for diagnosis of COPD includes: the patient presenting with symptoms of breathless, cough and sputum production, spirometry results indicating a ratio of FEV₁ (forced expiratory volume in 1 second) to FVC (forced vital capacity) of <70%^[59].
3. Baseline FEV₁ <70% predicted
4. Must be in clinically stable period of their condition as determined by a senior thoracic physician (ie. no exacerbations for 6 weeks)
5. May have respiratory failure on blood gas criteria (ie. PaO₂ <60 mmHg or PaCO₂ >50mmHg)
6. May be a current inpatient within Concord Repatriation General Hospital

Exclusion Criteria

Potential subjects were excluded if they demonstrated any of the following:

1. History of head and neck surgery
2. Neurological impairment or progressive neurological disease (including traumatic brain injury, bulbar and pseudobulbar palsy)

3. Reported clinical symptoms or diagnosis of gastro-oesophageal reflux disease

These conditions are known to be associated with swallowing disorders and impaired LPS.

Medical Assessment

Following subject identification, each case subjects' medical histories were presented to both the attending and supervising Thoracic Physicians to determine potential suitability for the study. Adherence to the TSANZ criteria^[59] and Respiratory Function Test results were used to confirm each case subject's diagnosis of COPD. Any case subjects with possible indications of GORD were excluded from the study in effort to reduce bias upon LAR assessment^[17]. Once potential case subjects were deemed to satisfy all inclusion and exclusion criteria, they were approached for consent to participate in the study.

Respiratory Status

Pulmonary Function testing was completed on each case subject to determine the severity of COPD. Tests were conducted on all subjects according to American Thoracic Society criteria (ATS 1995). Respiratory function tests were performed utilising body plethysmography (Sensormedics Vmax). Pulmonary function testing results for the case subjects is summarised in table 4.1.

Table 4.1: FEV₁ values for case subjects

Case	FEV₁% Predicted Value
1	44
2	66
3	41
4	27
5	19
6	46
7	23
8	21
9	25
10	30
11	32
12	24
13	68
14	42
15	33
16	38
17	49
18	44
19	62
20	33

Laryngopharyngeal Sensitivity (LPS) Testing

LPS was assessed through implementation of the Laryngopharyngeal Sensory Discrimination Testing (LPSDT) technique^[52].

Topical Xylocaine Viscous was applied to both nares to facilitate toleration of the nasendoscopy procedure. Anaesthetic spray was not utilised as this may have influenced sensory testing results. The nasoendoscope (Pentax FNL-10 AP) was attached to the Pentax AP-4000 air-pulse sensory stimulator and then passed transnasally through to the laryngopharynx, until it was situated approximately 3mm above the arytenoid eminence. Establishing the presence of light reflection from the nasoendoscope onto the arytenoid eminence in addition to deflection of arytenoid tissue when an air pulse is triggered, ensured the accuracy of the distance between and correct positioning of the nasoendoscope and arytenoid eminence. Air pulses were then delivered to the arytenoid eminence via the Pentax AP-4000 air-pulse sensory stimulator, initially at 6.0 mmHg.

The aim was to elicit a response known as the Laryngeal Adductor Reflex (LAR). The LAR is the involuntary transient adduction of the vocal cords in response to air pulse stimuli. The administration of the stimulus followed a descending and ascending threshold testing protocol as described by Aviv et al, 1993^[14]. The initial air pressure delivered was 6.0 mmHg. If the LAR was triggered at 6.0mmHg, the air pulses delivered were reduced by 0.5 mmHg increments until the LAR was no longer observed. Air pressure was then increased by 1.0 mmHg increments until the LAR was observed again. If no LAR was triggered at 6.0 mmHg, air pulses were increased in 1.0 mmHg increments until the LAR was observed. Once the LAR was elicited, air pulses were systematically reduced by 0.5 mmHg until the LAR was no longer observed. The lowest air pressure to trigger the LAR on three repetitions was recorded as the "LAR threshold". LAR thresholds have been reported to vary in stroke patients from 2.0-9.9

mmHg, however data for other disease groups is not yet known. LAR thresholds for normal controls have been reported between 2.0 to 5.0 mmHg^[14]. The Pentax AP-400 air-pulse sensory stimulator is unable to generate air pulses greater than 9.9 mmHg. For the purposes of this study, if no LAR was observed at 9.9 mmHg, the LAR threshold was determined to be 9.9 mmHg. LAR testing was conducted unilaterally only, as none of the case subjects were considered to be at risk of asymmetrical sensory impairment. Any subject with potential neurological or head/neck aetiology, and therefore at risk of asymmetrical sensory impairment, had been excluded at time of recruitment. The senior thoracic physician performed the LPSDT testing. The physician was blinded to the patient's results on respiratory function testing but not the COPD diagnosis.

Subjects were positioned sitting upright in a chair for the LPSDT procedure. LPS testing was conducted first, followed promptly by the endoscopic assessment of swallowing. The subject's positioning was not altered between assessments and they were not informed regarding the ascending and descending testing protocol for the LPS assessment. They were also not informed as to when the air pulse was being delivered. Air pulses were presented at irregular intervals so that the subject would not know when the stimulus was to be delivered.

Prior to LPSDT testing, each subject was instructed: "As the scope passes through your nose and into your throat, you may feel a little discomfort however you should not experience pain. Once the scope is in place we will release a few puffs of air through the scope and into your throat. Try to relax and just breathe normally."

Control Subjects

The control group consisted of 11 healthy volunteer subjects: 7 male and 4 female between the ages of 41 and 79 (mean=70.4, SD = 11.6, median=76). All control subjects were recruited for the purposes of determining laryngopharyngeal sensation and age matched to case subjects. Control subjects underwent a detailed case history to obtain a comprehensive medical history and identify potential swallowing disorders. Potential control subjects were excluded if they had a history of any of the following: neurological disease, respiratory disease, GORD, significant medical illness, previous history of dysphagia, smoking or abnormal lung function result measured by spirometry.

All control subjects underwent LPS testing using the protocol specified earlier for the case subjects.

ANALYSIS

To ensure patient confidentiality at all times, data was entered into a MS Excel spreadsheet. Subjects were identified by enrolment code only. Only the principal investigator had password-protected access to this database. Statistical analyses were completed using the Statistical Package for Social Sciences (SPSS) version 11.0, Chicago IL. 2004.

Sample Size

Our null hypothesis was that there is no difference in LPS between COPD and healthy subjects. Based on a previous pilot study where a difference in populations of 0.5mmHg and a SD of 0.32 was obtained, sample size calculation was conducted using α 0.05 and β 0.10 (power = 90%). Using these figures, we calculated that we would require a minimum of 14 patients to test our null hypothesis.

Statistical Analysis

Initially all data were tabulated and reviewed descriptively for completeness and distribution. Several of the variables were found to be non-normally distributed. Consequently, non-parametric methods were employed to evaluate the relationship between the primary outcome, LAR threshold and all other endpoints due to the non-normal distribution and small sample size.

Mean, mode and standard deviation were derived for all variables. The groups were then compared for demographic variables such as age, gender, admission diagnosis and respiratory function. Any differences between the groups were sought using odds ratios with 95% confidence intervals applied.

Cross tabulation and Fishers exact analysis were employed to examine the relationship between the categorical endpoints of each group; FEV₁ values, age and gender.

The non-parametric t-test for independent samples, Mann Whitney U was employed to evaluate the relationship between LAR threshold and each group.

4.3 RESULTS

This section will examine the relationship between presence of COPD and LPS (as defined by LAR threshold).

Baseline Characteristics

During the study period, a total of 33 subjects were recruited. 11 healthy control subjects and 22 case subjects with a confirmed diagnosis of COPD. Of the control subjects, all 11 underwent LPSDT. Of the case subjects, 2 were unable to tolerate the LPSDT procedure and subsequently withdrew from the study. These 2 case subjects do not form part of the final study group (n=20) and do not feature within the analysis that follows.

Table 4.2 summarises descriptive data for all case subjects. For the purposes of maintaining confidentiality, all subjects will be referred to by enrolment number only.

Table 4.2: Case subject descriptive data

Variable	Case Group (COPD)	Control Group (non-COPD)	P Value
Age (Mean, SD)	71.7, 6.8	70.4, 11.6	Not sig.
Gender (%)	80% male 20% female	64% male 36% female	Not sig.
FEV ₁ (Mean, SD)	38.35, 14.60	-	-
LAR threshold (Mean, SD)	9.27, 1.50	5.4, 1.96	p<0.001

Respiratory Status

Respiratory function testing demonstrated that all case subjects fell in the prescribed FEV₁ % predicted range for the diagnosis of COPD according to TSANZ criteria. TSANZ criteria for diagnosis of COPD include the patient presenting with symptoms of breathless, cough and sputum production, as well as spirometry results indicating a ratio of FEV₁ (forced expiratory volume in 1 second) to FVC (forced vital capacity) of <70%^[59]. Case subjects demonstrated FEV₁ % predicted values between 19% and 68% (mean = 38.35, SD = 14.60, 95% CI = 31.87 - 44.82).

There was no significant difference ($p>0.05$) in age between cases and controls as determined by a 2 sample t-test (assuming unequal variance).

Laryngopharyngeal Sensory Discrimination Testing (LPSDT)

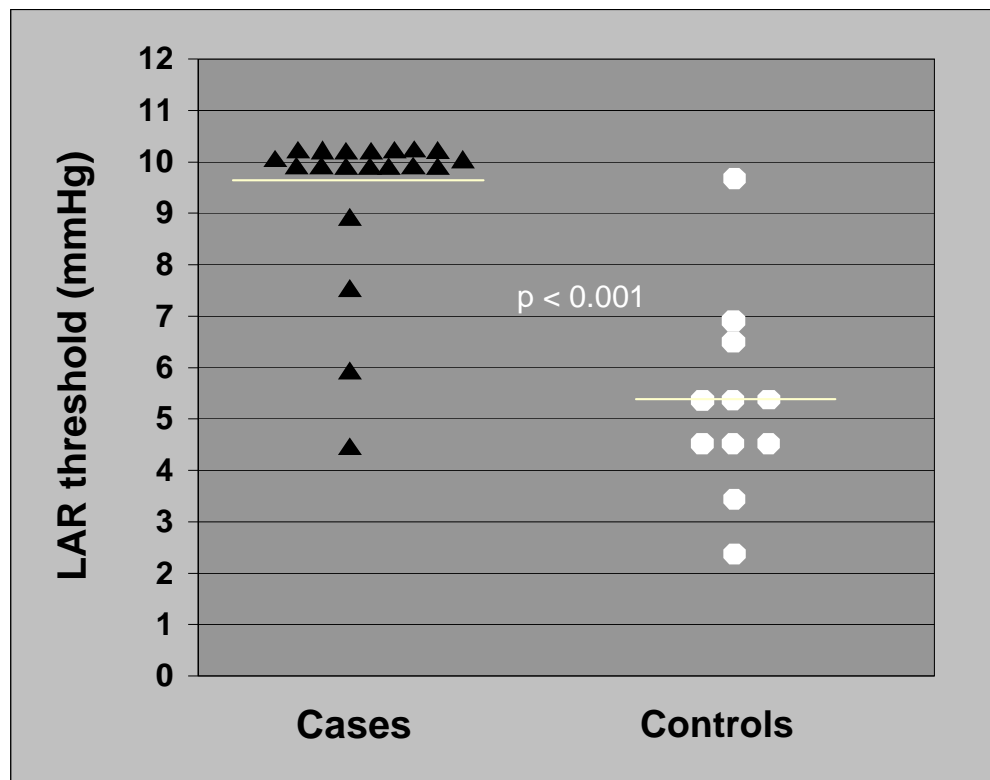
LAR thresholds were obtained for all control and case subjects. LAR threshold values for control subjects ranged between 2.0 – 9.9mmHg (mean = 5.4mmHg, median = 5.5mmHg, SD = 1.96, 95% CI = 4.08 – 6.72). For case subjects, LAR threshold range was 4.5 - 9.9mmHg (mean = 9.27mmHg, median = 9.9mmHg, SD = 1.50, 95% CI = 8.57 – 9.97).

A significance value of $p<0.001$ was calculated using the Independent Samples T-Test where equal variance was assumed (using Levene's Test for equality of variance) for the difference in LAR threshold between case and control subjects.

Table 4.3: LAR data for cases & controls

	Controls (n=11)	Cases (n=20)
LAR Threshold (mean [mmHg])	3.45	9.27
Range	2.00 – 5.00	4.50 - >9.90
p Value	-	<0.001**

Figure 4.1: LPSDT results



Sample Size and Power

As discussed in the Methodology section, sample size was calculated using α 0.05 and β 0.10, providing a power of 90%. A difference in populations of 0.5mmHg and a SD of 0.32 was obtained from a previous pilot study, allowing us to calculate that 14 subjects were required in order for the null hypothesis to be tested.

As the number of case subjects in the present study was 20, we can be confident that the sample size used was sufficient to accurately test and subsequently reject our null hypothesis that states there is no difference in LPS between COPD and healthy subjects.

4.4 DISCUSSION

The associations and descriptive data evaluated in the results section of this paper will be discussed in view of their relevance to swallow dysfunction, risk of aspiration and aspiration pneumonia.

Relationship between COPD and LPS

Results revealed that patients with COPD have a significantly impaired level of LPS (as defined by LAR threshold) when compared with healthy controls ($p < 0.001$). This allows us to reject our original null hypothesis and prove that a relationship does exist between LPS and the presence of COPD.

The significance of a severely impaired LAR threshold has several implications. A number of researchers have completed studies examining the effect of impaired LPS on risk of aspiration and aspiration pneumonia. Aviv et al (1997)^[13] studied LPS testing with Modified Barium Swallow (MBS) as a predictor of aspiration pneumonia after stroke.

This author found that the combination of LPS testing and MBS assessment was prognostic of patients at high risk of developing aspiration pneumonia. He also reported that those patients with bilateral sensory deficits (as defined by LPS testing) regardless of whether they showed evidence of aspiration on MBS, were found to be at the greatest risk of developing pulmonary complications due to aspiration. This has important implications for the results of the current study. In this study, 95% of the COPD subjects also demonstrated impaired LPS (LAR threshold >5.0mmHg). Extrapolating from Aviv et al's study^[13], this would imply that 95% of the COPD subjects in this study (demonstrating sensory deficits) are at high risk of developing aspiration pneumonia.

Setzen et al (2001)^[48] conducted a study examining LPS deficit as a predictor of aspiration. The authors examined 40 patients with dysphagia, dividing them into 2 groups; those with apparent normal sensitivity and those with severe sensory deficits as defined by absent LAR. Liquid and puree consistencies were administered and the patients were evaluated for aspiration and pharyngeal muscle contraction. Results revealed that pharyngeal muscle contraction was impaired in 90% of those with absent LAR. Aspiration on thin liquid was observed in 100% and aspiration on puree was noted in 60% of the patients with absent LAR. A statistically significant result of $p < 0.001$ was obtained for the differences in incidence of aspiration and pharyngeal muscular weakness when compared to the group with normal LPS. The conclusion was made that a strong relationship exists between sensory loss and motor deficits, and that the combination of these 2 features may be used to predict those patients at greater risk of aspiration.

As an extension of Setzen et al's (2001)^[48] study, Aviv et al (2002)^[93] also investigated LAR and pharyngeal squeeze as predictors as laryngeal penetration and aspiration. The results from this study were similar to those of Setzen et al (2001)^[48]. These authors again report a strong association between motor and sensory deficits, concluding that

those with absent LAR were more likely to demonstrate laryngeal penetration and aspiration than those with an intact LAR ($p < 0.0001$). These investigators also reported a significant difference in integrity of pharyngeal muscular contraction (as defined by pharyngeal squeeze) between the 2 groups. Those with absent LAR demonstrating increased incidence impaired pharyngeal squeeze ($p < 0.0001$) when compared to those with intact LAR.

Pursuing the concept that impaired LPS and pharyngeal squeeze were prognostic of aspiration, Setzen et al (2003)^[47] researched the association between LPS deficits, pharyngeal motor function and the prevalence of aspiration with thin liquids. These researchers divided 204 consecutive patients into a number of different study groups depending on the severity of deficit in LPS and pharyngeal motor function. They then examined how the combination of LPS deficit and pharyngeal motor deficit may affect the prevalence of aspiration. These authors concluded that regardless of pharyngeal motor function, those with severe LPS deficits were associated with aspiration of thin liquids ($p < 0.05$).

Finally, Perlman et al (2004)^[53] examined the risk of aspiration on pureed consistency as determined by LPS and pharyngeal squeeze. Patients were grouped according to level of sensory integrity and pharyngeal strength. These authors demonstrated that an increased incidence of pureed food aspiration was noted when impaired pharyngeal squeeze was present for the normal and moderate sensory loss patients ($p < 0.001$). However, frequency of aspiration between those with normal and impaired pharyngeal squeeze in the severe sensory loss group was not statistically significant. They concluded that patients with impaired pharyngeal motor function at different levels of sensory loss are at greater risk for aspiration of pureed consistency foods, when compared to those with normal pharyngeal motor function. Further, they suggested that hypo-pharyngeal muscle tone may be more predictive for aspiration of pureed foods than laryngopharyngeal sensation.

While the results of this study demonstrated a high incidence of LPS impairment in patients with COPD, the integrity of pharyngeal motor function in this population is unknown. A study examining the relationship between LPS, pharyngeal squeeze and swallow function in COPD patients should be investigated in future studies.

Relationship between FEV₁ and LPS

There was no relationship found between severity of LPS impairment (as defined by LAR threshold) and severity of COPD (as defined by FEV₁). While the diagnosis of COPD was strongly related to LPS impairment when compared to controls, severity of COPD did not correlate with deterioration in LPS.

This may imply that the presence of COPD is enough to predict impairment in LPS.

A larger sample size, including non-COPD subjects with corresponding FEV₁ % predicted values, may be able to define if a relationship truly exists or not. Additionally, if LAR thresholds can be more accurately determined in the upper range (should LPSDT be modified to allow pressures greater than 9.9mmHg), this may also assist in establishing a clearer relationship.

4.5 STUDY LIMITATIONS

While the findings on the association between LPS and COPD in this study are of significance, the study does suffer from several potential limitations. In the current study design the control group was selectively matched to the case group for age. COPD typically occurs in older populations as lung damage from tobacco use takes a period of time to present as airways disease; hence the mean age for the COPD subjects for this study was considerably high (mean = 71.65 years). For these reasons,

it was considered that selectively age-matching the controls to cases was required to accurately ascertain the relationship between COPD and LPS, and potentially remove age as a confounding variable. The aim was to demonstrate that the difference in LPS between COPD subjects and healthy controls is more than what can be attributed to increased age alone. The literature discussed below describes the relationship between age and LPS and supports the rationale for utilising this methodology.

Aviv et al (1994)^[95] and Aviv (1997)^[96] examined age related changes in laryngopharyngeal sensation. In the 1994 study^[95], 672 trials were performed on 56 subjects divided into three age categories: 20 to 40, 42 to 60, and 61 to 90 years of age. The researchers found that there was a statistically significant difference ($p < 0.05$) between the 20-40 year age group and the 61-90 year age group. There was also a statistically significant difference ($p < 0.05$) between the 41-60 year and 61-90 year age groups. The differences in sensation between age groups were significant in the study by Aviv et al (1994)^[95], however it is interesting to note that the mean LAR thresholds for each of these age groups were well below those found in this current study. The mean LAR threshold for the 61-90 year age group in Aviv's study^[95] was 2.68 +/- 0.63 mmHg, whereas the mean LAR threshold for control subjects (mean age 70.36) in the current study was 5.4 mmHg. Therefore, despite the fact that increasing age may contribute to a reduction in LPS, the substantial difference in LPS found in this study between COPD and controls, has been demonstrated to not be attributed to age alone. It is apparent that COPD itself has considerable impact upon LPS.

Similarly, Aviv and colleagues (1997)^[96] further investigated effects of aging on sensitivity of the pharyngeal and supraglottic areas. This study also found significant differences in LPS with increasing age ($p < 0.05$). The mean LAR threshold of the eldest age group (>61 years) was 2.97 +/- 0.78mmHg. This evidence further supports the need to exclude age as a confounding variable and illustrates that the differences in LPS found in this study are correctly attributed to the presence of COPD.

This study has identified that patients with COPD have significantly reduced mechanosensitivity in the laryngopharynx. The cause of sensory impairment may be related to a number of variables. The effect of inhaled corticosteroids and inhaled anticholinergics on laryngopharyngeal sensation is unknown. These medications are used widely in COPD management yet it is possible they may have an adverse affect on sensory mucosa in the laryngopharynx. Presence of chronic cough resulting in laryngeal oedema, a symptom commonly occurring in COPD, also cannot be excluded as a contributor to reduced sensation. Finally, Gastro-Oesophageal Reflux Disease (GORD) is known to result in impaired LPS as described by Phua et al (2005)^[17]. While patients with symptomatic GORD were excluded from the current study, occult GORD cannot be eliminated as a factor. One method of accounting for the presence of GORD in future research would be to perform 24 hour ambulatory oesophageal dual channel pH manometry as a part of the study protocol.

4.6 CONCLUSION

This study has revealed that patients with COPD have impaired laryngopharyngeal sensation, which suggests that this population may be at increased risk of aspiration.

Future studies examining LPS in this population are encouraged to use more rigorous procedures to exclude those patients with occult GORD.

CHAPTER 5:

STUDY TWO:

IMPAIRED LARYNGOPHARYNGEAL SENSITIVITY (LPS) IN PATIENTS WITH COPD: THE RELATIONSHIP TO SWALLOW FUNCTION

5.1 STUDY AIMS

1. To determine the relationship between LPS and swallow function in patients with proven COPD
2. To determine whether LPS predictive value may be used as a method of evaluating risk of dysphagia, as identified by the Mann Assessment of Swallowing Ability (MASA) and Endoscopic Assessment of Swallowing in patients with COPD

5.2 METHODOLOGY

LPS and swallow function were assessed in case subjects during a clinically controlled period of their respiratory condition. The primary physician assessed the stability of the case subject's condition through clinical assessment. All assessments were conducted at The Respiratory Unit, Concord Repatriation General Hospital, under the direct supervision of senior thoracic physicians with experience in managing patients with COPD.

Please refer to Study One for full details regarding case subjects, inclusion and exclusion criteria, medical assessment and pulmonary function testing.

Questionnaire

The Sydney Swallowing Questionnaire (SSQ)^[92] is a self-reporting questionnaire that examines an individual's view of their swallowing ability. This was used to determine the case subject's perception of their swallow function at the time of study participation (see Appendix D). The SSQ was completed by each case following pulmonary function testing, in the presence of the Study Speech Pathologist. Instructions were delivered by the Study Speech Pathologist, were consistent between all case subjects and are described below. The purpose of the SSQ is to focus upon the case subject's perception of their swallowing ability specific to food and fluid consistencies, meal duration and dysphagic symptoms. Where possible, the case subject completed the questionnaire unassisted. The Speech Pathologist assisted SSQ completion in cases of poor literacy or visual impairment (n=2).

Prior to administration of the SSQ each subject was given the following instructions. "Please fill in this questionnaire as per the instructions described at the top as best you can".

Bedside Examination of Swallowing

The Mann Assessment of Swallow Ability (MASA)^[21] was utilised to clinically assess each case subject's swallow function and provide a severity of dysphagia (see Appendix E). The MASA is a validated and reliability tested assessment of swallowing ability that has been standardised on stroke patients. Upon completion it provides a quantifiable score of swallowing ability, which enables the clinician to classify the patient in terms of dysphagia severity.

The MASA evaluates cranial nerve sensory and motor function specific to the anatomical structures necessary for swallowing. The MASA also acknowledges the

patient's status of communication, chest and airway protection, prior to examination of the oral and pharyngeal stages of swallowing. The MASA was administered by the Study Speech Pathologist following the pulmonary function testing and SSQ, and prior to LPS assessment. It was completed at the patient's bedside for inpatients and in a clinic room within the Respiratory Unit for outpatients.

Laryngopharyngeal Sensitivity (LPS) Testing

Please refer to Study One for full methodology details regarding LPS testing.

Endoscopic Assessment of Swallowing

Endoscopic Assessment of Swallowing (EAS) was achieved through evaluation of the case subject swallowing a variety of substances while visualising the oropharynx, hypopharynx and larynx through a nasoendoscope. The nasoendoscope implemented for this project was the Pentax FNL-10 AP. The author and Dr Giselle Carnaby-Mann developed the EAS scoring form for the purpose of this study (see Appendix F). The current study was part of the validation process for the EAS tool.

All endoscopic assessments were viewed on a standard colour television and recorded on VHS video cassette by a super VHS VCR.

Substances trialed:

- 90ml water (dyed with 0.5ml blue food colouring)
- 5 x 5ml teaspoons of Goulburn Valley apple puree (dyed with 0.5ml blue food colouring)
- 1 plain dry biscuit (Arnotts Milk Coffee biscuit)

The substances trialed were selected on the basis that they represent a broad range of the diet and fluid consistencies that individuals consume on a daily basis. The

consistencies were believed to demonstrate dysphagic characteristics such as laryngeal penetration, aspiration and pharyngeal residue in patients with swallow dysfunction, and corresponded to those items used in standard clinical swallowing evaluations.

The amounts administered were also considered to be adequate to demonstrate evidence of swallow dysfunction. All food and fluid measurements were determined with standardised 5ml and 20ml syringes. Trial amounts were kept consistent between all subjects. Puree was administered via teaspoon and water from a cup. The fluid and puree fruit consistencies were dyed blue to assist in visualisation of the dysphagic characteristics described above. All subjects were first administered apple puree, followed by the water and finally the biscuit. Order of delivery was kept consistent between all subjects.

Prior to administration of the EAS protocol, each subject was instructed to: "Please eat / drink this water / puree / biscuit as you normally would".

The EAS was performed on all subjects immediately following LPS testing. Positioning of subjects remained consistent with LPS testing. The senior thoracic physician controlled the nasoendoscope whilst the Study Speech Pathologist provided the subject with the food and fluids to be consumed. The senior thoracic physician was aware of the subject's results on LPS testing, but not of results from pulmonary function testing, SSQ and MASA.

All subjects consumed all amounts of puree fruit and water. If laryngeal penetration or aspiration was observed, swallowing strategies were trialed immediately to reduce aspiration risk. All subjects consumed at least half of the dry biscuit in order to adequately demonstrate potential dysphagic characteristics on this consistency. If the patient demonstrated pharyngeal residue or some other difficulty on swallowing the first half of the biscuit, they were not required to consume the remaining half. Any patients

who demonstrated evidence of dysphagia during the study were later referred to the Respiratory Speech Pathologist for ongoing swallowing management.

ANALYSIS

To ensure patient confidentiality at all times, data was entered into a MS Excel spreadsheet. Subjects were identified by enrolment code only. Only the principal investigator had password-protected access to this database. Statistical analyses were completed using the Statistical Package for Social Sciences (SPSS) version 11.0, Chicago IL. 2004.

Sample Size

Please refer to Study One for details regarding sample size.

Statistical Analysis

Initially all data were tabulated and reviewed descriptively for completeness and distribution. Several of the variables were found to be non-normally distributed. Consequently, non-parametric methods were employed to evaluate the relationship between the primary outcome, LAR threshold and all other endpoints due to the non-normal distribution and small sample size.

Mean, mode and standard deviation were derived for all variables. The groups were then compared for demographic variables such as age, gender, admission diagnosis and respiratory function. Any differences between the groups were sought using odds ratios with 95% confidence intervals applied.

Cross tabulation and Fishers exact analysis were employed to examine the relationship between the categorical endpoints of each group; FEV₁ values, age, gender, aspiration, vallecular residue and piriform residue.

The non-parametric t-test for independent samples, Mann Whitney U was employed to evaluate the relationship between LAR threshold and each group.

5.3 RESULTS

This chapter describes the analysis of descriptive data for the case group using demographic and clinical figures (derived from the LPSDT, SSQ, MASA and FEV₁ % predicted values). The relationships between COPD and swallow function, as measured by the LPSDT, SSQ, MASA and EAS will also be discussed.

Baseline Characteristics

During the study period, a total of 33 subjects were recruited. 11 healthy control subjects and 22 case subjects with a confirmed diagnosis of COPD. Of the control subjects, all 11 underwent LPSDT. Of the case subjects, 21 were evaluated with SSQ, 22 with MASA, and 20 underwent LPSDT and EAS assessments. The 2 case subjects who did not complete LPSDT and EAS assessments withdrew from the study due to their inability to tolerate the LPSDT procedure. Therefore, these case subjects do not form part of the final study group (n=20) and do not feature within the analysis that follows.

Table 5.1 summarises descriptive data for all case subjects. For the purposes of maintaining confidentiality, all subjects will be referred to by enrolment number only.

Table 5.1: Case subject descriptive data

Variable	Case Group (COPD)	Control Group (non-COPD)	P Value
Age (Mean, SD)	71.7, 6.8	70.4, 11.6	Not sig.
Gender (%)	80% male 20% female	64% male 36% female	Not sig.
FEV ₁ (Mean, SD)	38.35, 14.60	-	-
SSQ score (Mean, SD)	215.47, 160.93	-	-
MASA Score (Mean, SD)	192.05, 2.86	-	-
LAR threshold (Mean, SD)	9.27, 1.50	5.4, 1.96	p<0.001
Aspiration count	5	-	-
Valleculae residue count	17	-	-
Piriform residue count	18	-	-

Respiratory Status

Please refer to Study One for details regarding results on pulmonary function testing.

Sydney Swallowing Questionnaire (SSQ)

Results of the SSQ indicated that many of the subjects felt they did not have any swallow function difficulties for either solids or liquids. Out of a possible score of 1700, results ranged from 66 to 698 (mean = 215.47, SD = 160.93, 95% CI = 142.2 – 288.7).

For the purposes of this study, if the response value was greater than 20 for any given question, the result was considered to be affirmative.

3 out of the 20 (15%) (95% CI = 5.2 - 36) case subjects studied indicated that they felt they had difficulty with swallowing. Of these subjects, all three (15%) noted difficulty

swallowing solid foods: 2 (10%) (95% CI = 2.7 - 30) found foods of hard and dry consistency difficult, whereas the third (5%) reported hard, dry and soft foods difficult to swallow. 2 out of the 3 (10%) (95% CI = 2.7 - 30) had previously noted sensations of food getting stuck in the throat, needing to swallow more than once to clear a bolus and coughing/choking on fluids. 1 out of the 3 (5%) (95% CI = 0.8 - 23.6) affirmed a history of coughing/choking on food and the need to cough up and spit out food. All 3 (15%) (95% CI = 5.2 - 36) subjects acknowledged that they had difficulty swallowing however did not describe it as severe. Only 2 of the 3 (10%) (95% CI = 2.7 - 30) reported that their swallowing problem interfered with their enjoyment or quality of life. These results are summarised in the table below.

Table 5.2: SSQ data summary

Feature on Sydney Swallowing Questionnaire (SSQ)	% Cases (n=20)
Admitted swallowing difficulty at time of assessment	15 (95% CI = 5.2 - 36)
Difficulty with hard foods	15 (95% CI = 5.2 - 36)
Difficulty with dry foods	15 (95% CI = 5.2 - 36)
Difficulty with soft foods	5 (95% CI = 0.8 - 23.6)
Sensation of food getting stuck in throat	10 (95% CI = 2.7 - 30)
Need to swallow more than once for food to go down	10 (95% CI = 2.7 - 30)
Coughing / choking on fluids	10 (95% CI = 2.7 - 30)
Coughing / choking on foods	5 (95% CI = 0.8 - 23.6)
Need to cough up / spit out food	5 (95% CI = 0.8 - 23.6)
Admitted swallowing problem is mild-moderate	15 (95% CI = 5.2 - 36)
Swallowing difficulty interferes with quality of life	10 (95% CI = 2.7 - 30)

There were no reports of case subjects having difficulty in initiating a swallow, swallowing saliva, swallowing thick liquids, or nasopharyngeal penetration / regurgitation. No case subjects reported requiring excessive amounts of time (>30 minutes) to consume an average meal.

Mann Assessment of Swallowing Ability (MASA)

MASA results for the case group revealed that all subjects, while having a respiratory condition that may place a patient at risk of dysphagia and/or aspiration, did not present with explicit dysphagia on bedside examination. MASA scores for case subjects ranged from 186-196, (mean = 192.05, median = 192.5, SD = 2.86, 95% CI = 190.78 – 193.3), corresponding to the cut-off for within normal limits according to the Mann Assessment of Swallowing Ability. The normal range for the MASA is 178 – 200^[21].

It should be noted that despite achieving scores that were within normal limits, all case subjects lost points on the section that examines Respiration and Respiratory Rate for Swallow due to their underlying respiratory diagnosis. While previous studies have shown that there is no correlation between presence of gag reflex and laryngopharyngeal sensation^[14], an interesting find was that 60% (95% CI = 38.6 - 78.1) of case subjects presented with absent gag reflex, while a further 25% (95% CI = 11.1 - 46.9) exhibited a diminished gag reflex bilaterally.

Endoscopic Assessment of Swallowing (EAS)

Results from the Endoscopic Assessment of Swallowing demonstrated that 90% (95% CI = 69.9 – 97.2) of case subjects demonstrated pharyngeal residue post swallow for all consistencies trialed. 25% (95% CI = 11.1 – 46.9) of case subjects exhibited some degree of laryngeal penetration or aspiration. 10% demonstrated audible aspiration (1 subject on thin fluid and the other on biscuit), and 15% displayed silent aspiration on thin fluid. Presence of silent aspiration was agreed if the patient did not cough or make another attempt to clear the aspirate after approximately 10-15 seconds. Of the 3 patients who demonstrated silent aspiration on thin fluid, aspiration was eliminated with implementation of neck flexion in 2 of the patients. All case subjects that presented with

clinical evidence of dysphagia were referred on for further Speech Pathology intervention.

Table 5.3: EAS data summary for vallecular & piriform residue

Site of residue	NAD	Trace residue unilateral / able to clear	Residue uni/bilateral, attempts to clear	Obvious residue bilateral / no spontaneous clearance
Valleculae	15%	5%	30%	50%
Piriform fossae	10%	5%	35%	50%

Table 5.4: EAS data summary for laryngeal penetration / aspiration

	Obvious staining below vocal folds / requires suctioning	Some staining / cleared with prompt	Trace staining / cleared spontaneously
Laryngeal Penetration / Aspiration	-	15%	10%

Relationships between LPS, MASA, SSQ, EAS, FEV₁ and Age

Correlations were found to be significant at the level of $p < 0.05$ using Pearson's correlation coefficient for the relationship between MASA score and EAS results for presence of laryngeal penetration / aspiration, vallecular residue and piriform residue (refer to table and graphs below).

Table 5.5: Relationship between EAS & MASA

EAS	MASA (mean, SD)	p Value	r Value
Laryngeal penetration / aspiration	192.05, 2.86	0.04	-0.457
Vallecular residue	192.05, 2.86	0.01	-0.544
Piriform residue	192.05, 2.86	0.01	-0.539

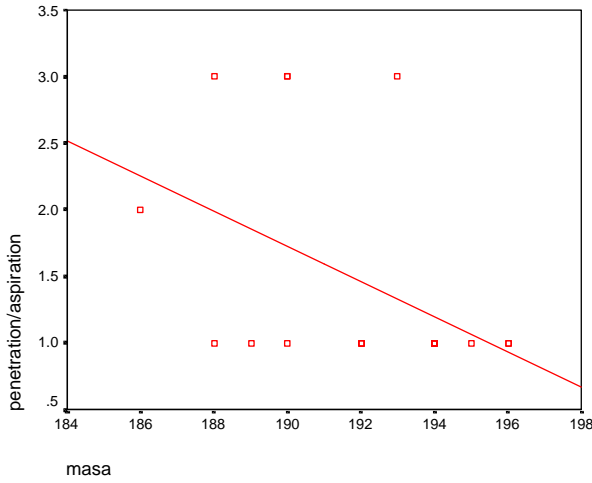


Figure 5.1:
Correlation between incidence of laryngeal penetration / aspiration (on EAS) and MASA score

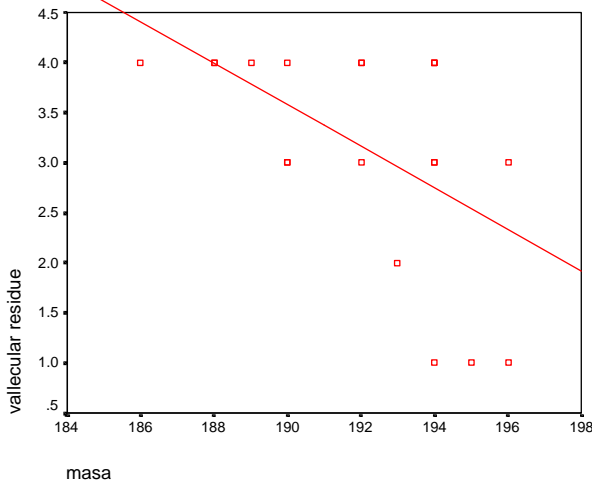


Figure 5.2:
Correlation between incidence of vallecular residue (on EAS) and MASA score

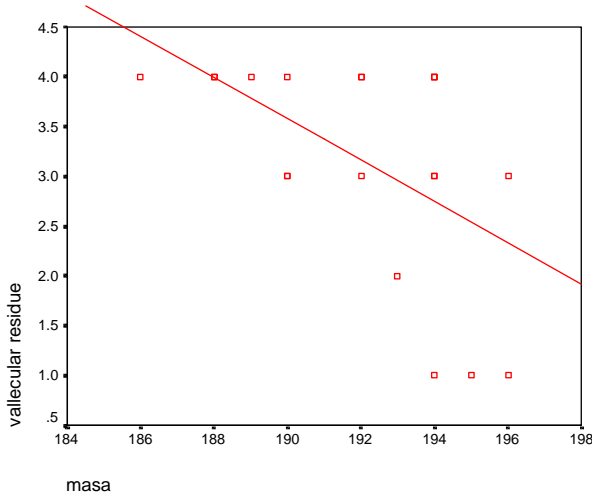


Figure 5.3:
Correlation between incidence of piriform fossae residue (on EAS) and MASA score

No significant correlations were found between the remaining variables.

5.4 DISCUSSION

The associations and descriptive data evaluated in the results section of this paper will be discussed in view of their relevance to swallow dysfunction, risk of aspiration and aspiration pneumonia.

Relationship between COPD and LPS

Results from Study One revealed that patients with COPD have a significantly impaired level of LPS (as defined by LAR threshold) when compared with healthy controls ($p < 0.001$). Therefore we have proved that a relationship does exist between LPS and the presence of COPD.

The significance of a severely impaired LAR threshold has several implications. A number of researchers have completed studies examining the effect of impaired LPS on risk of aspiration and aspiration pneumonia. Aviv et al (1997)^[13] studied LPS testing with Modified Barium Swallow (MBS) as a predictor of aspiration pneumonia after stroke. This author found that the combination of LPS testing and MBS assessment was prognostic of patients at high risk of developing aspiration pneumonia. He also reported that those patients with bilateral sensory deficits (as defined by LPS testing) regardless of whether they showed evidence of aspiration on MBS, were found to be at the greatest risk of developing pulmonary complications due to aspiration. This has important implications for the results of the current study. In this study, 95% of the COPD subjects also demonstrated impaired LPS (LAR threshold > 5.0 mmHg). Extrapolating from Aviv et al's study^[13], this would imply that 95% of the COPD subjects in this study (demonstrating sensory deficits) are at high risk of developing aspiration pneumonia regardless of their results on EAS.

Setzen et al (2001)^[48] conducted a study examining LPS deficit as a predictor of aspiration. The authors examined 40 patients with dysphagia, dividing them into 2 groups; those with apparent normal sensitivity and those with severe sensory deficits as defined by absent LAR. Liquid and puree consistencies were administered and the patients were evaluated for aspiration and pharyngeal muscle contraction. Results revealed that pharyngeal muscle contraction was impaired in 90% of those with absent LAR. Aspiration on thin liquid was observed in 100% and aspiration on puree was noted in 60% of the patients with absent LAR. A statistically significant result of $p < 0.001$ was obtained for the differences in incidence of aspiration and pharyngeal muscular weakness when compared to the group with normal LPS. The conclusion was made that a strong relationship exists between sensory loss and motor deficits, and that the combination of these 2 features may be used to predict those patients at greater risk of aspiration.

In the present study, an association was also observed between motor and sensory deficits. In 16 of the 20 COPD subjects studied, no LAR was exhibited. Of these 16 subjects, 15 also demonstrated pharyngeal residue post swallow on the EAS examination. One explanation for this post swallow pharyngeal residue is reduced pharyngeal muscle contraction. Comparing Setzen et al's conclusions^[48] to this study's results, we can also postulate that the 15 of the 20 (75%) of COPD patients studied, who demonstrated a LAR threshold of greater than 9.9mmHg and pharyngeal residue post swallow, may be at risk of aspiration. However, direct measurement of pharyngeal contraction was not evaluated in this present study sample.

As an extension of Setzen et al's (2001)^[48] study, Aviv et al (2002)^[93] also investigated LAR and pharyngeal squeeze as predictors as laryngeal penetration and aspiration. The results from this study were similar to those of Setzen et al (2001)^[48]. These authors again report a strong association between motor and sensory deficits, concluding that

those with absent LAR were more likely to demonstrate laryngeal penetration and aspiration than those with an intact LAR ($p < 0.0001$). These investigators also reported a significant difference in integrity of pharyngeal muscular contraction (as defined by pharyngeal squeeze) between the 2 groups. Those with absent LAR demonstrating increased incidence impaired pharyngeal squeeze ($p < 0.0001$) when compared to those with intact LAR.

Pursuing the concept that impaired LPS and pharyngeal squeeze were prognostic of aspiration, Setzen et al (2003)^[47] researched the association between LPS deficits, pharyngeal motor function and the prevalence of aspiration with thin liquids. These researchers divided 204 consecutive patients into a number of different study groups depending on the severity of deficit in LPS and pharyngeal motor function. They then examined how the combination of LPS deficit and pharyngeal motor deficit may affect the prevalence of aspiration. These authors concluded that regardless of pharyngeal motor function, those with severe LPS deficits were associated with aspiration of thin liquids ($p < 0.05$).

Finally, Perlman et al (2004)^[53] examined the risk of aspiration on pureed consistency as determined by LPS and pharyngeal squeeze. Patients were grouped according to level of sensory integrity and pharyngeal strength. These authors demonstrated that an increased incidence of pureed food aspiration was noted when impaired pharyngeal squeeze was present for the normal and moderate sensory loss patients ($p < 0.001$). However, frequency of aspiration between those with normal and impaired pharyngeal squeeze in the severe sensory loss group was not statistically significant. They concluded that patients with impaired pharyngeal motor function at different levels of sensory loss are at greater risk for aspiration of pureed consistency foods, when compared to those with normal pharyngeal motor function. Further, they suggested that hypo-pharyngeal muscle tone may be more predictive for aspiration of pureed foods than laryngopharyngeal sensation.

While the results of this study did not demonstrate a significant relationship between LPS impairment and incidence of aspiration, a repeat study with larger sample size and control group may do so. While the COPD patients in this study had a strong tendency to demonstrate pharyngeal residue post swallow, it is unclear if this was related to pharyngeal muscular contraction. The relationship between LPS and pharyngeal squeeze in COPD patients should be investigated in future studies.

Relationship between LPS and Swallow Function

There was no relationship found between LPS (as defined by LAR threshold) and swallow function (as defined by the EAS). The limited sample size may be responsible for this result, as previous studies have indicated that deficits in LPS are highly correlated with increased risk of aspiration^[13, 47, 48, 93, 94]. The size of the sample may have resulted in only a selected “milder” group of COPD subjects being represented thus obviating any relationship to aspiration. Further if EAS had been performed on control subjects (as well as cases), a relationship may have been identified.

In view of the descriptive results on presence of COPD and swallow dysfunction on EAS, it is possible that a history of COPD alone may be sufficient to assume that a patient will experience sub-clinical dysphagia, in particular presence of undetected pharyngeal residue, however this issue requires further investigation.

Relationship between COPD and Swallowing Function

Patients with COPD in this study demonstrated a strong tendency to exhibit pharyngeal residue post swallow on EAS. The patients studied also did not display efforts to clear residue with a secondary swallow, or report pharyngeal stasis. The impairment of LPS in this population may have resulted in the lack of response to this pharyngeal residue.

If pharyngeal residue is not detected, no attempts are made to clear the pharynx and the individual may consequently be placed at greater risk of aspiration due to build up and overflow or inhalation from the pharyngeal recesses.

In association with our findings, Eisenhuber et al (2001)^[49] also examined pharyngeal retention as a predictive factor for aspiration. Using videofluoroscopic assessment of patients with dysphagia, 386 patients were studied with potential deglutition disorders. 108 of these patients presented with pharyngeal retention. The amount of residual contrast material observed in the valleculae or piriform sinuses was graded as mild, moderate or severe. The frequency, grade and type of aspiration were also assessed. This author's results demonstrated that residue was caused by pharyngeal weakness or paresis in 95% of the 108 assessed. In 65% of patients with pharyngeal retention, post-deglutitive over-flow aspiration was observed. Post-deglutitive aspiration was diagnosed in 25% of patients with mild, 29% with moderate and 89% with severe pharyngeal residue ($p < 0.05$). This study concluded that pharyngeal retention is a strong indicator of aspiration risk, and deduced that risk of aspiration increases with increasing severity of pharyngeal retention.

In concordance with the findings of Eisenhuber et al^[49], this study identified that 90% of COPD patients demonstrated pharyngeal residue on EAS. While the severity of residue was not graded during the endoscopic procedure, the presence of this residue may place the patient at greater risk of aspiration. However, the incidence of aspiration was low in this study. One reason for this may have been that the quantities of material administered to the patient were insufficient to demonstrate post-deglutitive aspiration in our population. Further, the inclusion of more sensitive videofluoroscopic assessment methods may have improved the detection of aspiration events.

Relationship between MASA and EAS

In this study, there was a significant inverse correlation between clinical swallowing results on the MASA and EAS for case subjects. As a COPD patient's score on the MASA declined, the chance of that subject demonstrating aspiration, vallecular or piriform residue on EAS increased.

However, the total MASA scores for the COPD patients' fell in the "within normal limits" range for this assessment. This may be due to the presence of a ceiling effect for COPD on this examination. The MASA was developed for and standardised on stroke patients, not on patients with a history of respiratory disease. The COPD patients' performance may simply be represented within the upper tier of this test. It may be appropriate that the MASA is re-evaluated for use with COPD patients, or that the weighting of certain sections of the examination be adjusted for this population in order to provide a more realistic severity rating of swallow dysfunction.

Relationship between SSQ and EAS

There was no significant correlation between patients' performance on the SSQ and results on the EAS. This finding supports the evidence that patients with COPD have reduced laryngopharyngeal sensitivity on LPS testing. Poor results on LPS testing imply that a COPD patient is unable to provide an accurate history of their swallow function due to reduced sensory awareness as defined by a marked reduction in laryngopharyngeal sensitivity.

These results are supported by the findings of Reid (1998)^[9], who documented that COPD patients' subjective reports of swallowing difficulties were inaccurate of their actual swallow ability when comparison was made between questionnaire answers and results on Modified Barium Swallow assessment.

5.5 STUDY LIMITATIONS

There was a high incidence of post swallow pharyngeal residue in the COPD patients studied. The cause for this pharyngeal residue is unclear. Contributing factors may include pharyngeal weakness, paresis and pharyngeal incoordination. Given this, a possible strategy to account for these impairments may be the inclusion of manometry in the assessment procedure in future studies. Whilst providing further information of pharyngoesophageal pressures and bolus transit, this procedure also has questionable validity due to the accuracy of transducer placement in the pharynx. This technique is most effective in cases where the transducer can be fixed to a specific and accurately determined site such as the upper oesophageal sphincter. Current methods that place the transducer in the pharynx permit variability due to the air space and poor adherence to specific structures.

Another variable that may have influenced the presence of pharyngeal residue is the effect of the nasoendoscope on intra-oral pressure. A reduction in intra-oral pressure may result in inefficient stripping wave during the pharyngeal swallow, therefore resulting in increased residue counts within the pharyngeal recesses following swallowing. However, this is unlikely in view of similar results obtained in studies of swallowing in COPD using videofluoroscopy^[8, 9, 85].

Finally, while the EAS is able to provide useful information regarding swallow function during the pharyngeal phase, it does not directly assess presence of oral phase disorders. Endoscopic assessment of swallowing involves placement of the endoscope at the velopharyngeal port during the swallowing. In this position, only the pharynx and larynx can be visualised and subsequently oral phase difficulties cannot be observed. The focus of this study however, was primarily to examine pharyngeal swallowing disorders and their relationship to LPS integrity. Further studies should consider

examining oral sensation, as clearly the oral phase of swallowing may contribute to or suggest sensitivity changes that may influence findings from the EAS.

5.6 Conclusion

This study has revealed that patients with COPD exhibit a high frequency of post swallow pharyngeal residue and demonstrate poor insight into their swallowing ability likely due to poor laryngopharyngeal sensitivity. These findings suggest that this population may be at increased risk of aspiration and require objective assessments to provide an accurate assessment of their swallowing function.

Future studies examining dysphagia in COPD are encouraged to explore the role of motor function in assessing swallowing ability.

CHAPTER 6: SUMMARY

There is limited literature describing the incidence and nature of swallowing disorders in patients with COPD. The aetiology of this including the role of sensation have not previously been examined in this population.

Sensory integrity is critical to airway protection and preclusion of aspiration. Impaired laryngopharyngeal sensitivity (LPS) has been associated with an increased risk of aspiration in conditions including stroke. However, impaired LPS has not been examined with respect to aspiration risk specifically in COPD.

The aims of this study were to investigate the effect of COPD on laryngopharyngeal sensation using Laryngopharyngeal Sensory Discrimination Testing (LPSDT) and to determine whether a relationship between LPS and swallow function in patients with proven COPD exists.

Our study found that subjects with COPD had impaired laryngopharyngeal sensation as denoted by significantly higher LAR threshold when compared to their normal healthy counterparts ($p < 0.001$). Our study also found that subjects with COPD frequently demonstrated dysphagic characteristics. Positive correlations were identified for the relationships between bedside swallow assessment and endoscopic swallow assessment results for the presence of laryngeal penetration / aspiration ($p < 0.04$), vallecular residue ($p < 0.01$) and piriform residue ($p < 0.01$).

These results suggest that patients with COPD have significantly reduced mechanosensitivity in the laryngopharynx. Patients with COPD also have impaired swallow function characterised primarily by pharyngeal stasis. These changes strongly imply that patients with COPD are at increased risk of aspiration.

APPENDIX A - Ethics Approval

Contact: Secretary:- CSAHS Ethics Review Committee – CRGH Zone
Concord Repatriation General Hospital
Concord NSW 2139
Telephone: (02) 9767 5622 Fax: (02) 9767 7883

Our Reference: CH62/6/2001-008 (7.6 of 22/02/2001)

21 March 2001

Dr Alvin Ing
Department of Respiratory Medicine
Concord Repatriation General Hospital

Dear Dr Ing

Re: CH62/6/2001-008 – A Ing, N Clayton, M Peters
The Effect of Chronic Obstructive Pulmonary Disease on Laryngopharyngeal
Sensitivity and Dysphagia

Thank you for submitting the revised Patient Information Sheet for the above study trial, which has addressed the concerns raised by the Human Research Ethics Committee at its meeting of 22 February 2001. As you have now fulfilled all the necessary conditions, I have pleasure in advising that ethical approval to proceed with this study has been granted by the Chairman on behalf of the Human Research Ethics Committee. Please find enclosed:

- Copy of the approved version of the Patient Information Sheet and Participant Consent Form for your files.

After 12 months, the Committee requires a brief progress report on the research it has approved and a final report at the conclusion of the study.

These reports should:-

1. Be accompanied by abstracts of articles or publications (if any) arising from the study.
2. Confirm security of records.
3. Confirm compliance with approved consent procedures and documentation.

The investigator should also report immediately to the Ethics Committee anything which might affect ethical acceptance of the protocol, including:-

- serious adverse events on subjects
- proposed changes in the protocol
- unforeseen events that might affect continued ethical approval of the project.

Please note that approval is valid for twelve months only. The Committee requires you to submit for its consideration a report on progress of the project by 21 March 2002. Ethical approval will lapse unless the report is received.

Please quote Concord Hospital File No: CH62/6/2001-008 in all correspondence.

Yours Sincerely

J. Turner
Virginia Turner
Secretary

CSAHS Human Research Ethics Committee – CRGH - Zone



CONCORD
REPATRIATION GENERAL
HOSPITAL



University of Sydney

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APPENDIX B - Participant Information Form

RESEARCH STUDY INTO THE EFFECT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON LARYNGOPHARYNGEAL SENSITIVITY AND DYSPHAGIA

INFORMATION FOR PARTICIPANTS



You are invited to take part in a research study into The effect of chronic obstructive pulmonary disease (COPD) on laryngopharyngeal sensitivity and dysphagia. The aim is to assess sensitivity in the throat of people with smoking induced airways diseases. We hypothesise that people with COPD are at risk of developing difficulties with swallowing due to a change in throat sensitivity. This study will provide information on how to manage COPD patients with respect to their eating and drinking, so as to minimise the risk of developing chest infections as a result of aspiration (food / fluid going down the "wrong way").

Dr Alvin Ing (Consultant Thoracic Physician, Concord Hospital)
Nicola Clayton (Speech Pathologist, Concord Hospital)

Procedures

If you agree to participate in this study, you will be required to attend the Respiratory Unit on 2 separate occasions. The first visit will involve lung function testing and assessment of swallowing function. The second visit will entail a nasendoscopy. A nasendoscopy is a standard examination of the throat and involves a thin tube-like device with a camera on one end inserted through the nose and down to the level of your throat. During this study, we will introduce puffs of air into your throat via the flexible endoscope. You may be required to indicate that you have felt the puffs of air by raising your hand.

Possible Discomforts, Side Effects and Risks

During the insertion of the endoscope, some discomfort may be experienced around the nose. All efforts will be made to minimise any discomfort, including the use of local anaesthetic to reduce nasal sensation. A specialist endoscopist, Dr Alvin Ing, will be responsible for your care at all times, during this procedure.

Allergic reaction to local anaesthetic is a rare possibility. You will feel some mild temporary irritation of the nose and the upper throat, as the endoscope is places into position. You may develop a slightly runny nose, cough or sneeze while the instrument is in position. Nasal bleeding and prolonged discomfort is unlikely. There is also a possibility that you experience some changes in your breathing pattern. Your breathing patterns will be monitored carefully throughout the study. Changes in breathing patterns can be corrected when the endoscope is removed.

There is a rare but possible risk of laryngospasm, which is characterised by involuntary movements of the vocal cords. Breathing may become difficult. The study will be terminated immediately when it occurs and you will be monitored for further respiratory difficulties.



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Confidentiality

All aspects of this study, including results, will be strictly confidential and only the investigators named above will have access to information on participants. A report of the study may be submitted for publication, but individual participants will not be identified in the report.

Potential Benefits

While we intend that this research study furthers medical knowledge and may improve treatment of disorders associated to smoking related airways diseases in the future, it may not be of direct benefit to you.

Withdrawal from the Study

Participation in this study is entirely voluntary: you are in no way obliged to participate and – if you do participate – you can withdraw at any time. Whatever your decision, please be assured that it will not affect your medical treatment or your relationship with medical staff.

When you have read this information, Dr Alvin Ing or Miss Nicola Clayton will discuss it with you further and answer any questions you may have. If you would like to know more at any stage, please do not hesitate to contact them on **(02) 9767 6712**. This information sheet is for you to keep.

This study has been approved by the Ethics Review Committee – CRGH Zone of Central Sydney Area Health Service. If you have any concerns or complaints about the conduct of the research study, you may contact the Secretary of the Ethics Review Committee – CRGH Zone, on (02) 9767 6233. Alternatively, if you wish to speak with an independent person within the Hospital about any problems or queries about the way in which the study was conducted, you may contact the Patient Representative on (02) 9767 7488.

APPENDIX C - Participant Consent Form

**RESEARCH STUDY INTO THE EFFECT OF
CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON
LARYNGOPHARYNGEAL SENSITIVITY AND DYSPHAGIA**

PARTICIPANT CONSENT FORM



I,(name) of
.....(address)

have been invited to participate in the above named research study and have discussed the study with **Dr Alvin Ing** (Consultant Thoracic Physician) or **Nicola Clayton** (Speech Pathologist).

- I acknowledge that I have received and read the Participant Information Sheet, which includes the aims of this study, the procedures involved in this study, including any inconvenience, risk, discomfort or side effects, and of their implications.
- I understand that my participation in this study is entirely voluntary and that I can withdraw at any stage. If I withdraw, this decision will not affect in any way, my future treatment or my relationship with my doctors and other members of my health care team.
- I also understand that the information related to my participation in the study is strictly confidential. I agree that research data gathered from the results of the study may be published, provided that I cannot be identified.
- I understand that the research project will be carried out according to the principles in the National Health & Medical Research Council Statement on Human Experimentation.
- I understand that if I have any questions relating to my participation in this research study, I may contact Dr Alvin Ing on (02) 9767 6712, who will be happy to discuss them with me.
- I understand that if I have any questions about my rights as a research subject or on any other administrative matters, I may contact the Concord Hospital Ethics Review Committee on (02) 9767 6233.
- I also understand that if I wish to speak with an independent person within the Hospital about any problems or queries about the way in which the study was conducted, I may contact the Patient Representative on (02) 9767 7488.

I hereby freely agree to participate in this research study.

I also state that I have / have not participated in any other research project in the past 3 months. If I

have, the details are as follows:
.....

Name (print):

Signature: **Date:**

Name of Witness:

Signature of Witness: **Date:**



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APPENDIX D - Sydney Swallowing Questionnaire (SSQ)

THE ST GEORGE
HOSPITAL



DEPARTMENT OF
GASTROENTEROLOGY

THE UNIVERSITY OF
NEW SOUTH WALES



Sydney Swallow Questionnaire

Name: _____

DOB/Sex: _____

Date: _____

This questionnaire is designed to help us establish the severity of your swallowing problem. It is quite straightforward and should easily be completed within 10 minutes. All the information given will remain **strictly confidential**

For each question put an "X" on the line below to indicate how severe your swallowing problem is. For example, put the "X" towards the **lefthand end** of the line if your problem only **minor**, in the **middle** if it is **moderate** and at the **righthand end** if you have **severe** difficulty. If you have **NO** problem or difficulty asked about in the question you should place the "X" at the **FAR LEFTHAND** end of the line

1. How much **difficulty** do you have swallowing at **present**?

NO DIFFICULTY
AT ALL

UNABLE TO SWALLOW
AT ALL

2. How much difficulty do you have **swallowing THIN liquids**?
(eg: tea, soft drink, beer, coffee)

NO DIFFICULTY
AT ALL

UNABLE TO SWALLOW
AT ALL

3. How much difficulty do you have **swallowing THICK liquids?**
(eg: milkshakes, soups, custard)



4. How much difficulty do you have **swallowing SOFT foods?**
(eg: mornays, scrambled egg, mashed potato)



5. How much difficulty do you have **swallowing HARD foods?**
(eg: steak, raw fruit, raw vegetables)



6. How much difficulty do you have **swallowing DRY foods?**
(eg: bread, biscuits, nuts)



7. Do you have any difficulty **swallowing your saliva?**



8. Do you have any difficulty **starting a swallow?**




9. Do you ever have a **feeling of food getting stuck** in your throat when you swallow?

NEVER OCCURS OCCURS EVERYTIME I SWALLOW



10. Do you ever **cough or choke** when swallowing **solid foods**?
(eg: bread, meat or fruit)

NEVER OCCURS OCCURS EVERYTIME I EAT



11. Do you ever **cough or choke** when swallowing **liquids**?
(eg: coffee, tea, water, beer)

NEVER OCCURS OCCURS EVERYTIME I DRINK




12. How long does it take you to **eat an average meal**?

Please **TICK ONE**

Less than 15 minutes	_____
About 15-30 minutes	_____
About 30-45 minutes	_____
About 45-60 minutes	_____
More than 60 minutes	_____
Unable to swallow at all	_____

13. When you swallow does food or liquid ever **go up behind your nose or come out of your nose**?

NEVER OCCURS OCCURS EVERYTIME I SWALLOW



APPENDIX E - Mann Assessment of Swallowing Ability (MASA)

Mann Assessment of Swallowing Ability (MASA)

Alertness	2 no response to speech	5 difficult to rouse	8 fluctuates	10 alert
Co-operation	2 no cooperation	5 reluctant	8 fluctuating cooperation	10 co operative
Auditory comprehension	2 no response to speech	4 occasional motor response if cued	6 follows simple conversation with repetition	8 follows ordinary conversation with little difficulty
Respiration	2 chest infection suctioning	4 coarse basal creps chest physio	6 fine basal creps	8 spunum upper airway other condition
Respiratory rate (for swallow)	1 no independent control	3 some control/ uncoordinated	5 able to control breath rate for swallow	10 chest clear
Dysphasia	1 unable to assess	2 no functional speech sounds / single words	3 expresses self in limited manner short phrases / words	4 mild difficulty finding words or expressing ideas
Dyspraxia	1 unable to assess	2 groping/ inaccurate/ partial or irrelevant responses	3 speech crude / defective in accuracy or speed on command	4 speech accurate after trial & error minor searching mov'ts
Dysarthria	1 unable to assess	2 speech unintelligible	3 speech intelligible but obviously defective	4 slow with occasional hesitation or slurring
Saliva	1 gross drool	2 some drool consistently	3 drooling at times	4 frothy / expectorated
Lip seal	1 No closure unable to assess	2 incomplete seal	3 unilaterally weak poor maintenance	4 mild impairment occasional leakage
Tongue movement	2 no mov't	4 minimal mov't	6 incomplete mov't	8 mild impairment in range
Tongue strength	2 gross weakness	5 unilateral weakness	8 minimal weakness	10 full ROM
Tongue coordination	2 no mov't unable to assess	5 gross incoordination	8 mild incoordination	10 NAD
Oral preparation	2 unable to examine	4 no bolus formation no attempt	6 minimal chew thrust gravity assisted	8 Lip or tongue seal bolus escape
Gag	1 no gag	2 absent unilaterally	3 diminished unilaterally	4 diminished bilaterally
Palate	2 no spread or elevation	4 minimal mov't nasal regurg / air escape	6 unilaterally weak	8 slight asymmetry mobile
Bolus clearance	2 no clearance	5 some clearance/ residue	6 significant clearance / minimal residue	8 fully cleared
Oral transit	2 no mov't observed	4 delay > 10 secs	6 delay > 5 secs	8 delay > 1 sec
cough reflex	1 none observed/ unable to assess		3 weak reflexive cough	5 NAD
cough voluntary	2 no attempt / unable to assess	5 attempt inadequate	8 attempt bovine	10 NAD
Voice	2 aphonic unable to assess	4 wet / gurgling	6 hoarse	8 mild impairment slight huskiness
Trachae	1 trachae / cuffed		5 trachae / fenestrated	10 no trachae
Pharyngeal phase	2 no swallow unable to assess	3 pooling / gurgling laryngeal elevation incomplete	8 laryngeal elevation mildly restricted slow initiation incomplete clearance	10 immediate laryngeal elevation clearance of material
Pharyngeal response	1 not coping / gurgling		5 cough before/ during / after swallow	10 NAD
Diet recommendation	NBM risk too great	thick vitaminised diet	modified soft	soft
fluid recommendation	NBM	thick fluid (batter)	thick (honey)	thick (nectar)
Swallow integrity	definite	probable	possible	unlikely
dysphagia	dysphagia	dysphagia	dysphagia	dysphagia
Aspiration	aspiration	aspiration	aspiration	aspiration

Total =

APPENDIX F - Endoscopic Assessment of Swallowing (EAS)

E.A.S Endoscopic Assessment of Swallowing

COMPONENT	RATINGS			
Palate	Flaccid / removed	Bilateral weak	Unilateral weak	NAD
Velopharynx	Nasal regurgitation	Weak seal / mod regurgitation	Weak seal / mild regurgitation	NAD
Oropharynx / BOT	Atrophic/ excised	Extended deficit	Unilateral deficit	NAD
	No Movement	Moderate reduced ROM	Mild reduced ROM	NAD
Hypopharynx	Patulous / Bilateral weakness	Complete unilateral weakness	unilateral asymmetry	NAD
	No mov't / clearance	Bilateral weak / mod residue	Unilateral mov't / mild residue	NAD
PPW	Cervical osteophyte >1	Cervical osteophyte	Osteophyte non obstructive	NAD
Epiglottis	Fixed / immobile	Incomplete mov't	Mild tethering	NAD
	Severe Edema / erythema	Mod edema / erythema	Mild edema / erythema	NAD
Valleculae	Obvious residue bilateral / no spont clearance	Residue uni/ bilateral, attempts to clear	Trace residue unilateral / able to clear	NAD
Piriform sinus	Obvious residue bilateral / no spont clearance	Residue uni/bilateral, attempts to clear	Trace residue unilateral / able to clear	NAD
Larynx	Poor airway patency / bilateral VF paresis	Unilateral VF paresis	Paretic VF/ Asymmetry mov't -	NAD
	Severe Edema / erythema of glottis	Mod edema / erythema glottis	Mild edema / erythema glottis	NAD
PES	Nil opening / severe residue/ continuously open	Mod residue post swallow / bolus back-flow on trials	Minimal residue post swallow / no bolus back-flow	NAD
	Severe Edema / erythema, redundant tissue	Mod edema / erythema, +/- redundant tissue	Mild edema / erythema, +/- hyperemia	NAD
Tracheal Staining	Obvious staining below VF/ requires suctioning	Some staining / cleared with prompt	Trace staining / cleared spontaneously	NAD
Food Trials	Nil – at risk	Semi solids	Thick liquid	Thin liquid
Maneuvers				
Risk Rating	Definite	Probable	Possible	Unlikely
<i>Dysphagia</i>				
<i>Aspiration</i>				

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