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Perception of Symptoms during Induced Bronchoconstriction between African American and Caucasian Asthma Patients

by

Grace Hardie, MS, RN

**DISSERTATION**

**Submitted in partial satisfaction of the requirements for the degree of**

**DOCTOR OF PHILOSOPHY**

**in**

Nursing

**in the**

**GRADUATE DIVISION**

**of the**

**UNIVERSITY OF CALIFORNIA**

**San Francisco**

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by

Grace Hardie, Ph. D.

## DEDICATION

To Michael, my husband, for your love, your support, and your understanding during these long and stressful times of school and of writing this dissertation. I thank you for giving me "space" and always stating "you can do it!" Without you I could not have achieved this goal.

To my wonderful daughter, Nicole, and her equally wonderful husband, Benjamin. Words cannot express how much your love, caring, and support have meant to me. Not only did both of you take the time to "listen to me," but when I called in desperation for some "TLC" you both responded.

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**Perception of Symptoms during Induced Bronchoconstriction between African American and Caucasian Asthma Patients.**

Grace Hardie, R.N., Ph.D.
University of California, San Francisco
San Francisco, California

The purpose of the study was to ascertain differences in the perception of breathlessness between African American and Caucasian asthma patients during induced airflow obstruction and bronchodilation.

The death rate in the U. S. from asthma is three times higher, and emergency room visits are greater, for African Americans than Caucasians. The words that African Americans use to describe their breathlessness have not previously been studied. Thirty-two, 16 per group, African American and Caucasian mild asthmatics using beta agonist only were studied. Breathlessness was measured by Borg and VAS scale; word descriptors were measured by an open ended questionnaire. The baseline lung function and breathlessness scores were comparable. Five significant word descriptors were described by both African American and Caucasian asthma patients. African Americans used upper airway word descriptors; Caucasians used chest symptom descriptors. There was no difference between African Americans and Caucasians in their ability to perceive airflow obstruction, and they responded equally well to medications that causes bronchodilation. African Americans with asthma use different words than Caucasians to describe the respiratory sensations they experience during airflow obstruction. It is paramount to inform and educate both the general public and healthcare providers about ethnic differences in the language of breathlessness.

Susan Janson

Susan Janson, D.N. Sc., Graduate Advisor

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# Chapter One:
# The Study Problem

## Introduction

Breathlessness is one of the most common symptoms people with asthma report during episodes of bronchoconstriction (Pfeiffer, Marsac, & Lochart, 1989; Turcotte, Corbeil, & Boulet, 1990). Some people with asthma can accurately sense a marked decrease in lung function caused by airflow obstruction whereas others sense the same decrease caused by airflow obstruction only as a small change; this suggests that some patients with asthma have a lowered perception of airflow obstruction (Turcotte, et al., 1990). People with a lowered perception may be at risk of dying from asthma due to an inability to sense the need for urgently needed care. Ethnic differences in the perception of breathlessness during episodes of airflow obstruction in patients with asthma have not been studied. The death rate from asthma is three times higher for African Americans with asthma than for Caucasians (Malveaux, Houlihan, & Diamond, 1993, Haire-Joshu, Fisher, Munro, & Wedner, 1993). In view of these facts, it is essential to determine if the perception of breathlessness is different for the same degree of bronchoconstriction between African American and Caucasian patients with asthma. Having African Americans and Caucasians with asthma describe, in their own words, the sensation of breathlessness that they experience during a methacholine challenge should illustrate whether or not the language of breathlessness is unique or shared across cultures.

Currently the specific words or phrases that African Americans use to describe their asthma symptoms are not known, but the language of

breathlessness—word descriptors—were derived from studies of samples that included only Caucasians (Simon, Schwartzstein, Weiss, Fencl, Seghtsoonian, & Weinberger, 1990; Elliott, Adams, Cockcroft, Macrae, Murphy, & Guz, 1991). The language of breathlessness may be culturally distinct and needs to be studied. New information could directly affect clinical asthma management by influencing communication between patients and clinicians. This study seeks to enlarge our knowledge and understanding of the effects of ethnicity on the language of breathlessness. Symptom monitoring using ethnically sensitive descriptions rather than word descriptors imposed by clinicians could be important in improving communication between clinicians and patients

## Statement of the Problem

Common symptoms of asthma, e.g., dyspnea, chest tightness, and cough, generally reflect increased airflow obstruction. For successful symptom management people with asthma must be able to perceive the severity of their symptom(s) in order to seek appropriate treatment and to obtain symptom relief. The most common approach asthma patients use to control their symptoms is to take medication, specifically an inhaled beta agonist. Recent studies have sought to quantify the perception of bronchoconstriction, or airway obstruction, because of the subjective and individualized nature of the symptom (Roisman, Peiffer, Lacronique, LeCae, & Dusser, 1995; Turcotte, et al., 1990). Poor perception of bronchoconstriction may be one of the factors contributing to asthma death since blunted perception was found in asthma patients who experienced a near fatal asthma episode (Roisman, et al., 1995; Kikuchi, Okabe, Tamura, Hida, Homma, Shirato, & Takishima, 1994). Yet, the relationship between the perception of symptoms and the degree of airflow obstruction is poorly understood (Noseda,

Schmerber, Prigogine, & Yemault, 1993; Boulet, Deschesnes, Turcotte, & Gignac, 1991). The inability of asthma patients to perceive the severity of their bronchoconstriction poses the risk of their delaying treatment, and this may contribute to fatal or near-fatal asthma episodes (Roisman, et al., 1995; Boulet, et al., 1991).

Malveaux and colleagues have suggested that both the recognition and treatment of asthma are influenced by a patient's ethnicity (Malveaux, et al., 1993). Since the 1980's the mortality and morbidity from asthma for African Americans has risen by 7% while asthma prevalence within this ethnic group has risen by 22% (Malveaux, et al., 1993). Such factors as poverty, fear, lack of access to care, and the underestimation of the severity of symptoms may hinder African Americans from seeking immediate care for their symptoms (Malveaux, et al., 1993). If African Americans with asthma indeed underestimate their symptom severity they would face an increased risk of experiencing a fatal to near fatal asthma attack (Haire-Joshu, et al., 1993).

The differences in perception of bronchoconstriction between African American and Caucasian patients with asthma have not been studied. That African American patients with asthma have the highest morbidity and mortality rates suggests that understanding their subjective perception of breathing difficulty is warranted (Lougheed, Lam, Forkert, Webb, & O'Donnell, 1993). Since the perception of breathlessness is highly variable, an asthma patient may not recognize this symptom as a threat, but rather try to adapt to the existence of the symptom instead (Brand, Rijcken, Schouten, Koeter, Weiss, & Postma, 1992). In patients with asthma a blunted perception of airflow obstruction is potentially dangerous since the severity of the asthma exacerbation is minimized and may therefore be undertreated both by the patient and the physician (Kikuchi, et al., 1994). Conversely, the effect that this blunted perception has on the perception of

bronchodilation also needs to be determined. An inability to perceive that the airway is "tight" or "open" will directly influence whether or not a patient uses the inhaled beta agonist for rescue treatment of airflow obstruction. Understanding the ethnic variations in perception of airflow obstruction will allow for the development of individualized self-management approaches (Boulet, et al., 1994; Brand, et al., 1992).

Almost all of the research on the perception of bronchoconstriction has involved white cohorts. The extension of this research to African Americans with asthma is essential. Some asthma patients modulate or tolerate symptoms associated with their diminished lung function or bronchoconstriction; the symptom(s) that influence their decision to use their inhaler is not known. Determining what symptom(s) influence the perception of acute bronchoconstriction among African American and Caucasian patients with asthma will facilitate not only more accurate assessment but treatment that could potentially reduce the incidence of fatal episodes while providing better control of the asthma symptoms (Lougheed, et al., 1993; Quirk & Jones, 1990).

## Significance

Worldwide, asthma afflicts more than 4% of the population; in the United States that figure is 5% (Sullivan, 1996; Jones, 1996). Moreover, asthma care is economically costly. In 1990 the yearly medical cost per asthma patient was estimated to be $640.00 with the majority of this cost being spent on the management of asthmatics after acute hospitalizations (Sullivan, 1996). Until recently, asthma management did not focus on the prevention of asthma episodes but rather on treating the presenting symptom(s). However, in the last decade, both the prevalence and incidence of asthma within the population at

large has increased, and during this same period the mortality from asthma among African Americans has increased by 7% (Haire-Joshu, et al., 1993; NAEPP, 1992). Both the rising cost of asthma care and the increased prevalence of asthma indicates the need for alternative measures of management and assessment that change the emphasis of care to control and prevention of asthma excerbations.

The emergence of asthma as a significant health problem is corroborated by the complexity and the variability of asthma symptoms. Despite more effective beta agonist agents, the mortality rates from asthma for African Americans is almost three times the rate for Caucasians (Kelso, Self, Rumbak, Stephens, Garrett, & Arheart, 1995). If the sensory perception of bronchoconstriction is different for African Americans with asthma and if treatment is prescribed later in an acute exacerbation, then differences in symptom perception may be a factor in increased mortality rates in this ethnic group.

**Asthma: Implications of Ethnicity**

The lack of regular care, the delay in seeking treatment, and the quality of prior experience with health care professionals are interrelated influences upon the health seeking behavior of African Americans with asthma (Haire-Joshu, et al., 1993). Haire-Joshu, et al., (1993) conducted interviews and focus groups of adult African Americans with asthma to determine how attitudes impacted on self-management. From 81 interviews (Haire-Joshu, et al., 1993) the most common reason for seeking episodic care as opposed to regular care was the lack of satisfaction with health care providers. Thus, self-care and the use of over the counter medications became the predominant approaches to symptom management. This episodic care approach has fostered a belief for some patients with asthma that "if I didn't die" then the symptoms are treatable or controllable.

Moreover, for African Americans with asthma without health care coverage the emergency room becomes the primary care provider. If the attitude of the health care provider, either implicit or explicit, is negative towards an individual seeking care, that individual may delay seeking treatment to avoid further negative or degrading interactions with health care providers. (Haire-Joshu, et al., 1993; Targonski, Persky, Orris, & Addinton, 1994). In a related context, African American patients with asthma have hesitated to participate in research due to an undercurrent of distrust and fear in seeking outside help (Janson-Bjerklie, Ferketich, Benner, & Becker, 1992; Haire-Joshu, et al., 1993).

At present, the traditional symptoms of wheezing, chest tightness, and dyspnea are not applicable to all persons with asthma. Thus, elucidating both the subjective sensations and the word descriptions that African American and Caucasian patients with asthma use to describe their airflow obstruction will serve to quantify the symptoms.

Of particular concern are asthma patients with a blunted perception of airflow obstruction who fail to respond appropriately to the worsening of their symptoms for they may be at a greater risk for a fatal episode. Whether or not a blunted perception of airflow obstruction occurs in African Americans with asthma has not been studied. Recent studies have documented an association between irregular use of an inhaled beta agonist with more severe, difficult to control, asthma exacerbations and with a decline, over time, in lung function; additionally, an increase in airway responsiveness to methacholine without altering bronchodilator responsiveness has been noted (Taylor, Sears, Herbision, Flannery, Print, Lake, Yates, & Lucas, 1992; Cheung, Timmers, Swinderman, Bel, Dijkman, & Sterk, 1992). The possibility that asthma patients with a lowered ability to perceive airflow obstruction and who use a short acting inhaled beta

agonist regularly or excessively may actually worsen their bronchoconstriction is clinically alarming (Kikuki, et al., 1994; Boulet, et al., 1991).

Inadequate asthma symptom control with appropriate pharmacotherapy may contribute to the present increase in asthma morbidity and mortality in African Americans compared to Caucasians (Koenig, et al., 1992; Johnson, Burlew, & Stiles, 1995). Two physiological studies (Koenig, et al., 1992; Johnson, et al., 1995) found a lowered affinity and binding of the airway beta receptors of African American patients with asthma, thereby suggesting the existence of ethnic differences in response to the inhaled beta agonists. These researchers (Koenig, et al., 1992) found that African Americans with asthma not only had a reduction in the number and the binding capabilities of their airway beta receptors but, also, a reduced and different response than Caucasians. This finding is significant since the standard treatment for quick relief of asthma symptoms is the use of short acting beta agonist inhalers. The great probability that this group of bronchodilators may provide adequate symptom relief while only modestly controlling airflow obstruction for this ethnic group is frightening and requires further research. Hopefully, the clinical assessment of an asthma patient's ability to perceive airway narrowing will become a routine extension of asthma management for health professionals.

The differences in physiology and sensory perception between African American and Caucasian asthma patients have also not been studied (Wong, Pavord, Williams, Britton, & Tattersfield, 1990), in particular, the differences in the perception of breathlessness, bronchoconstriction, and bronchodilation (Koenig et al., 1992; Sherman, Tollerud, Heffner, Speizer, & Weiss, 1993). No studies have compared the sensation of symptoms during induced bronchoconstriction between African American and Caucasian patients with

asthma. Until the symptoms of airflow obstruction are documented, the timing of adequate treatment will not be optimal.

Therefore, quantifying the perception of breathlessness will allow patients with asthma to regain self-control over their symptoms (Janson-Bjerklie, et al., 1992; Quirk & Jones, 1990). Additionally, the subjective sensation of bronchoconstriction and bronchodilation by word descriptions based on ethnicity has not been elucidated and these descriptors will provide valuable new information.

## Purpose of the Study

The overall objectives of this study are to determine (1) whether African American and Caucasian patients with asthma differ in the perception of airflow obstruction and bronchodilation, and (2) whether asthma symptoms are described differently by these two ethnic groups during induced bronchoconstriction and bronchodilation. The specific aims of this study are to compare and contrast (a) the perception of the symptom of breathlessness (airflow obstruction) between the two ethnic groups at the provocative dose of methacholine that causes a 30% fall from baseline in the forced expiratory volume in 1 second (FEV1); (b) the word descriptions of the sensations these two ethnic groups describe at the provocative dose of methacholine; (c) the perception of the bronchodilation by the change in the symptom of breathlessness between these two ethnic groups; (d) the word descriptions of the sensations these two ethnic groups describe at maximal bronchodilation; and (e) the response to the bronchodilator question at various levels of airflow obstruction (PC15, PC20, and PC30) from these two ethnic groups.

To provoke airflow obstruction the methacholine challenge will be used as a laboratory analog of an asthma exacerbation. The perception of bronchoconstriction during a methacholine provocation test will provide insight into whether ethnic subgroups perceive asthma symptoms differently (Boulet, et al., 1994). Moreover, what is not established is the relationship between symptoms, severity, and the perception of breathlessness; nor has it been determined which symptom(s) are most important in association with increasing airflow obstruction.

# Chapter Two:
# Review Of Literature

## Overview of Asthma

### Definition of Asthma

Asthma is characterized by specific symptoms (wheezing, dyspnea, and chest tightness) that are highly variable and are relieved by the use of an inhaled bronchodilator (Woolcock, 1996; Busse, Masiak, & Young, 1994). The hallmark features that characterize asthma are (a) an obstruction to airflow that reverses with bronchodilators and (b) an exaggerated airway reactivity to allergens or to other environmental stimuli. Asthma is associated with allergies (atopy), IGE production, and a genetic predisposition (Landau, 1995; Woolcock, 1996). For example, an asthma patient who responds to seasonal stimuli may be symptomatic only during that particular season, whereas asthma patients who respond to a variety of stimuli may experience daily symptoms in varying degrees of severity and duration (Barnes & Liew, 1996).

The second feature, airway reactivity, confirmed by a bronchoprovocative agent such as histamine or methacholine, is a physiologic feature of asthma that is termed airway hyperresponsiveness (Gold, 1994). The methacholine (Mch) challenge test is sensitive to asthma but lacks specificity since airway reactivity can be demonstrated in other people without asthma, e.g., people with chronic bronchitis (Neukirch, Liard, Segala, Korobaeff, Henry & Cooreman, 1992). However, the bronchoprovocative challenge test has become an important

measurement tool in assessing the perception of airflow obstruction and the presence of airway responsiveness (Gold, 1994).

A third feature, airway inflammation with infiltration of the airway mucosa by lymphocytes, mast cells, and eosinophils, is less widely agreed upon as a characterizing feature, but it is gaining acceptance (Woolcock, 1996; Howarth, Bradding, Montefort, Peroni, Djukanovic, Carroll, & Holgate, 1994). What clearly distinguishes asthma from other obstructive disorders is that the symptoms commonly persist throughout a person's life, usually occurring intermittently rather than persistently (Barnes & Liew, 1996; Boushey, 1997).

The influence of ethnicity in defining and characterizing asthma has not been explained. A useful approach to determine ethnic differences in the symptom(s) of breathlessness and the perception of airflow obstruction is by methacholine challenge which will be used in this study as a laboratory analogy.

Agreement exists that spirometry is the hallmark method to assess airflow obstruction and that the tests of maximal expiratory flows—forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), peak expiratory flows (PEF) and forced expiratory flows 25-75 (FEF 25-75)—are the accepted diagnostic measures even though their specificity for asthma is lacking (ATS, 1987; Gold, 1994). Normally, airflow obstruction is confirmed when the FEV1/FVC ratio is decreased and if, after two puffs of inhaled beta agonist, a 12% improvement in airflow is demonstrated (ATS, 1987). Diagnostically, the ratio of FEV1/FVC should be 80% in healthy adults; this ratio decreases with aging (ATS, 1987). Individuals with mild airway obstruction may not have a reduction in the FEV1/FVC ratio but they do demonstrate a definitive concave shape to their expiratory flow loop (Weinberger, 1992; Gold, 1994)). Although a reduction in the expiratory volumes of the lung is found in other pulmonary disorders, the

FEV1 remains the most valid measure to confirm the diagnosis of asthma (ATS, 1987).

## Overview: Approaches to the Assessment of Breathlessness

### Bronchial Challenge

To further substantiate a diagnosis of asthma after spirometry a bronchial challenge is performed to confirm an exaggerated airway response; this test is highly predictive for a clinical diagnosis of asthma. Exaggerated airway responsiveness is confirmed if the subject's FEV1 falls by 20% (PC20) in response to a dose of 8 mg/ml or less of the bronchoprovocative agent (Sterk, Fabbri, Quanjer, Cockcroft, O'Byrne, Anderson, & Malo, 1993). Bronchial challenges, most frequently, use methacholine or histamine, although physical stimuli (exercise) and sensitizing agents (allergens) can also be used to determine the degree of airway responsiveness (Perpina, Pellicer, de Diego, Compte, & Macian, 1993). Conversely, airway hyperrereactivity may not be a constant feature for some asthmatics. A negative response to the methacholine challenge may occur in asthma patients whose symptoms are seasonal; a small percentage of patients never respond (Perpina, et al., 1993; Gold, 1994). A negative challenge in an asthma patient with seasonal symptoms would need to be repeated during the patient's symptomatic phase (Perpina, et al., 1993).

Recently, these challenge tests have been used as a stimulus in studies to assess the perception of breathlessness associated with airflow obstruction (Turcotte, et al., 1990; Lougheed, Lam, Forkert, Webb, & O'Donnell, 1993). During a bronchial challenge the degree of airway hyperresponsiveness to a specific stimuli is indicated by a leftward shift in the dose response curve that is

often associated with an increased slope (Sterk, et al., 1993). The degree of airway hyperresponsiveness (AH) is correlated with asthma severity; severe asthmatics would have a more pronounced leftward shift of the dose response curve (Sterk, et al., 1993). When standardized laboratory procedures are followed, bronchial challenges provide a highly reliable and valid measure of airway hyperresponsiveness (Sterk, et al., 1993; Malo, Pineau, Cartier, & Martin, 1983). A bronchial challenge is an objective method to assess breathlessness by inducing airflow obstruction. (Turcotte, et al., 1990; Chinn, Burney, Britton, Tattersfield, & Higgins, 1993). With respect to bronchial challenge, the terms high and low perceivers are commonly used to categorize the sensory response of asthma patients to induced airflow obstruction. Whether or not these terms apply to the perception of airflow obstruction across ethnicity's is not known.

**Symptom Assessment**

A principal concern for asthma patients is their symptoms. Because asthma is a disease characterized by distressing symptoms, patients must learn to control or abate the symptoms and self-manage the disease (Janson-Bjerklie, et al., 1992). The nature of the symptoms experienced by people with asthma varies widely. The symptoms are difficult to characterize and quantify because they are triggered by different stimuli and respond to different medications. For example, the intensity of breathlessness can vary widely, and an increase in breathlessness can be perceived as frightening or as life-threatening for some people with asthma. Others with comparable airway obstruction will not perceive this same intensity and the quality of breathlessness will not be as threatening (Janson-Bjerklie, et al., 1993; Boulet, et al., 1994). The weight or severity a patient accords to a symptom such as breathlessness can be disproportionate to an objective

measure of airflow obstruction such as FEV1 or PEF (Quirk & Jones, 1990; Janson-Bjerklie, et al., 1993). Janson-Bjerklie and colleagues (1993) noted that patients who used self-care strategies perceived less danger and distress from their symptoms because they felt "in control" of their symptoms. However, unless individuals with asthma can accurately perceive the severity of their symptoms they cannot modify selfcare. The relationship between symptoms, severity, and perception is not clearly understood nor is it understood which symptoms are correlated with increasing airflow obstruction.

Asthma patients need to understand when and what medications to take, especially when they have several different prescribed inhalers, for symptom control. Asthma patients who lack regular health care and who treat their symptoms episodically by using over the counter medications (OTC) generally undertreat their symptoms and have greater hospitalization rates (Gottlieb, Beiser, & O'Connor, 1995). The use of OTC medications is indicative of the belief that the symptoms are treatable, controllable, and thus not serious (Haire-Joshu, et al., 1993). This misconception about asthma symptoms was articulated in a study of patients whose primary source of health care was an acute care setting, the emergency room; they were compared with patients who had a private physician (Haire-Joshu, et al., 1993). Interestingly, patients who used the acute care setting as their source of primary care felt more confident in their use of a metered dose inhaler (MDI) than those patients who had a primary care doctor. Haire-Joshu, et al., (1993) hypothesized that this confidence represented less awareness for these patients about the different aspects of asthma management because they were exposed to minimal or inconsistent education (Haire-Joshu, et al., 1993). The more frequent the emergency room visits the greater the asthma instability (Haire-Joshu et al., 1993; Janson-Bjerklie, et al., 1992).

## Review of Literature

The literature is reviewed in the order of the study objectives. The order is as follows: (1) perception of the symptoms of airflow obstruction; (2) mechanisms of bronchoconstriction; (3) word descriptors; (4) physiological differences: airway responsiveness; (5) ethnicity and perception of breathlessness; and (6) perception of bronchodilation.

## Perception of the Symptoms of Airflow Obstruction

Breathlessness is the most common symptom associated with airflow obstruction (Turcotte, et al., 1991; Peiffer, et al., 1989). Due to the subjective and individualized nature of this symptom, recent studies have sought to quantify the perception of breathlessness during induced airflow obstruction (Roisman, et al., 1995; Turcotte, et al., 1991). Brand and colleagues (1990) studied the perception of breathlessness (dyspnea) during a histamine challenge of asymptomatic hyperresponders in an attempt to identify why some asthma patients can sense a marked decrease in their lung function whereas others can sense only a small change (Brand, et al., 1990; Turcotte, et al., 1991).

Brand et al., (1990) randomly selected 412 middle aged subjects, with moderate to mild disease, who recorded by Borg scale their dyspnea before and after a standardized histamine challenge (PC10 $\leq$ 16 mg/ml of histamine). Prior to enrollment, only 16.5% of all the subjects reported symptoms on the self-report symptom questionnaire. Subjects who reported dyspnea, wheeze, or asthma symptoms were defined as asthmatics and assigned to group one (n = 32); those who reported cough, phlegm, or bronchitis were defined as chronic bronchitics and were assigned to the second group (n = 36). The third group was comprised

of asymptomatic subjects (n = 344). The mean FEV1 for group one was 2.54 L ± .68, group two FEV1 was 2.89 L ± .68, and group three FEV1 was 2.97 L ±.75. The histamine dose that induced a PC10 was not provided. Rather, subjects who responded to ≤ 8 mg/ml were termed hyperresponders (Brand, et al., 1990). Dyspnea, described as either breathlessness or shortness of breath, was measured using a zero (no symptoms) to ten (maximal bearable) Borg scale (Brand, et al., 1990). Before the challenge, 72.3% of all the subjects rated their dyspnea as zero on the Borg scale compared to 24.3% (100 subjects) who rated their dyspnea as zero after the challenge (Brand, et al., 1990). Subjects who reported wheezing on the pre-entry questionnaire also recorded more dyspnea on the Borg scale. The median change in the Borg scale before and after the challenge was two (Brand, et al., 1990). Additionally, subjects who had reported symptoms at baseline reported higher dyspnea (OR 4.01) on the Borg scale (Brand, et al., 1990).

In contrast, the asymptomatic hyperresponders, poor perceivers of airway obstruction, had a PC10 ≤ 16 mg/ml of histamine and no change in their Borg scale (Brand, et al., 1990). The dose of histamine at PC10 was comparable in both the symptomatic and asymptomatic hyperresponders (Brand, et al., 1990). Asymtomatic asthma patients with variable or infrequent airway obstruction were unable to perceive airflow obstruction. This result may be related to the fact that the sensation of breathlessness comes and goes and is not perceived as airflow obstruction (Brand, et al., 1990; Turcotte, et al., 1990). The asymptomatic group was not asked to describe their sensation of bronchoconstriction using any words other than "breathlessness". It is possible, had they been given the option, that they would have chosen other words to describe their sensations.

Other variables, e.g., age, smoking history and PC10, also influenced study outcomes. The confirmation AH by a PC10 to ≤ 16 mg/ml of histamine suggests that the FEV1 may not have been decreased far enough (Boulet, et al., 1994) to

induce symptoms especially in the asymptomatic group. Presently, the standard indicator of AH is a PC20 to ≤ 8 mg/ml of a bronchoprovocative agent (Sterk, et al., 1993). When the smoking histories of groups one and two were combined, 40% of all men and 22% of all women were current smokers (Brand, et al., 1990). Current smokers were 1.66 times more likely to have an increased Borg score (Brand, et al., 1990; Turcotte, et al., 1989). Moreover, smokers had increased Borg scores unrelated to airflow obstruction (Turcotte, et al., 1989). Both studies suggest that temporal adaptation to persistent symptoms may have resulted in lower scores since the mean age of the sample ranged from 50 ± 9.3 to 52 ± 8.5 years (Brand, et al., 1990; Turcotte, et al., 1989). All three groups were older, and the likelihood that they had adapted to their symptoms must be considered. The interaction of smoking (groups one and two) and age with the Borg scores was not explained. This study (Brand, et al., 1990) has major limitations, but it was one of the first studies to evaluate the perception of bronchoconstriction and to try to distinguish between hyperresponders and poor responders. One important finding was that the degree of airway obstruction is not a determinate of perceived dyspnea; this finding emphasizes the complexity and enigmatic origin of sensory perception (Brand, et al., 1990).

**Induced Bronchoconstriction: Methacholine and Bradykinin**

The VAS was used by Roisman and colleagues (1995) to assess if the perception of bronchoconstriction was influenced by the type of bronchoconstricting agent used to induce airflow obstruction and by the degree of airway inflammation present . Mild asthmatics (n = 18) participated in this parallel two treatment group study. The two groups had comparable baseline FEV1s; group A (n = 9) had a mean FEV1 of 89% predicted compared to 91% of

predicted for group B (n = 9). Group A, mean age 34.4 ±5, received only beta agonist for symptom control whereas group B, mean age 29.1 ± 3.2, received beta agonist for symptom control and an inhaled corticosteroid (ICS) (flunisolide) twice a day. All of the subjects had a methacholine and bradykinin challenge, bronchoalveolar lavage, and a bronchial biopsy. At baseline, subjects were asked to rate the magnitude of their breathlessness on a 100 mm horizontal VAS scale anchored at either end with "not at all breathless" or the "worst imaginable breathlessness". Breathlessness was further defined as a "sensation felt during an asthma attack in the past irrespective of chest wall discomfort" (Roisman, et al., 1995). Two to three minutes after each challenge dose subjects were instructed to make a vertical mark, relative to the two extremes, that indicated the magnitude of their breathlessness at that time. After each dose of methacholine or bradykinin subjects were given a new VAS sheet thus limiting recall bias.

Baseline increases in VAS scores were plotted against the FEV1 at baseline and the Δ FEV1 after each bronchoconstricting agent. Subjects without ICS had an increased VAS score only after Mch. This increase in VAS score was correlated with the decrease in a subject's FEV1 ($p < 0.01$); this same correlation did not exist for bradykinin ($p < 0.35$) and the VAS scores did not increase (Roisman, et al., 1995). In the ICS group the increased VAS scores from both Mch and bradykinin correlated with a decrease in FEV1 ($p < 0.01$) (Roisman, et al., 1994). The provocative doses (PD15) of Mch and bradykinin were comparable between both study groups. In the ICS group, the VAS scores increased comparatively with both provocative agents and the VAS increase was dose dependent on the agonist given ($p < 0.02$) (Roisman, et al., 1994). Gender may have influenced the VAS scores since 78% of the ICS group were men whereas 63 % of the non-ICS were women (Marks, Yates, Ceyhan, Campos, Scott, & Barnes, 1996).

For the non-ICS group, the difference in the perception of breathlessness between the two bronchoconstricting agents suggests that these two agents may induce bronchoconstriction differently. The mean maximal decrease in FEV1 was comparable; methacholine resulted in a 25.7 L ± 1.6 reduction and bradykinin a 28.3 L ± 2.9 reduction (Roisman, et al., 1994). The effect of ICS on temporal adaptation was not discussed. By using two treatment groups it is possible that two very different types of perception experiences occurred. It is likely the two groups were not comparable. The use of a control group could have resolved these concerns (Woods & Catanzaro, 1988). How bradykinin induces bronchoconstriction when compared to the direct action on the airway smooth muscle of methacholine was not delineated. It is known that bronchoconstriction induced in asthmatics by bradykinin is mediated by cholinergic and peptidergic reflexes resulting in its weak action on airway smooth muscle (Roisman, et al., 1995). Furthermore, in all subjects the intensity of increase in VAS score was dose dependent on the constricting agonist ($p < 0.01$) and independent of the Δ FEV1 (Janson-Bjerklie, et al., 1986; Roisman, et al., 1995). The VAS/FEV1 slope did reflect the magnitude or percentage of change in airway obstruction, thereby indicating that the VAS is a sensitive tool to measure breathlessness (Roisman, et al., 1995).

The outcomes of this study are confusing since ICS is known to reduce the perception of bronchoconstriction both by temporal adaptation and by altering the down regulation of beta receptors (Tattersfield & Barnes, 1992; Barnes, 1990). Earlier studies, using a VAS, confirmed a lowered perception of symptoms in asthma patients using ICS compared to those using beta agonist only (Tattersfield & Barnes, 1992). Roisman ,et al., (1994) proposed several reasons for the reduced perception of breathlessness in the non-ICS group induced by bradykinin: (1) the site or mechanisms that induced bronchoconstriction may

have been different and (2) the effect of bradykinin may not be related to its bronchoconstrictor action.

**LAR and EAR Effects on Bronchoconstriction**

Antigen, exercise, and histamine challenges were used to determine differences in the perception of breathlessness in a study of mild asthmatics (FEV1 ≥ 80%) controlled by as-needed beta agonist only (Turcotte, et al., 1990). Turcotte and colleagues (1990) questioned why some asthma patients do not sense a reduction in their lung function whereas others can sense even a slight change. The eight subjects, with a mean age of 26 ± 10, were atopic, non-smokers, and had a history of exercise induced asthma. The mean FEV1 was 94.5% percent predicted; females comprised 63% of the sample.

To assess both the early (EAR) and late asthmatic response (LAR) in acute bronchoconstriction, histamine and exercise challenges were performed before and after an antigen challenge (Turcotte, et al., 1990). On day one all subjects had a histamine challenge, on day two an exercise study, on day three an antigen challenge, on day four a repeat histamine challenge, and on day five a repeat exercise challenge. Subjects scored their dyspnea on a Borg scale, labeled 0 (no symptoms) to 10 (maximal bearable), prior to and two minutes after the last dose of histamine, antigen, or exercise challenge. AH was demonstrated by the provocative dose of histamine that caused a 20% fall (PC20) in the baseline FEV1 (Turcotte, et al., 1990). The eight subjects clearly demonstrated AH; the summed (histamine one and two) dose of histamine, PC20, was 1.67 mg/ml. As a group, the maximal Borg score at PC20 ranged from a mean of 1.0 to 1.25 suggesting a lowered perception of breathlessness for the degree of airway responsiveness. When the percent change of FEV1 was plotted against the change in the Borg

score an inverse relationship was present; this was not statistically significant. Thus the relationship between the intensity of breathlessness, as measured by the Borg scale, for a given decrease in FEV1 was not demonstrated (Turcotte, et al., 1990). Three of the study subjects had a greater fall in FEV1 (≥ 20%) but failed to perceive a greater intensity, measured by the Borg, of breathlessness; their perception of breathlessness was the same for all three challenges. (Turcotte, et al., 1990). Three other subjects did not perceive the LAR until 90 minutes post challenge but accurately perceived the EAR (Turcotte, et al., 1990). These findings did not demonstrate a difference in perception of breathlessness between EAR and LAR; the sample size was very small.

Several factors influenced the study outcomes. First, the group had mild airway disease with a mean FEV1 ≥ 95% predicted. This could explain the low mean dyspnea (Borg ≤ 3) scores. Secondly, the subjects were asked only to score their sensation of breathlessness, and they might not have perceived the sensation as breathlessness but rather as chest tightness, wheeze, or some other sensation. In reference to the subjects with a delayed perception of breathlessness of the LAR, Turcotte, et al., (1990) proposed that constriction of the large airways was more acutely sensed than constriction of small airways; the small airways primarily constrict in the LAR whereas the large airways constrict in EAR (Turcotte, et al., 1990; Bierman, Spiro, & Peteram, 1984). McFadden, et al., (1984) noted that during exercise induced bronchoconstriction the less severe changes (airflow obstruction) in airway caliber primarily affected the larger airways with more severe obstruction affecting the smaller, more peripheral, airways (McFadden, Kiser, & deGroot, 1973; Bierman, et al., 1984). Assuming this is accurate, then small airway constriction would not be acutely sensed in asthma patients with a blunted perception of breathlessness thereby placing them at risk for near-fatal episodes (Janson-Bjerklie, et al., 1987; Kikucki, et al., 1994).

To replicate their earlier study, Turcotte and Boulet (1993) enrolled 28 young (mean age 24), mild asthma patients controlled by inhaled beta agonists only. The mean FEV1 for the study sample was 92% of predicted. Airflow obstruction was induced by antigen, allergen, and Mch (in place of histamine) challenges to assess the perception of breathlessness during EAR and LAR. Subjects were asked to evaluate their breathlessness, by scoring their dyspnea on the Borg scale, prior to challenges and at regular intervals during the EAR and LAR. Breathlessness and dyspnea were used as interchangeable terms. The average PC20 with Mch induced bronchoconstriction was 1.60 mg/ml; the mean Borg score for EAR was 2.0 compared to 0.7 for the LAR (Turcotte & Boulet, 1993). The EAR Borg score was inversely related to the rate of fall in the FEV1 ($p < 0.001$); in particular, during LAR the slower the fall in the FEV1 the weaker the perception of breathlessness ($p < 0.001$). One hypothesis for the poorly perceived LAR is that during slow and progressive bronchoconstriction temporal adaptation occurs resulting in an underestimation of the severity of the obstruction (Burdon, et al., 1982; Brand, et al., 1992). The perception of breathlessness that results from rapid airflow obstruction may be mediated by different mechanisms and thus perceived differently (Marks, et al., 1996). This changed perception of breathlessness could be the result of a lowered or blunted perception; however, data supporting this notion is lacking (Burdon, et al., 1992; Pfeiffer, et al., 1989).

The Turcotte and Boulet (1993) study has some important limitations. First, the occurrence of the LAR usually involves airway inflammation and the inflammatory process contributes to a lowered perception of breathlessness (Cockcroft, et al., 1995; Roisman, et al., 1995). Second, considering (a) that 18 out of the 28 subjects were dual responders to EAR and LAR and (b) that dual responders perceive the EAR more intensely with a lowered perception during LAR, this data might have been skewed (Roisman, et al., 1995). Third, the use of

Mch may have contributed to a more accurate perception of breathlessness because of its direct effect on airway smooth muscle (Roisman, et al., 1995). Even though histamine also causes contraction of bronchial smooth muscle with secondary bronchoconstriction via reflex neurogenic pathways, its effect on increased microvascular permeability might cause a different perception of breathlessness (Gold, 1994; Sterk, et al., 1993). Fourth, because the subjects were very mild asthma patients, it is not surprising that the Borg scores were low since a 20 % reduction in their airflows may have been insufficient to induce significant symptoms. Finally, without a definition of breathlessness or dyspnea it is unclear what symptom or sensation the subjects rated on the Borg scale.

Determining the exact mechanisms that cause breathlessness during spontaneous airflow obstruction is important because poor perception of breathlessness is associated with poor asthma control (Janson-Bjerklie, et al., 1987). In order to effectively treat their symptoms, asthma patients must first be able to perceive they are having difficulty breathing. Therefore, it is essential to understand what symptoms are important to asthma patients and how they perceive their symptom(s); next it is important to match a treatment with a specific symptom. The traditional symptoms of wheezing, chest tightness, and dyspnea may not be applicable to all asthma patients; instead, determining what symptoms are important should be a priority.

## Perception Studies: Intensity, Awareness, Characteristics, and Near-Fatal Episodes

### Perception of Intensity

In 1987, Janson-Bjerklie and colleagues found younger asthmatics experienced more intense dyspnea compared to older asthmatics during similar levels of airway obstruction. These researchers examined the intensity of

dyspnea to determine if specific variables influenced the degree of dyspnea experienced by asthmatics. A total of 31 asthmatics, with a mean age of 31, who demonstrated at least a 20% reduction in their FEV1 with 15% reversibility, were enrolled. On day one, methacholine-induced bronchoconstriction was performed on all of the subjects. Thirty seconds after each concentration they were asked to rate their dyspnea on a visual analog scale (VAS). The 100 mm VAS was anchored at either end with "no difficulty breathing" and "extreme difficulty breathing". Airway resistance (Raw) and thoracic gas volume (TGV) measured by body plethysgraphy documented that all the subjects reached a PC20 (Janson-Bjerklie, et al., 1987). With a possible dyspnea score of 1 to 100, the baseline score was 9 (± 10) with a mean dyspnea score of 35.2 (± 19.7) at PC20. Increased frequency of asthma attacks and a greater smoking history were correlated with dyspnea intensity at PC20. Age was negatively correlated with dyspnea intensity ($r = .41$; $p < 0.02$) indicating that for younger asthmatics the intensity of dyspnea was greater at PC20 than for older subjects in this cohort. The actual VAS scores were not presented. These investigators proposed that asthmatics with greater AH tended to experience more frequent symptoms, based on self report data, and that these factors contributed to their experiencing a greater level of dyspnea. In fact, asthma patients with greater awareness of their symptoms may be more sensitized (attuned to their symptoms), therefore, are better able to perceive discrete changes in their breathing (Janson-Bjerklie, et al., 1987). As noted earlier, changes in the airway caliber of the larger airways are more acutely sensed (McFadden, et al., 1984; Bierman, et al., 1984); the increased awareness of symptoms exemplifies this notion. This was one of the first studies to utilize the term awareness in regards to dyspnea. The investigators did not explore whether subjects experienced any other sensations they may have been aware of when they rated their dyspnea.

**Perception: Awareness**

In a later study, Connolly and colleagues explored impaired awareness to induced bronchoconstriction in elderly and young asthmatics (Connolly, Crowley, Charan, Nielson, & Vestal, 1992). Connolly, et al., noted, in an earlier 1988 study, that 40% of elderly asthmatics were symptomless, based on self-report, even though their peak flows were diminished by as much as 40% . To explore this question of reduced awareness to airflow obstruction 67 subjects were studied. The sample included 17 elderly and 16 young asthmatics with matched normal non-asthmatic controls (17 per group). Elderly was defined as individuals over the age of 60, whereas the "young" category was defined as under the age of 40. The cohort was comprised of four groups: (1) elderly asthmatics, with a mean age of 69, and a mean FEV1 percent predicted of 78% ; (2) elderly normals, with a mean age of 67, and a mean FEV1 percent predicted of 110%; (3) young asthmatics, with a mean age of 31, and a mean FEV1 percent predicted of 104%; and (4) young normals, with a mean age 28, and a mean FEV1 percent predicted of 105%. Two methacholine challenges were performed on two different days. Immediately after subjects reached a PC20 they were asked to rank their awareness of chest tightness, discomfort, or breathlessness using a four point scale (1= no symptoms to 4= pronounced symptoms requiring immediate treatment). Subjects were also instructed to ignore the non-respiratory side effects, such as flushing and salivation from the methacholine, and to rank their overall respiratory discomfort.

To confirm reproducibility of the "rank awareness" scale, subjects were asked to rank symptoms on two different days. Elderly asthmatics averaged (both days) a 27.4% fall in their FEV1 with an awareness score of $2.0 \pm 1.7$ compared to the younger asthmatics who averaged a 21.5% fall in their FEV1 ($p < 0.001$) with a

3.1 ± .11 awareness score. Thus, for a greater fall in FEV1, the elderly asthmatics were less aware ($p < 0.001$) or failed to perceive their symptoms; this finding was attributed to temporal adaptation (Connolly, et al., 1992). No relationship existed between the awareness scores on day one and the effect of the cumulative doses of methacholine administered overall to any of the four groups. This finding suggests that cumulative doses of methacholine (day one and two) did not influence how subjects scored their symptoms.

Unfortunately, the elderly asthmatics were not comparable to the younger asthmatics since they were taking many different, inhaled and oral, medications and were twice as likely to use their beta agonist inhaler regularly (Connolly, et al., 1992). This difference in disease severity (the elderly normal and asthmatic were sicker) is significant and directly affects perception of breathlessness (Boulet, et al., 1994). Boulet, et al., (1994) also noted that the perception of bronchoconstriction tended not to change in the elderly since, as a group, they scored their symptoms as zero unrelated to the degree of airflow obstruction. Use of the awareness scale was a novel approach to assessing perception because it allowed subjects to rank three different symptoms thereby addressing the individual experience of symptom perception. More importantly, the use of three symptoms to rank awareness added weight to the argument that different symptoms may be associated with similar levels of bronchoconstriction. Unfortunately, the authors reported the awareness rank data only as global scores. What the individual and group scores were of the three different symptoms was not presented. This ranked symptom data could have provided valuable insight into symptom perception and the association between specific symptoms and word descriptors.

**Perception: Characteristics**

Another group of investigators (Boulet, et al., 1994) sought to determine the specific characteristics of asthmatics who fail to perceive bronchoconstriction. To examine the characteristics of high and low perceivers of induced bronchoconstriction, symptomatic asthmatics with a mean age of 34± 30.5 and a FEV1 ≥ 50% were studied (Boulet, Le Blanc, & Turcotte, 1994). All of the 150 Caucasian asthmatics studied had a PC20 of ≤ 16 mg/ml to histamine. A perception score (Ps20), derived from the Borg scale, was devised to identify poor perceivers during bronchoconstriction and to compare the characteristics of high and low perceivers. Subjects were asked to rank their overall sensation of respiratory discomfort defined as breathlessness immediately before and after a histamine concentration. The actual Ps20 score was determined by averaging the last two perception scores immediately before and after a subject demonstrated a 20% fall in FEV1. The Ps20 was normally distributed across the sample; subjects whose Ps20 fell 1 SD above the mean were classified as hypoperceivers (n =19) and 1 SD below the mean as hyperperceivers (n =24). For hypoperceivers the mean Ps20 was 0.55 ± .07 and the mean Borg score of 0.11 ± .06 compared to a mean Ps20 of 6.68 ± .26 and a mean Borg of 2.21 ± .34 for the hyperperceivers (Boulet, et al., 1994). Other studies have shown that changes in lung volume (Orehek, Beaupre, Badier, Nicoli, Delpeirre, 1982), speed of bronchoconstriction (Lougheed, et al., 1993), age, anxiety, and duration of asthma (Connolly, et al., 1992) can affect perception of dyspnea (Boulet, et al., 1994). In this study by Boulet, et al.,, once age, sex, baseline FEV1, PC20, and the number of emergency room visits in a year were accounted for, the group differences were negated. No other differences in the characteristics between the hypoperceivers and hyperperceivers were found. A wide intersubject variability to symptom perception was noted. Neither the age nor other demographics predicted

perception of asthma symptoms. These investigators emphasized the importance of perception scoring during bronchial challenges. This information on how subjects perceive acute asthma symptoms will identify poor perceivers or those subjects who fail to perceive worsening of their asthma symptoms. Once poor perceivers are identified, then individualized self-management strategies can be implemented.

Several factors limited the ability of these investigators to determine differences between the group characteristics. For example, 76 out of 110 subjects had a baseline Borg score of zero indicating a symptom free cohort or an insensitive Borg scale. The fact that subjects were asked to rate their symptoms immediately after completing each challenge dose was problematic since during this time interval a rapid reduction in perception occurs (Burdon, et al., 1982). Other investigators have found obtaining perception scores at two to three minutes after the challenge dose avoids the immediate temporal adaptation to the constricting agent (Cornier, Boulet, Deschesnes, Simard, & Leblanc., 1993; Burdon, et al., 1982). The use of histamine rather than methacholine, which has direct action on airway smooth muscle and an indirect vagal effect, possibly reduced the perception scores since it is believed that bronchoconstriction of large airways is more acutely sensed (McFadden, et al., 1973; Bierman, et al., 1984). Indirect evidence indicates that methacholine induces bronchoconstriction in the proximal airways thus augmenting perception of airway obstruction (Roisman, et al., 1995). Also contributing to the inability to identify characteristics of low perceivers is that the actual descriptions of the symptoms may be of more importance. Other investigators have also had limited success in correlating breathlessness with a change in the Borg scale (Lougheed, et al., 1993; Turcotte, et al., 1990). The Borg scale is very sensitive in measuring the magnitude or intensity (Adams, Chronos, & Guz, 1985) of breathlessness caused by changes in

the inspiratory pressure (hyperinflation) that affect the smaller, more peripheral airways (Marks, Yates, Sist, Ceyhan, DeCampos, Scott, & Barnes, 1996). Studies have demonstrated that asthma patients perceive airway obstruction first in the larger airways then, secondly, in the smaller more peripheral airways (Bierman, et al, 1984). Airway obstruction may be perceived differently depending on the site or size of the airway; thus what a subject perceives may not be breathlessness but a more discrete symptom (Boulet, et al., 1994; Connolly, et al., 1992). The importance of identifying those asthmatics who poorly perceive worsening of their asthma and thus fail to modify their inhaler use until their symptoms are severe or uncontrollable cannot be underestimated. The ultimate goal of asthma management is to reduce the risk of fatal or near-fatal episodes.

**Perception: Asthma Severity**

In 1992 Janson-Bjerklie and colleagues measured asthma severity and life-threatening episodes by the Asthma Severity/Risk Index tool. A total of 95 asthmatics, with a mean age of 44, and an average FEV1 of 76% of predicted, were studied. An initial baseline pulmonary function test was performed on all subjects. During their 60 days of participation, subjects were instructed to record their peak expiratory flows (PEF) twice daily, record episodes of symptoms in a diary, rate the intensity of these symptoms, identify trigger factors, and describe what actions they took to control their asthma symptoms. Subjects were interviewed monthly and asked to describe significant episodes of increased asthma symptoms that occurred during the previous 30 days. The focus was on recounting any memorable (significant) asthma attacks then rating the intensity of their symptoms (wheezing, dyspnea, and chest tightness) during the past episodes.

Out of 95 subjects 11 had been previously intubated. The mean Asthma Severity/Risk Index score was 7.7 (± 2.4) out of a possible 25. A strong correlation (r = - 0.57) was found between FEV1 percent predicted and PEF. The greater the severity of airflow obstruction the greater the risk of asthma-related death (Janson-Bjerklie, et al., 1992). There was also a positive correlation (r = 0.65) between the Asthma Severity/Risk Index and a subject's ability to perceive the severity of an episode. This was an important finding since it validated that asthma patients could correctly assess the severity of their asthma episode. Previously, the degree of airflow obstruction had been considered the major determinate of the severity of an asthma episode. Dyspnea was the major symptom associated with perceived severity (r =0.41) and danger (r - 0.25); they were highly correlated with the Asthma Severity/Risk index scores (r = 0.41). Even though these asthmatics were aware of the severity of their symptoms, they postponed going to the emergency room (ER) due to a variety of reasons.

The prior study is based on recall data which may be biased, especially the possible over estimation of the intensity of a symptom. However, the histories from asthma patients regarding prior severe asthma episodes were a reliable indicator of the severity of the episode. The Asthma Severity/Risk Index was found to be a valid measure to identify those asthma patients who are at risk for asthma-related death. These investigators also noted that the emotions of fear and panic in an asthma patient were reliable indicators of the severity of the asthma episode. It would have been valuable to ascertain what sensation or perception these asthma patients who had accurately accessed episode severity recalled.

**Perception: Near-Fatal Asthma Episodes**

Kikuchi and colleagues (1994) investigated how perception of dyspnea was different in subjects who had experienced a near-fatal (NF) attack. To identify the exact mechanisms contributing to life-threatening attacks, a total of 22 asthmatics, 11 (mean age of 39 ± 17) who had experienced NF attacks, 11 (mean age of 32 ± 12) who had never experienced such attacks, and 16 (mean age of 33 ± 9) normal subjects were studied. The three groups were comparable except that the mean vital capacity and FEV1 was slightly larger in the NF group. The NF group had percent predicted VC of 117 % ± 15 and a FEV1 of 111% ± 15; the non NF group had a VC percent predicted of 104 ± 16 and a FEV1 of 96% ±16; and the normals had a VC percent predicted of 103% ± 10 and a FEV1 of 107 % ± 10 (Kikuchi, et al., 1994)

Each subject, using a rebreather mask, had incremental resistive breathing applied at minute intervals; their perception of dyspnea was measured at the same time. Subjects rated their sensation of breathing difficulty (dyspnea) using a Borg scale that ranged from 0 to 10. The mean Borg scale for asthmatics having experienced a NF episode was 1.0 ( indicative of a decreased perception of breathlessness) compared to 2.0 for asthma patients who had never experienced a near-fatal episode (Kikuchi ,et al., 1994). Although there was no statistical difference in dyspnea between these two groups, it was surprising that asthma patients who had prior severe episodes did not accurately perceive the severity of the resistive breathing. This blunted perception of dyspnea to resistive loading was also associated with a decreased chemosensitivity, or hypoxic response; the decreased chemosensitivity was positively correlated (rs = .70) with a NF asthma attack (Kikuchi, et al., 1994). The severity of an asthma attack may be underestimated by an individual who has experienced a previous near-fatal attack; by the time they seek help it could be too late.

Boulet and colleagues (1991) compared 19 asthmatics who had a near fatal (NF) asthma attack (mean age 39 ± 3.1) with a matched (n =19) control group (mean age 39 ± 2.8) to identify risk factors and to determine if the perception of bronchoconstriction varied between the two cohorts. NF episodes had occurred within 6 months to 5 years prior to study participation. The FEV1 of the NF group was 81% ± 4.4; the FEV1 of the control group was 79 % ± 3.8. All subjects had a Mch challenge to induce bronchoconstriction (PC20 ≤ 8 mg/ml) during which they rated their dyspnea on a Borg Scale. For four weeks after a Mch challenge, subjects were asked to record their peak flows (PEF) twice daily and to rate their daily asthma symptoms on a Borg scale. The mean Borg score between these two groups was not significantly different (NF = 3.0 ± 4 and controls = 2.5 ± 2.5) and no specific personality characteristics correlated with a NF episode (Boulet, et al., 1991). Subjects who had NF episodes also had an increased diurnal variation in PEF ($p \leq 0.0002$). A Minnesota Multiphasic Personality Inventory (MMPI) was given to all subjects. The MMPI revealed an association of poor control of asthma with a less adaptive personality ($p < 0.004$) and a reduced medication compliance with the NF group. The variability in the time between NF episodes was quite wide; moreover, how this variability affected a subject's perception and medication compliance was not addressed. An evaluation of self-management skills of the individual subjects would have strengthened this study by identifying the psychological dimensions of severe asthma.

There is not agreement on the sensations that define breathlessness. The symptoms and sensations associated with perception of airflow obstruction vary between and within individuals. In order to define the precise symptoms of airflow obstruction we need to understand how asthma patients perceive the sensation and then how they describe (in their own words) this sensation.

## Mechanisms of Perception of Bronchoconstriction

The possible mechanisms that contribute to airflow obstruction are complex and multi-dimensional. Early laboratory studies that induced bronchoconstriction provided objective data on the physiological mechanisms and respiratory mechanics of airflow obstruction (Burki, Mitchell, Chaudhary, & Zechman, 1978). More recently, clinical studies that induce bronchoconstriction have sought to quantify the sensory experience of breathlessness. Numerous physiological, pathological, and nonmechanical factors are associated with bronchoconstriction, including lung hyperinflation due to increased expiratory resistance, sensory input from the stretch, irritant and J receptors, decreased hypoxic chemosensitivity, impaired carotid chemosensitivity, airway inflammation, respiratory epithelium changes, and airway hyperresponsiveness, nocturnal awakenings, and temporal adaptation (Turcotte & Boulet, 1993; Lougheed, et al., 1993; Burki, et al., 1978). Multiple mechanisms are associated with bronchoconstriction. Of interest to this study are the sensations perceived by asthma patients during induced airflow obstruction.

### Determination of Bronchoconstriction

One method used to determine bronchoconstriction are studies of airway resistance (Turcotte, Tahan, Leblanc, Boulet, 1993; Burki, et al., 1978). Burki, et al., (1978) studied normal and asthma subjects to detect the sensory differences of bronchoconstriction during resistive inspiratory loading. Burki, et al., noted a wide variability in an asthma patient's ability to detect different thresholds of inspiratory loading; they suggested that chronic adaptation to the increased airway resistance was involved (Turcotte, et al., 1993). As a result, research

studies began to focus on the perception of airflow obstruction from induced bronchoconstriction.

Turcotte, et al., (1993) studied how rapid increases in airway resistance influenced the perception of airflow obstruction in normal and asthma subjects. A total of 18 subjects, 9 controls (mean age of 28 ± 1.7) and 9 asthma subjects (mean age 27 ± 2.8), were exposed to both acute and progressive expiratory resistance to mimic slow and acute airflow obstruction. Baseline lung function for the control group (mean FEV1 of 3.67 L) and the asthma group (mean FEV1 of 3.20 L) were comparable. All of the asthma subjects had a PC20 to Mch of ≤ 8 mg/ml. Subjects breathed through an apparatus with a one-way valve during which resistance was increased or decreased from 0-24 cm of H20/l/s in five minute sequences (Turcotte, et al., 1993). As airway resistance was increased or decreased subjects were asked to rate their perception of dyspnea (definition not provided) using a Borg scale. A linear relationship between increasing resistive loads and the Borg scores ($p < 0.0001$) was noted in both groups (Turcotte, et al., 1993). Turcotte, et al., suggested that the asthma group better perceived airway resistance even though the Borg scores were not significantly higher. It is unclear how Turcotte et al reached this conclusion since the change in Borg scores from increased to decreased resistive breathing did not differ. They hypothesized that during progressive loading, acute perception of dyspnea would be lower due to temporal adaptation (1993). Instead, the findings suggest that factors other than respiratory effort contributed to dyspnea intensity, e.g., the lack of increase in lung volumes (Schwartzstein, et al., 1990). This study demonstrated that dyspnea associated with resistive breathing was not perceived as intensity (Turcotte, et al., 1993). How this finding relates to sensory perception of symptoms of airflow obstruction, however, is unclear.

O'Donnell, et al., studied how hyperinflation affects bronchoconstriction in COPD subjects (O'Donnell, & Webb, 1993; Mahler & Harver, 1992). O'Donnell, et al., examined the effects of lung hyperinflation on the perception of breathlessness. To determine the interaction between the level of inspiratory muscle activity and sensory input, 23 subjects with severe COPD (FEV1 of 36% predicted) were studied. All of the subjects participated in graded exercise testing during which their lung volumes were measured by plethysmography. During exercise testing, subjects were asked to rate their breathlessness (not defined) using a Borg scale. The investigators noted that the level of breathlessness was related to the level of exercise ventilation. During an acute asthma attack, hyperinflation occurs; yet, how this phenomenon relates to the sensory perception of bronchoconstriction in asthma was not explained. The findings support the notion that multi-dimensional factors contribute to the perception of airflow obstruction. In addition, these three studies (Turcotte, et al., 1993; Boulet, et al., 1994; O'Donnell, et al., 1993) have defined and interpreted the same phenomenon, breathlessness, differently. This lack of consensus regarding the definition of breathlessness and the sensory perception of breathlessness limits generalizability of the findings across studies.

According to Boulet and colleagues, residual airway inflammation is another mechanism contributing to changes in perception of bronchoconstriction (Boulet, Turcotte, & Brochu, 1994), They studied symptom reporting of asthma patients in remission (remission was defined as no asthma symptoms or use of asthma medications in the last two years). Patients had a diagnosis of atopy; their asthma was confirmed by a physician. A total of 30 asthma patients (mean age of 32; mean FEV1 91% predicted) in remission (termed ex-asthmatic), and 28 matched controls (mean age of 31; mean FEV1 94% predicted) recorded peak flows twice daily for two weeks prior to study entry (Boulet, et al., 1994). The Mch challenges

were performed on separate days. Dyspnea, during the challenges, was measured by the Borg scale and neither the measurement method nor the definition of dyspnea was provided (Boulet, et al., 1994).

AH, a PC20 to ≤ 8 mg/ml, occurred in 11 asthmatics in remission indicating airway reactivity even though they denied clinical symptoms. Ten ex-asthma patients had a PC20 to ≤ 12.2 mg/ml; eight ex-asthma patients had a negative Mch challenge. According to Boulet, et al., the positive Mch response of asthma patients in remission indicates that ongoing airway inflammation persists long after symptoms subside. Another explanation could be presence of airway remodeling without inflammation (Gold, 1994). A correlation between increased AH and dyspnea was present ($r_s = 0.546$). There were no significant differences in PEFR, in duration of asthma, or in duration of remission between the two groups. Nor were there any group differences in the perception of dyspnea or bronchoconstriction (not defined) at PC20 . Of those asthma patients in remission, 50% denied symptoms; however, the lack of an open-ended question regarding symptoms likely biased a person's response (Wood & Catanzaro, 1988). How this denial of symptoms correlated with a lowered perception of "bronchoconstriction" was not explained. Furthermore, Boulet, et al., (1994) did not explain how they differentiated bronchoconstriction from dyspnea nor how they measured both. The physical sensations asthma patients use to describe dyspnea (magnitude, intensity, character) and bronchoconstriction have many similarities. In actuality, for asthma patients, the two sensations may be the same with distinction between the two derived from exposure to health care language (Janson-Bjerklie, Carrieri, Hudes, 1986).

## Word Descriptors

The word(s) used to describe breathlessness or dyspnea vary according to the person experiencing the sensory change in breathing. It is not uncommon that different diseases are characterized by the same or different sensations (Simon, Schwartzstein, Weiss, Lahive, Fencl, Teghtsoonian, & Weinberger, 1989). The sensation of dyspnea is a prime example. Dyspnea is frequently defined as an uncomfortable awareness of breathing difficulty. More recent research has concluded that dyspnea is a singular sensation varying only by intensity. Conversely, Comroe (1974) considered dyspnea to be a term that subsumes many sensations. Early word descriptors for dyspnea were derived from normal volunteers; these studies used various techniques including breath holding, inspiratory loading, inspiratory resistance, carbon dioxide inhalation, and pacing of breathing to measure dyspnea (Simon, et al., 1989). From these studies, word clusters describing the sensation of breathlessness resulted. An early descriptor was "I feel that my breath stop" which was clustered under the term "suffocating". It is debatable if the sensory sensation of breathlessness that normal volunteers experience is applicable to individuals with airway obstruction. Understanding the subjective sensation of breathlessness that patients perceive and the words they use to describe this sensory experience will facilitate an appropriate and individualized response to the management of their symptoms. All of the studies to date are of Caucasian cohorts. How the language of breathlessness applies to different ethnic groups is unknown.

**Dyspnea Word Descriptors**

Most asthma patients describe their airway obstruction using expressive words for the symptom sensation (Carrieri-Kohlman & Janson-Bjerklie, 1990). Janson-Bjerklie and colleagues (1992) noted that patients were able to recognize severe episodes of asthma based on their own "language" or knowledge about their symptoms. The language of breathlessness has been the source of numerous studies in COPD but few in asthma (Burdon, Juniper, Killian, Hargreave, & Campbell, 1982; Simon, et al., 1989). The language of breathlessness that African Americans use to describe their perception of breathlessness has not been studied.

In 1986, Janson-Bjerklie, et al., studied symptom perception to obtain the verbal descriptors subjects used to describe their sensations of dyspnea (Janson-Bjerklie, Carrieri, & Hudes, 1986). A convenience sample of 68 subjects with mixed pulmonary diseases was enrolled. The pulmonary disease categories included: emphysema-bronchitis (n = 27), asthma (n = 23), restrictive disease (n = 13), and vascular disease (n = 5). The mean age of the study sample ranged from 34 ± 21; 68% of the sample were retirees. Two interviews were conducted to elicit information from the subjects about their physical and emotional sensations during dyspnea episodes. The instruments used to assess the sensory experience included the VAS, Grade of Breathlessness Scale (GBS), Asthma Symptom Checklist (ASC), Bronchitis-Emphysema Checklist (BESC), Profile of Mood States (POMS), and the Norbeck Social Support Questionnaire (NSSQ).

When the subjects were asked to describe their dyspnea, a consensus or a clustering of sensations in the categories of suffocation, tightness, and congestion resulted. The most frequent phrase used, 85% of the time, to describe dyspnea by all the subjects was "hard to move air"; in contrast, the asthma group described

"chest tightness" 79% of the time (Janson-Bjkerlie, et al., 1986). For asthma patients the term "chest tightness" may describe the sensation of airway obstruction more succinctly. Subjects across disease categories were asked to rate their "usual" and "worst" dyspnea using a VAS. Asthma subjects rated their "usual" dyspnea the lowest (25.3 mm) but also had the highest rating for "worst" dyspnea (87.83 mm). In contrast, subjects with vascular disorders had the highest "usual" dyspnea (55 mm); this group also had the next highest "worst" rating of dyspnea (82.6 mm). What "words" the asthma subjects associated with the "usual" and "worst" dyspnea experiences unfortunately were not ascertained.

A limitation of recall data is that when a subject is asked to recall it is not uncommon for the severity of the episode to be exaggerated (Woods & Catazanaro, 1988). Recently, Mahler, et al., (1996) validated the reliability of recall data for descriptors of breathlessness (Mahler, Harver, Lentine, Scott, Beck, & Schwartzstein, 1996). The Janson-Bjerklie, et al., study exemplified the importance of the language of breathlessness and how word descriptors reflect the individual sensory perception of breathlessness.

In a similar study, Mahler, et al., (1996) examined descriptors of breathlessness across seven different pulmonary and cardiac disorders. Mahler, et al., sought to replicate the findings of Simon and colleagues (1990) for the purpose of documenting that individuals with different diseases experience distinct qualities of breathlessness. A total of 218 subjects with complaints of breathing difficulty were selected from seven disease categories—COPD, asthma, cystic fibrosis, congestive heart failure (CHF), interstitial disease (ILD), deconditioning, and neuromuscular disease (NM). The average age of the groups was comparable (mean age 59 ± 16 ). The level of lung function was variable; the lowest mean FEV1 was 56% in the ILD group while the highest mean FEV1 was 103% in the NM group. Individuals with COPD comprised the largest group (n =

85) and the asthma group was the second largest (n = 56). After baseline PFT, subjects were given, at random, one of four different forms of the same 15 statement questionnaire. They were instructed to respond to each question by circling either yes or no. The average number of descriptors selected across all disease groups was 10; from these 10 descriptors, subjects were instructed to select the "three best" that characterized their breathlessness (Mahler, et al., 1996). This resulted in a 10-cluster word grouping (e.g., work/effort, exhalation, and tight). Some examples of the word descriptors in a cluster were: "my breathing requires effort", "my breathing does not go out all the way", and "my chest feels tight".

When the data was analyzed, subjects were grouped by diagnosis to a specific cluster(s) that was unique to that diagnosis; this cluster included the three top descriptors assigned to that diagnosis (Mahler, et al., 1996). The alignment of the diagnosis with a cluster represented a subject's perception of breathlessness. To illustrate this point: asthma subjects selected word descriptors in the cluster categories of "work/effort" and "tight". In comparison, COPD subjects selected word descriptors only in the cluster of "work/effort". The cluster of "work/effort" has been described as analogous to the "lifting of a weight" (Demediuk, Manning, Lilly, Fencl, Weinberger, Weiss, & Schwartzstein, 1992). The sensation of effort implies intensity with sensory mediation to the respiratory muscles arising from the cortex. Frequently, effort is associated with inspiratory loading and, as a result, a subject's sensory perception is enhanced during inspiration. Thus, individuals who sense breathlessness more during inspiration would select word descriptors associated with this sensory experience.

Demediuk, et al., (1992) made an important distinction by suggesting that the sensations of effort and breathlessness are not the same nor are they mediated by

the same mechanisms. The word descriptors asthma subjects selected were notable since two distinct clusters, "exhalation" and "tight", were identified only with asthma. These descriptors may represent an association between the qualitative response (Simon, et al., 1990) and the underlying disease that produces the symptom. At the same time, these two descriptors, "exhalation" and "tight", suggest a mechanical description of breathlessness.

The symptom(s) that each diagnostic group associated with their breathing discomfort was also ascertained. For example, the primary symptom descriptor asthma subjects identified with was "wheezing"; COPD subjects identified with the symptom descriptor of "distress"; CHF subjects identified with the symptom descriptor of "suffocation"; and the symptom descriptor of "shallow" was identified by subjects with NM disease. The exact relationship between word descriptors and the varied mechanisms causing airflow obstruction is not known (Mahler, et al., 1996). One possible physiological explanation regarding the descriptor "my chest feels tight" is that the descriptor reflects bronchoconstriction and airway tone (airway obstruction) (Elliott, Adams, Cockcroft, Macrae, Murphy, & Guz, 1991 ). For subjects with ILD the word descriptors "rapid" and "inhalation" may reflect a physiological process defined by mechanical descriptors; these descriptors, in turn, show a pattern of qualitative responses (Elliott, et al., 1991).

These findings by Mahler, et al., are thought provoking, but limitations to generalizability are evident. The age, the level of lung function, and the Caucasian ethnicity of this cohort caution application of these clusters of word descriptors to other ethnic groups. The next step is to validate if these word descriptors apply to other ethnic groups.

**Qualitative Differences**

Current physiological evidence indicates that there is no unique peripheral site that mediates dyspnea but rather that there are multiple sites (Simon, et al., 1990). Some mediating sites for a sense of respiratory effort proposed by Simon, et al., (1990) include sensory receptors in the airways, diaphragm, and intercostals; they suggest that all these sensory receptors may interact or be involved in the perception of breathlessness. In normal volunteers, Simon, et al., (1989) noted an association between different sensations and the stimuli that produced breathlessness. In 1990, Simon, et al., sought to replicate their earlier study (1989) but in individuals with cardiopulmonary disease who experienced shortness of breath. From their 1989 study of normal volunteers in whom breathlessness was induced, a list of 19 descriptors were compiled. Their 1990 study was designed to validate whether or not qualitative differences existed between the sensation of breathlessness noted in normal volunteers and breathlessness experienced by patients with cardiopulmonary disorders.

A total of 53 subjects with shortness of breath were selected from seven disease categories (asthma, COPD, CHF, NM. pulmonary vascular disease, ILD, and first to second trimester pregnancy) (Simon, et al., 1990). The age of the study groups was quite different; the asthma group was youngest (mean age 40 ± 13) whereas the COPD was the oldest (mean age of 65 ± 10). Baseline lung function indicated the sample had moderate to severe disease with wide variability; the COPD group was the lowest (FEV1 of 39% predicted) and the ILD was the highest (FEV1 of 60% predicted). Each subject received one of the five different versions of the questionnaire consisting of the 19 descriptors derived from the earlier study. As an investigator read the 19 descriptors each subject was asked to select the descriptor that applied to their "uncomfortable awareness of

breathing". After a subject had selected from the initial grouping of descriptors each subject was asked to choose the best three descriptors. Based on these descriptors subjects were instructed to grade the intensity of their breathlessness by selecting a numerical value from the Borg Scale. Using cluster analysis the descriptors were classified into groupings characterized by a subject's sensory experience of dyspnea. A total of 14 cluster groupings resulted with eight clusters comprised of a single descriptor (e.g., the cluster "exhalation" was described as "my breath does not go out all the way") (Simon, et al., 1990). The other six cluster groups were comprised of two to three different word descriptors. The clustering of more than one word descriptor under a cluster reflected a shared sensory experience regardless of the disease process (Simon, et al., 1990).

One example of single descriptors associated with a disease category and not shared with other categories was asthma. The descriptors of "exhalation", "concentration", and "tight" were only aligned with asthma thereby suggesting a different sensory experience of breathlessness mediated by a different physiological mechanism (Simon, et al., 1990). This association was also noted in the earlier study by Janson-Bjerklie and colleagues (1986). The only descriptor shared between asthma and COPD was "heavy" which was surprising since both conditions are characterized by airway obstruction (Demediuk, et al., 1992). Simon and colleagues ( 1990) proposed that the sensation of breathlessness is qualitatively different with a different mechanism mediating breathlessness in each condition. The idea of qualitative differences in breathlessness runs counter to prior belief which proposed that breathlessness, regardless of disease etiology, was the same phenomena and mediated with similar sensory or physiological mechanisms (Elliott, et al., 1990; Demediuk, et al., 1992). Interestingly, when all the subjects were asked to rate the intensity of their breathlessness, the mean intensity Borg score for all seven conditions was between 5 (moderate) to 8

(moderately severe). The fact that the intensity of breathlessness was rated similarly across groups contrasts with the quality of the sensation of breathlessness that was different across groups. This further suggests that the quality of the sensation of breathlessness is a distinguishing feature of asthma.

Several limitations of this study are evident. The groups were different in age, level of lung function, and disease severity. Age has been demonstrated to be a significant confounder (Boulet, et al., 1994). Over time, with aging, temporal adaptation to a particular sensation directly changes, by frequently lowering the sensory perception of a symptom. With wide variability in lung function and disease severity, perception of a symptom can be either acutely sensed or conversely sensed with a lowered perception (Boulet, et al., 1994). Gift (1991) noted that acute dyspnea experienced by asthma patients was different from chronic dyspnea during acute phases. The impact of cultural, social, educational, and ethnic backgrounds on the language of breathlessness was acknowledged but not addressed. It is not known if African Americans with asthma would select the same word descriptor for breathlessness as Caucasians due to the subtleties of language.

Assuming that word descriptors (Janson-Bjerklie, et al., 1986; Simon, et al., 1990) are accurate in representing the underlying disease process, then a greater understanding of the interrelationship of symptoms with mechanisms and their contribution to breathlessness may result. The identification of the types of respiratory sensations experienced with a specific disease can assist in a differential diagnosis by adding specificity to diagnostic testing. This is contrary to current practice since a physician normally uses clinical reasoning and diagnostic testing to search for a diagnosis. Hearing a patient's "voice" offers an interactive approach to management of symptoms. There are several drawbacks to the static word descriptor forms proposed by these researchers. The cluster

groupings and word descriptors represent terms and words from Caucasians. The language of word descriptors by ethnic groups, in particular African Americans, may be radically different. How subjects with asthma describe their symptoms influences both pharmacological treatment and assessment of the severity of an asthma episode by the health care provider. Clarifying the language of breathlessness across ethnic groups is essential to prevent life-threatening asthma episodes.

## Ethnicity and the Perception of Breathlessness

What words African Americans use to describe the sensation of airflow obstruction has not been studied nor is it known what sensation(s) prompts them to use their beta agonist inhaler. If African Americans have a low perception of symptoms or of airflow obstruction, then they may be unable to perceive worsening of their symptoms; a subsequent delaying of treatment could result in a life-threatening attack (Kikuchi, et al., 1994). Prevalence studies have attempted to define the relationship between ethnicity and asthma in children and adolescents (Crain, et al., 1994; Gold, Wupij, Wang, Speizer, Pugh, Ware, Ferris, & Dockery, 1994).

### Perception of Symptoms and Culture

Several studies have examined the presence of asthma and wheezing among ethnic groups. In a large survey by Crain, Weiss, Bijur, Hersh, Westbrook, & Stein (1994) of 1285 inner-city children (662 families), a questionnaire was administered in either English or Spanish to the "self-designated" head of the household. Eight questions were asked about the incidence of asthma, the

presence of wheezing or "whistling", the presence of "whistling" at night, the effects of breathing on speech, and the number of visits that were made to a doctor in the last year. The sample population included whites (n = 173), African Americans (n = 361), Hispanics (n = 619), and other ethnic groups (n = 48). In comparing the prevalence (per 100) of wheezing, 6.4% of all the white children reported wheezing compared to 5.8% of all the African American children. When the categories of asthma and wheeze were combined there was not a difference in prevalence rates.

The inability to demonstrate any group differences may be related to use of the standardized questionnaire. If Crain, et al., had used open ended questions to elicit information the responses from the participants could have been dramatically different. Defining asthma in several different ways, including word descriptors, would have been beneficial. Illustrating this point is the word descriptors used by Hispanics and African Americans describing asthma as "wheezy illness". Additional descriptors used were "whistling", "noisy breathing", and the inability to speak complete sentences due to wheezing. When 13 - 14 year olds from different ethnic groups were asked about their asthma/wheezing, some of the teenagers did not understand the meaning of these two words; when the word asthma was changed to "chest illness" more positive responses resulted (Robson, Woodman, Burgess, Crane, Pearce, Shaw, D'Souza, Crossland, & Beasley, 1993). All of these descriptive terms suggest the presence of asthma and wheezing even without a physician confirmed diagnosis of asthma. These few descriptors are an indicator that the language of breathlessness is different.

**Effects of Gender and Race on Perception**

To determine the significance of gender and race on the incidence of asthma/wheeze in children and adolescents, lung function screening was conducted (Gold, et al., 1994; Robson, et al., 1993). The trend across these studies reflects an increase in the incidence and prevalence of asthma among African American children, in particular, young males (Gold, et al., 1994; Crain, et al., 1994). Adolescent African American boys with a history of asthma/wheeze had a lower absolute FEV1 (5.7%) compared to Caucasian boys (16.9%) with comparable histories (Gold, et al., 1994). The exact pulmonary function data were not presented nor was it noted if lung function was corrected for ethnicity. If lung function values were not corrected for ethnicity this fact alone could be responsible for the differences in lung function. These investigators (Gold, et al., 1994) noted a trend (data was not presented) of less medication used by adolescent black boys than black girls. The inability to determine exact race and gender differences is in part due to the type of data collection methods that have been used in past studies. Use of more ethnically sensitive measurement tools is essential.

All of the findings reviewed here are primarily from Caucasian cohorts except for the few prevalence studies. Whether or not this data applies to adult African Americans with asthma has yet to be determined. Determining what symptoms influence the perception of acute airflow obstruction among African American and Caucasian asthmatics is needed; this would facilitate accurate assessment and treatment to reduce the incidence of potentially fatal episodes (Lougheed, et al., 1993; Quirk & Jones, 1990). Culture, socio-economic status, health seeking behavior, and language are only a few of the determinants that affect, both

directly and indirectly, the perception of airflow obstruction and the language of breathlessness across cultures.

## Physiological Differences: African Americans and Caucasians

The health impact of asthma for African Americans is great. Not only is asthma more prevalent but it is more severe for African Americans (Haire-Joshu, et al., 1993; Targonski, et al., 1993). Sherman, et al., (1993) sought to determine if differences in AH could be a factor contributing to this increase in prevalence. In discussing AH, it is important to note that AH can exist without bronchoconstriction (Brand, et al., 1992). Poverty and social factors (e.g., lack of access to care, dietary influences, environmental exposures, and social attitudes towards asthma) adversely affect health outcomes for African Americans (Targonski, et al., 1994). Other factors associated with increased prevalence are genetic differences. It has been documented that African Americans have smaller lung volumes, have higher IgE levels, and lower peripheral leukocyte counts than Caucasians (Koenig, et al., 1992; Johnson, 1993).

### Airway Responsiveness and Ethnicity

To investigate the relationship of AH and pregnancy in black and white women, questionnaires were given three days post- partum (Sherman, et al., 1993). In this case control study, 62 black and 238 white women participated. Data regarding respiratory symptoms prior to pregnancy, e.g., cough, wheeze, phlegm, and shortness of breath, were collected. Serum IgE levels were drawn prior to delivery; six to ten weeks after delivery, baseline lung function testing and Mch challenges were performed. The mean FEV1 for black women was 2.67

L in contrast to 3.09 L for white women. Only 66 subjects out of 300 had a positive PC20 to Mch (black women n = 21; white women n = 45) to ≤ 8 mg/ml. The black female subjects with AH also had higher serum IgE levels, a lower FEV1 and FVC, than the white female subjects (Sherman, et al., 1993).

When all the covariates were accounted for only the serum IgE was predictive of AH. The prevalence of AH in black women was 14.5% compared to 6.3 % for white women; it was not stated if the PFT values had accounted for the 13% reduction in lung volumes for African Americans. The disparity in the sample size between the two ethnic groups was a limitation. Whether or not hormonal levels (subjects were only 6-10 weeks post delivery) skewed Mch challenge data was not explained. Although this study has weaknesses, it was the first comparative study of AH and the influence of ethnicity.

**Beta Receptors and Ethnicity**

Altered responsiveness of the beta receptors and the effects of ethnicity have been examined in regards to cardiovascular medications. The efficacy of anti-hypertensive medications in African American and Caucasians has been assessed (Sherwood & Hinderliter, 1993; Johnson, Burlew, & Stiles, 1995; Mills, Dimsdale, Ziegler, & Nelsen, 1995). It is hypothesized that both α– and β–adrenergic receptors, independently or synergistically, can contribute to the increase in vascular resistance found in hypertension. By the stimulation of endogenous catecholamines, either an increase in the vascular α or a decrease in the β adrenergic receptors may account for the elevated vascular resistance (Sherwood & Hinderliter, 1993).

To study vascular responsiveness 26 healthy male subjects, 13 African Americans and 13 Caucasians, matched by age, weight and blood pressure, were

enrolled. To participate, a subject's screening blood pressure had to range from 140-160 for systolic and diastolic of 90 to 100 mm Hg. The standard protocol for blood pressure (BP) assessment was implemented. One week after baseline values were obtained receptor responsiveness testing was performed. Subjects were rested initially, then BP readings were obtained. While a subject was supine the standardized isoproterenol receptor responsiveness test was administered; doubling bolus doses of isoproterenol were given until a subject's heart rate increased by 25 beats per minute (Sherwood & Hinderliter, 1993). The physiological vascular responses that were monitored included baroreflex sensitivity and minimal forearm vascular resistance.

These investigators found that black hypertensives had a relatively heightened β-receptor responsiveness index, $F = 9.56$ ($P < .005$), but were less receptive to β blocker therapy (Sherwood & Hinderliter, 1993). Black subjects also had a heightened α-adrenergic receptors responsiveness, $PD_{25}$, of $F = 5.18$ ($P < .05$). These investigators proposed that the lower levels of sympathetic activity in blacks, verified by lowered plasma norepinehrine, may explain the heightened β receptor responsiveness.

Johnson, et al., (1995) replicated this study but used methods to block the effects of the parasympathetic nervous system (PNS). Eight black males and eight white male subjects, who were matched for specific variables, were enrolled. Standardized BP assessment was obtained, and atropine was administered to block the PNS followed by the β receptor sensitivity study. They noted similar findings and, in particular, that black male hypertensives needed twice the dose of isoproterenol to achieve chronotropic responses than white males. Other investigators (Johnson, 1993; Mills, et al., 1995) have validated these findings; they proposed that the down regulation of the β receptors resulted from adaptation to excessive stimulation by the Sympathetic Nervous System (SNS). A

major limitation in both of these studies was that only males were enrolled thus limiting generalizability. Both groups of investigators (Johnson, 1993; Mills, et al., 1995) did not state if dietary sodium intake was restricted in the study groups since sodium will directly affect vascular resistance. Nor did the investigators provide information regarding a subject's family history of hypertension.

**Beta Receptor Responsiveness: Vascular Blunting**

In a similar study, a blunting or attenuation, of forearm vasodilatation mediated by the beta 2-adrenergic receptors was also noted in young normotensive black males (Lang, Stein, Brown, Deegan, Nelson, Huai, Wood, and Wood, 1995). Nine normotensive black males (mean age 31 ± 8.0) and thirteen normotensive while males, (mean age 32 ± 5.6) were enrolled. Family histories of hypertension and diabetes were equally distributed between the two groups. A standardized protocol of isoproterenol infusion was implemented; SNS activity in the forearm was measured by isotope-dilution techniques (Lang, et al., 1995). Because dietary sodium levels influence both SNS activity and vascular tone, dietary sodium intake was restricted in both groups for five days before study participation. Lang, et al., (1995) noted in hypertensive black males a decreased β–adrenoreceptor sensitivity (decreased from 41.5 ± 8.6 to 14.6 ± 6.7) compared to white males; they did not differentiate which fibers were of primary importance (β one or two). Watkins and colleagues (1995) in a similar study confirmed that the beta 2 adrenoreceptor fibers were responsible for the attenuated vasodilatation in African American males. Lang, et al., (1995) also found that the vasodilatation response to isoproterenol was markedly reduced in black males who exhibited only a 3.5 increase in blood flow compared to a 9 fold increase in blood flow in white males. These findings of racial differences in

beta2 adrenoreceptors raises concerns about the effectiveness of long term regular therapy with beta2 agonists in African American asthma patients (Koenig, et al., 1992; Cheung, et al., 1992).

A major limitation of these three studies is the inability to generalize these outcomes beyond males. There is no clinical evidence that women respond exactly like men, even though, from a physiological standpoint it is a reasonable assumption. In vitro studies (Johnson, 1993) have resulted in different outcomes (no difference in beta-receptor density was observed) due to the fact that neural and hormonal effects on ß- receptors were controlled for. Physiological studies that focus on ethnic differences are essential to understanding why the prevalence of specific diseases, asthma and hypertension in particular, is higher in African Americans.

Only one study has compared AH in African Americans and Caucasians. This fact illustrates the paucity of clinical studies that have focused on ethnicity and asthma. Sherman, et al., (1993) did demonstrate ethnic differences in AH in post-partum women but how this compares to African Americans with asthma needs to be substantiated by clinical studies. The studies on hypertension and African American men indicate that differences in the beta adrenergic receptors do exist. The possibility that an altered responsiveness of beta receptors also occurs from use of inhaled beta agonists in African Americans who have asthma has not been fully documented. Determining if there are differences in lung function and sensory perception is essential due to the increased prevalence of asthma within the African American community. Identification of ethnic differences will enable us to improve clinical outcomes for African Americans with asthma and facilitate long-term asthma management plans specific to a person's ethnicity.

## Perception of Bronchodilation

Understanding the physiopathology of the perception of airway obstruction is essential for successful clinical management. However, few studies have addressed the perception of bronchodilation in the laboratory setting (Gottfried, Altose, Kelsen, & Cherniak, 1981). Assessing the reversibility of airflow obstruction by comparing indices of forced expiration and plethysmographic airway resistance (Raw) in subjects with chronic obstructive lung disease (COPD) and asthma provided valuable data but had limited clinical application (Van Noord, Smeets, Clement, Van De Woestijne, & Demedts, 1994). The way(s) that subjects respond to a bronchodilator in the laboratory and in their own home may be quite different. Assessment of airway reversibility in the laboratory by pulmonary function testing (PFT) and the use of PEF at home are widely accepted. It is only recently that the perception of bronchodilation has been studied. If asthma subjects cannot perceive airway obstruction, they may also not perceive when their airways are dilated. It is important to determine if asthma subjects can perceive bronchodilation accurately after an acute asthma episode. The perception of bronchodilation may also be highly variable within ethnic groups.

Noseda and colleagues (1994), using bronchodilator challenges, studied subjects with both asthma and COPD to characterize their subjective perception of bronchodilation. A total of 16 asthma subjects (mean age of 60) and 20 COPD subjects (mean age of 62) were enrolled. Subjects who demonstrated a 15% reversibility to a bronchodilator and exhibited symptoms of wheezing and episodic breathlessness were classified as asthma: those subjects who did not meet the prior criteria were classified as having COPD. All of the subjects had an

FEV1 ≤ 60% of predicted; the asthma group had a mean FEV1 of 42% predicted whereas the COPD group had a mean FEV1 of 38% predicted.

After baseline PFT, all subjects inhaled, by dosimeter, increasing doses of terbutaline at set intervals until a maximal dose of 800 μg was achieved. Subjects were blinded to the fact that they were receiving a bronchodilator (Noseda, et al., 1994). Before and two minutes after each dose of terbutaline, subjects were asked to rate their change in amount of shortness of breath using a bipolar VAS scale. After each dose of terbutaline (time was not specified), plethysmography measurements were obtained of specific inspiratory (sRin) and expiratory resistance (sRex) and FEV1. The level of perception was scored on the VAS scale. Subjects marked their change in the amount of shortness of breath on the VAS immediately after spirometry but before their first dose of terbutaline. A 25% cut-off in VAS line length after the fifth dose of terbutaline differentiated high perception from low perception (Noseda, et al., 1992). A modest correlation ($r = 0.513$) existed between VAS/Δ FEV1 and in VAS/Δ sRin ($r = 0.353$) for asthmatic subjects but was not significant ($p<0.05$). Only two of the asthmatic subjects met the criteria as low perceivers compared to seven of the COPD subjects. The majority, 14, of the asthmatic subjects were high perceivers indicating they were able to perceive bronchodilation. The one lung function parameter that correlated best with VAS, although not significant, was sRin. Noseda, et al., (1994) proposed that the decrease in inspiratory resistance was a better indicator of acute bronchodilation than an increase in expiratory volumes. Using shortness of breath (dyspnea) to measure the perception of airway obstruction may have been problematic since dyspnea is predominately an inspiratory sensation. As anticipated, asthma subjects had the greatest percent improvement in airflow after the bronchodilator. It is unclear if maximal bronchodilation (no further

improvement) was achieved since the criteria for maximal bronchodilation was not explained.

There are several important limitations to this study. The baseline lung function of both groups reflected moderate to severe disease, and disease severity is directly associated with lowered perception (Lougheed, et al., 1993). The COPD subjects were taking multiple medications (including oral prednisone); this contributed further to the group differences. The impact of age (the average age was from 60-62) was not discussed. Since repeated exposure to bronchoconstriction leads to temporal adaptation, it would be interesting to determine if the temporal adaptation occurs with repeated bronchodilation. The ability of these asthma subjects to detect the sensation of bronchodilation by the change in dyspnea was an interesting finding. It would have been valuable to determine if these same subjects perceived bronchoconstriction accurately.

It is important to determine if this same sensory bronchodilator response applies to African Americans with asthma. There are no studies specific to how African American asthma patients respond to acute bronchodilation. However, several studies have focused on African Americans and the physiological differences noted in the beta receptors and in airway responsiveness (Watkins, Dimsdale, & Zieger, 1995; Sherman, Tollerud, Heffner, & Speizer, 1993). Young, mild asthmatics (FEV1 $\geq$ 80%) from different ethnic groups were studied to determine the effects of continuous compared to as needed use of inhaled $\beta$–agonists on airway obstruction (Taylor, et al., 1992). Unpublished data has indicated that the young African Americans who used inhaled $\beta$ agonist routinely demonstrated a reduction in their FEV1; this suggests down regulation of the beta receptors (Drazen, et al., 1996). The implication of a difference based on ethnicity may also be pertinent to why perception of airflow obstruction may be different for African Americans with asthma.

## Awareness of the Language Descriptors

The perception of breathlessness and the ability of patients to sense accurately their airflow obstruction necessitates a rethinking of physiological processes with sensory responses. An unpleasant or uncomfortable awareness of breathing is associated with dyspnea (Schwartzstein, et al., 1990). In contrast, breathlessness is defined as "with breath held as in suspense or deprived of breath" (Random House Dictionary, 1968). The implications of these distinct definitions for two symptoms that many people consider synonymous suggests a different sensory experience. The language of breathlessness and/or dyspnea and the mechanisms mediating these sensations remain a source of debate. A qualitative difference between the terms dyspnea and breathlessness exists especially from the perspective of an individual's perception since the word "breath-less-ness" is easier to understand.

### Symptom Perception

The role of psychological factors in the presence of dyspnea has been widely researched (Janson-Bjerklie, et al., 1992; Carrieri-Kohlman, et al., 1993). Altered psychological responses, e.g. depression, panic-fear, anxiety, or loss of control, result from constant sensory stimulus driven by the physiological mechanisms of airway obstruction (Burdon, et al., 1982; Janson-Bjerklie, et al., 1993). Another viewpoint is expressed by Steele and Shaver (1992) who refer to the dyspnea experience as incorporating a cognitive interpretation of the event as threatening which they have, in turn, labeled as a noiceptive phenomenon. Other investigators (Boulet, et al., 1994) suggest that, like pain, sensory and affective dimensions are blended to reflect the intensity and magnitude of dyspnea

perception. The degree to which this level of awareness exists for the perception of breathlessness is questionable. The similarities of chronic pain to breathlessness are understandable at a very rudimentary level. The constancy of chronic pain (Dodd, 1987) is in some ways analogous to chronic dyspnea. Both of these sensations are always "felt" or perceived by the individual, and over time a tolerance or temporal adaptation to the sensation occurs (Burdon, et al., 1982). A prime example is the person with chronic pain who develops a tolerance for the pain resulting in a reduction of pain medication. Do such people become more tolerant of the pain or does their perception of the pain change? Unlike chronic pain, the sensation of breathlessness associated with asthma is variable; it comes and goes, thereby directly affecting the perception of this symptom. The unpredictability of breathlessness hinders exact determinants of the physiological mechanisms; word descriptors can provide insight into whether or not the sensation of breathlessness differs. Mahler, et al., (1996) clearly demonstrated through the use of word descriptors that qualitative distinctions in breathlessness occur across disease groups.

The way in which the perception of the symptom or the language of breathlessness is interpreted by an individual with asthma influences health seeking behavior. It is known that ethnicity affects symptom interpretation and symptom reporting (Di Pede, Viegi, Quakenboss, Boyer-Pfersdor, & Lebowitz, 1991). Di Pede and colleagues surveyed 981 people by self-administered questionnaires ["Anglos "(n = 789) and Mexican-Americans (n = 192)] to assess the prevalence of respiratory symptoms. The questionnaire focused primarily on the symptoms of chronic bronchitis (cough, phlegm, sputum, wheeze, and dyspnea); what "words" were used on the questionnaire to ask these questions were not identified. Even with frequent exposure to dust and chemicals (farm work) the symptom complaints of the Mexican American group surveyed were

not increased in comparison to the "Anglo" group. It is highly possible that both the language descriptors and interpretation of the terms by the Mexican American group resulted in a lower response rate. If a Mexican American respondent did not understand the term "wheeze" it is likely he or she would respond negatively to this question. Crain, et al., (1994) noted that children with asthma and their parents used unusual descriptors to describe wheezing, e.g., "whistle, squeaking, noisy breathing". Thus if a parent was not asked if their child made a "whistle" sound, an important symptom to guide clinical management would not have been ascertained. This fact illustrates the importance of why language and perception of symptoms must be ethnically sensitive in order to elicit accurate symptom information.

**Symptom Evaluation**

Symptom perception also involves identification and interpretation of the symptom based on prior experiences and beliefs (CSM, 1994; Harver & Mahler, 1990). Specific factors are known to affect the perception of symptoms, e.g., age, gender, socioeconomic status, social learning, beliefs, psychological orientation, and sensitivity to change. The perception of breathlessness is complex and multidimensional; but it can be a singular unchanging sensation for some individuals with asthma. The stimuli triggering breathlessness are highly variable and can be mediated by different physiological mechanisms. An individual, however, not only perceives different sensations but applies different word descriptors to the sensations. What one patient describes as breathlessness another may not; this represents the individual nature of symptom perception. The evaluative phase of symptom perception occurs when individuals determine or influence their symptom management. For individuals with asthma,

evaluating their level of breathlessness is crucial; the inability to accurately access or perceive their airflow obstruction can be life-threatening.

It is unclear to what degree prior experience affects how an individual interprets, evaluates, and mitigates symptom perception. For example, one mechanism that explains the poor perception of asthma symptoms is that during slow progression of airflow obstruction temporal adaptation occurs (Turcotte & Boulet, 1993). This was verified by Turcotte and Boulet (1993) who used the Borg scale to assess perception of breathlessness associated with bronchoconstriction from antigen challenges during early and late asthmatic responses. They (Turcotte & Boulet, 1993) found that the rate of fall in the FEV1 only correlated directly with an increased Borg scale rating during an early asthma response; this supported their premise that with a faster fall in FEV1 a temporal adaptation does not occur ($p < 0.001$). During a late asthma response, the slow progressive decrease in expiratory flows allows an asthmatic to tolerate these reductions over time. This is defined as temporal adaptation (Turcotte & Boulet, 1993). Investigators have shown that another explanation for this response may be the type of airways affected since the large and small airways constrict in an early response whereas only the small airways constrict in a late response (Bierman, Spiro, Petherman, 1984). The fact that large airway bronchoconstriction is more acutely sensed than the peripheral airways is important since these airways are constricted early on in an asthmatic episode (Roisman, et al., 1995; Boulet, et al., 1991).

Constriction of the large and small airways may exemplify the sensory distinction that Gift suggests between acute (large airways) and chronic (small airways) dyspnea (1991). Whether a patient with asthma can perceive sensory distinctions based on the type of airway constricted has not been established. Word descriptors indicate that a subject may "feel" the sensation of

breathlessness externally in the chest wall; breathlessness may be sensed diffusing over the chest, over the upper one-third of the chest (near clavicles), and/or over the base of the lung (or as subjects state "deep in my chest"). The scenario between perception, evaluation, and response to breathlessness may be as follows. With accurate perception, a person with asthma is able to perceive acute (large airway) bronchoconstriction based on intuitive knowledge from past experiences. The sensory load is possibly felt more across the upper one-third of the chest wall signaling the need for the person to use the beta agonist inhaler. Temporal adaptation comes into play here because of past, perceptual experiences from this specific sensory load; the association between symptom relief by use of the inhaler has resulted. Another conjecture is that small airway constriction and chronic dyspnea, accordingly to Gift (1991), are really quite different both perceptually and sensorially. Even though this concept has not been verified, the language of breathlessness indicates that sensorial differences in airflow obstruction exist. Word descriptors, e.g., "the air does not go all the way in", suggest that there is limited air movement across the entire chest wall. Subjects explain this sensation as "the air does not go into all the areas of the lung" (Hardie, 1997). Anecdotal information from subjects supports this contention; they perceive this "deep" entire chest wall sensation as frightening and a signal that they need to see their physician or go to the ER (Hardie, 1997). Each experience in the perception of breathlessness may actually be building blocks for their own self-management plan.

The problem arises when asthma patients are unable to read the signal of perception accurately and fail to intervene by taking their inhaled beta agonist medication. Several investigators have clearly identified the qualitative differences in perception of breathlessness elucidated by word descriptors (Janson-Bjerklie, et al., 1986; Mahler, et al., 1996). Verification of the existence of

different types of respiratory sensations, each with distinct characteristics and qualities, will allow for a broader view of symptom perception across ethnic groups. The perception of breathlessness is in the gestational stage. During this discovery stage of trial and error, the triad of perception, evaluation, and response is primarily subject based. To discover what works (relieves symptoms) and what doesn't requires designing a descriptor questionnaire that incorporates and evaluates mechanisms with interventions.

## Limitations of Current Knowledge

What is not understood or known is if the perception of airflow obstruction and the language of breathlessness varies by ethnicity, in particular, for African Americans with asthma. The questions regarding perception and ethnicity are numerous. Underlying sensory mechanisms and mediating pathways for perception are not understood. Variations in sensory perception varies with the intensity of stimulation but how this relationship is influenced by subject characteristics is not known. Our knowledge of symptom perception and word descriptors of breathlessness for African Americans with asthma is extremely limited. The present word descriptors for breathlessness are derived from samples of predominately Caucasian subjects do not acknowledge the impact of culture and language on symptom perception. Asthma patients are frequently asked by health professionals to describe their sensations of breathlessness using the symptom terms of shortness of breath, chest tightness, and wheezing; these terms are culturally limiting. The language of breathlessness has not been explored in African Americans with asthma. Insights into the perception of symptoms by word descriptors of airflow obstruction can facilitate self management approaches that are responsive (sensitive)to a persons ethnicity.

## Definition of Major Terms

To provide clarity and to increase understanding regarding the perception of bronchoconstriction the following terms are defined. This is meant in no way to be an inclusive dictionary of terms but rather a list of terms that may be interpreted differently based on a reader's expertise.

### Definitions

1. Airway Hyperresponsiveness (AH): A greater than normal reactivity in the airway caliber in response to various stimuli.
2. Forced Expiratory Volume in 1 second (FEV1): Volume of air expired in one second during performance of the forced vital capacity maneuver.
3. Forced Vital Capacity (FVC): The maximal volume of air forcibly expired from maximal inspiratory position.
4. Forced Expiratory Volume /Forced Vital Capacity (FEV/FVC): Ratio forced expiratory volume to forced vital capacity expressed as a percentage.
5. FEV1 %: Percent predicted of the FEV1.
6. Peak Expiratory Flow (PEF): Highest value for expiratory flow.
7. PC20: Provocative concentration of a bronchoconstricting agent that causes a 20 % fall in the baseline FEV1.
8. Mch: Methacholine
9. $\Delta$ : delta/change

# Chapter Three: Methodology

## Study Design

A descriptive cross-sectional design was used to compare the two cohorts, African-American and Caucasian patients with asthma, on the perception and symptom description of induced bronchoconstriction and induced bronchodilation. The overall objective of this study was to explore the effect of ethnicity on the perception and description of bronchoconstriction and the perception of maximal bronchodilation in African American and Caucasian adults with asthma. The specific aims of the study were to compare and contrast

a) the perception of breathlessness by the two ethnic groups at the provocative dose of Mch that causes a 30% fall from baseline in the FEV1;
b) the word descriptions for the sensations the two ethnic groups experience at the provocative dose of Mch;
c) the perception of bronchodilation as measured by the change in breathlessness by these two ethnic groups;
d) the word descriptions for the sensations the two ethnic groups experience at maximal bronchodilation; and
e) the response to the bronchodilator use question at PC15, PC20, and PC30 of these two ethnic groups. A PC30 was selected to ensure that bronchoconstriction was experienced.

Secondary aims were to determine differences between African American and Caucasians in

a) the provocative dose of methacholine (PC30), measured by the change in FEV1 from baseline (diluent);
b) the breathlessness score, measured by the Borg and VAS, at PC30;
c) the maximal bronchodilator dose (Max- BD), as measured by ≤ 5% change in the FEV1;
d) the breathlessness score, measured by the Borg and VAS, at Max-BD;
e) the word descriptors of breathlessness during the bronchoconstrictor and bronchodilator challenges; and
f) the response to the bronchodilator use question.

## Research Setting and Recruitment

Subjects were seen at a clinical asthma research satellite laboratory of the University of California, San Francisco. The clinical asthma research laboratory is located in Oakland, CA., an ethnically diverse community. The location of this laboratory facilitated easier recruitment of African Americans with asthma. Subjects were primarily recruited from advertisements in two local newspapers, though some were recruited from the Asthma Clinical Research laboratory at the University of California in San Francisco. During the initial telephone contact subjects were informed that participation in the study would not in any way jeopardize their present medical and/or nursing care, and that participation was voluntary. Informed consent was obtained from each participant prior to study participation. Institutional Review Board (IRB) approval from University of California San Francisco was granted on June 5, 1996. (Appendix A)

## Sample

### Characteristics of Sample

Thirty-two African American and Caucasian adults with mild to moderate asthma agreed to participate in the study. Both females and males, ages 18 to 60, (mean age 34.5± 9.7) were enrolled from July, 1996, through April of 1997. Of the 40 subjects enrolled eight were excluded for failure to meet study criteria. Thirty two subjects, 16 African Americans (mean age of 30.3 ± 2.4) and 16 Caucasians (mean age of 35.6 ± 4.6), completed the study.

**Criteria for eligibility:**

1) FEV1 ≥ 70% of predicted normal (NAEP Expert Panel, 1991; ATS, 1987);
2) PC30 ≤ 8 mg/ml;
3) Either African American or Caucasian;
4) Atopy - ≥ two positive skin prick reactions (wheal diameter > 3 mm);
5) Age - from 18 to 60 years old;
6) Diagnosis of asthma.

**Exclusion Criteria:**

1) Any significant coronary artery disease, or history of malignancy (≤5 years), diabetes mellitus, immune disorders, or hypertension;
2) PC30 ≥ 8 mg/ml;
3) Pregnancy;
4) A smoking history of ≥ 10 years; smoked any inhaled agents in the last year;
5) Use of either inhaled or oral corticosteroids or antibiotics in the last six weeks;
6) Exacerbation of asthma, a cold or flu-like symptoms, in the last six weeks;

7) A history of significant psychiatric illness;
8) Inability to read English.

Race has been shown to be an important determinant of lung function. African Americans have a smaller trunk:leg ratio than Caucasians (ATS, 1987). As a result, African Americans have smaller (13% less) static and dynamic lung volumes (ATS, 1987). Thus, prior to any pulmonary function testing, a 13% reduction in the predicted lung volumes (ATS, 1987) for African Americans was programmed as a permanent feature into the pulmonary function software; therefore, all of the PFT study results are corrected for race and body size. In addition, all of the subjects were using either a prescribed short acting inhaled beta agonist or an over the counter inhaled beta agonist, e.g., Primatene Mist, for asthma control.

With respect to education, 28.1% of the subjects were high school graduates and 10% had advanced degrees. Most (78%) were employed at least part-time and two were full-time students. Neither history of asthma duration nor income data was collected. Females comprised 65.6 % of the sample, with African American women comprising 37.5 % of the sample in contrast to 28.1% for Caucasian females. The baseline and clinical indices are described in Chapter Four: Results.

**Sample Size Calculations**

There are no published studies that have examined the differences in perception of bronchoconstriction based on ethnicity, and the exact differences in response to methacholine are unknown (Cockcroft, O'Byrne, Swystum, & Bhagat, 1995). Lougheed, et al., (1993) correlated the maximal response during a bronchoconstriction challenge, as percent change in FEV1, with breathlessness, as

measured by the Borg scale (r = 0.90), in Caucasian cohorts. Based on the expected differences between these two groups, a conservative, moderate effect size for a correlation coefficient of 0.50 and a $\beta$ of 0.2 a total (n = 28) was required (Hulley & Cummings, 1988). Utilizing an attrition rate of ten percent, a sample size of 32 was determined to be sufficient to detect significant differences between the groups.

## Data Collection Methods

### Study Variables

Breathlessness is one of the most common symptoms all asthma patients experience. However, the specificity of the experience of breathlessness in different ethnic groups has not been previously studied. The perception of breathlessness as a unique experience mediated by various sensory mechanisms has been documented in Caucasians (Simon, et al., 1990; Elliott, et al., 1991), but the replication of these same studies in African Americans with asthma has not occurred. The word descriptors of breathlessness, a qualitative approach, will identify specific words associated with the change in the perception of breathlessness during asthma episodes. The provocative concentration of methacholine that causes a 30% decrease in FEV1 was defined as the PC30 (Cheung, Timmers, Swinderman, Bel, Dijkman, & Sterk, 1992). Airway hyperresponsiveness (AH) was defined as a PC30 to $\leq$ 8 mg/ml of Mch. Study variables and methods of measurements are listed in Table 1.

**Table 1. Study Variable List**

| Variable Name | Variable Measurement | Type |
|---|---|---|
| Race | | Categorical |
| Breathlessness intensity | Borg & VAS | Interval |
| Breathlessness language | Word Descriptors | Categorical |
| PC30 | FEV1 L | Continuous |
| Max BD | FEV1 L | Continuous |
| Bronchodilator use question | Action response | Dichotomous |

**Screening Methods**

After consent was obtained, subjects completed an asthma demographic questionnaire. Women of childbearing age were asked to provide a urine sample for pregnancy testing prior to any procedures. A skin prick test to fourteen common allergens ("Dermatophagides pteronysinus", "Dermatophgoides farinae", mixed grass pollen, mixed tree pollen, mixed weed pollen, cat dander, and dog dander) was performed only if subjects lacked skin testing within the last three years. All visits were conducted between the hours of 8 A.M. and 5:30 P.M. Willingness to fill out the Borg and VAS Scale was discussed prior to implementation of the study procedures.

## Reliability and Validity of the Instruments to Measure Perception

Two measurement tools, the Borg and VAS, were used to measure the perception of breathlessness and the word descriptor questionnaire was used to describe the perception of breathlessness. The bronchodilator use question was

asked of all subjects at the provocative concentrations of Mch that caused a 15%, 20%, and 30% fall in their FEV1 from baseline (PC15, PC20, and PC30). The purpose of this last question was to explore what sensations or symptoms perceived by subjects influenced them to use their inhaler. One intent of this study was to correlate the subjective measure of the perception of breathlessness with an objective measure of airflow, the FEV1. Another intent was to have subjects describe in their own words their language of breathlessness.

**Borg Scale: Reliability and Validity**

Originally, the Borg scale was developed by Borg to measure perceived exertion in exercising patients (Borg, 1970). The Borg scale allowed only for ratio scoring in which subjects selected a numerical value that represented their magnitude or intensity (0 to 10) of dyspnea (Borg, 1970). The ratio scale allowed only for comparisons between stimuli without interindividual comparisons. To overcome these limitations descriptive categories (nothing at all to maximal) were added to the perceived exertion scale (Borg, 1982). These categories allowed for perceived exertion whereby subjects can select absolute descriptors, thus allowing for direct interindividual comparisons (Burdon, Juniper, Killian, Hargreave, & Campbell, 1982). The modified Borg Scale for breathlessness is a 10-point interval scale ranging from 0 (nothing at all) to 10 (maximal bearable). Different words are used to define the numerical values on the Borg scale by different investigators. Such terms as uncomfortable need to breathe, level of breathlessness, effort of breathing, intensity or magnitude of breathlessness, and dyspnea reflect some of the different scaling instructions used by investigators (Brand, et al., 1990; Adams, et al., 1985; Wilson & Jones, 1988; Turcotte, et al., 1990; Kikuchi, et al., 1994).

The reproducibility of the Borg scale was tested in six stable COPD subjects who participated in a progressive, incremental, exercise on an electrically braked bicycle ergometer (Muza, et al., 1990). All subjects had two exercises on the same day, after resting one hour, and a third exercise test was performed within 10 days. At minute intervals subjects were asked to rate their effort to breathe on the modified Borg scale (0= nothing to 10 = worst imaginable). Subjects were asked to rate "the sense of effort" required to breathe. Prior to the exercise test, subjects were read a script instructing them to point to the area on the Borg scale that best represented their sense of effort of breathing; they were informed that the increasing number on the scale indicated increased effort. The Borg scale was very reproducible (r = 0.96) in rating dyspnea (Muza, et al., 1990). The variability for sensation scaling assessed by the coefficient of variation for the Borg scale was 3 percent. The boundaries of the Borg scale—the maximum score a subject can select is 10—may be a constraint since subjects are forced to select from established categories (Muza, et al., 1990). Alternatively, the established categories on the Borg scale do provide accurate interindividual comparisons (Muza, et al., 1990).

The reliability and validity of the modified Borg scale has been verified (Burdon, et al., 1982; Mahler, 1991; Wilson, et al., 1989). The reproducibility (within-test reliability) of the Borg is advantageous for measuring perception; determining a change in the intensity of breathlessness, that is also reproducible, is an important outcome. The Borg Scale has been used to measure the perception of bronchoconstriction during bronchial challenges and in some ways it is considered the "gold standard" (Boulet, et al., 1994; Turcotte & Boulet, 1993). The Borg scale has been extensively used because it is easy to use, easily understandable, inexpensive, reproducible, and it provides categories that allow individuals to select either a word or number.

The major limitations of the Borg scale are recall and interviewer bias. To limit recall bias a new Borg Scale form was used for each challenge dose; subjects were not allowed to look at their previous scores. To prevent any influence on the symptom scoring, the investigator did not observe the scores nor were the outcomes of scores discussed with the subjects. To further limit interviewer bias, a written script was read to each subject initially on how to rate their breathlessness (the wording of the script is provided under Borg measurement procedures); subjects were asked to read the script before each scoring session. A verbal instruction was provided specifying that they could use the entire Borg scale to rate their breathlessness. Each Borg scale form was coded with the time, date, subject's initials, and the methacholine dose. The Borg scale was used for both the bronchoconstrictor and the bronchodilator challenges.

The Borg scale is considered to have an inbuilt ratio bias because it is used over a narrow range (Wilson & Jones, 1989; Mahler, 1990), and there is a tendency for scores to be restricted to the 0 to 5 range since 5 is categorized by the word "severe"(Wilson & Jones, 1989; Muza, et al., 1990). Moreover, the effect of the verbal descriptors on the Borg scale may impose a threshold of sensation intensity (Muza, et al., 1990). In order for a subject to mark up to a higher level, the prior threshold of an intensity would have to be exceeded. For example, to move from 5 = "severe" to 7 = "very severe" requires a threshold jump in the intensity of breathlessness. Conversely, the verbal descriptors may increase preference for the numerical values (e.g. 5) .

**Breathlessness VAS Scale: Reliability and Validity**

The VAS is a reliable and valid instrument used to measure the magnitude and quantification of breathlessness (Janson-Bjerklie, et al., 1986; Gift, 1989). The

VAS has shown strong correlation of breathlessness with changes in FEV1 when used in both bronchoconstrictor and bronchodilator challenges (Roisman, et al., 1995; Noseda, et al., 1993). The VAS scale is a 100-mm horizontal line, linear interval scaling, with the words "not at all breathless" and the "worst possible breathlessness" anchoring each end. The VAS is more sensitive to change than the Borg scale (Wilson & Jones, 1989; Roisman, et al., 1995). The VAS scale is not constricted by descriptors and the openness of the scale allows a subject to use the entire scale. For these distinct concerns the Borg scale and VAS were used together in this study.

In an early study of 34 normal adults the reproducibility of the VAS was evaluated fro validity and reliability (Adams, Chronos, & Guz, 1985). Subjects were fitted with a rebreather mask. During progressive increments in exercise (using a bicycle), inspiratory loading was added by changing the carbon dioxide concentrations as exercise workload was increased. Subjects were asked to quantify their sensation of breathlessness on a VAS by touching a potentiometer. Breathlessness was defined as "uncomfortable need to breathe". This exercise testing was repeated three times with varied levels of workload. The VAS was found to be highly reproducible with ventilatory (Ve = r = 0.72) and subjective parameters (interindividual) (Adams, et al., 1985; Mador, & Kufel, 1992). In a later study evaluating reproducibility of the VAS, slightly different findings were noted (Mador & Kufle, 1992). These investigators found that the VAS was reproducible at maximal levels of exercise but that variability occurred at lower levels of exercise. When the VAS is used to quantify breathlessness where exercise intensity is the study variable, it measures intensity changes (effort of breathing) instead of quantifying the sensation (Mador & Kufel, 1992). During bronchoconstriction challenges the VAS has been shown to accurately reflect the magnitude of breathlessness by the percent change in bronchoconstriction.

Roisman and colleagues found a strong correlation between a greater airflow obstruction or bronchoconstriction, represented as a reduction in the FEV1, and an increase in the VAS scores in asthma patients [VAS/FEV1] (1995). Noseda and colleagues (1995) validated these findings but noted the degree of interindividual variability related to the degree of bronchoconstriction (Janson-Bjerklie, et al., 1986).

The above studies demonstrate the test-retest reliability of the VAS. The construct validity, by T test score, was shown to be 12.35 ($p< 0.01$) in a study of 15 asthmatics (Gift, 1989; Wilson & Jones, 1989). The reliability and validity of the instrument is well documented. The major limitation of the VAS is that it is a highly subjective measure due to its visual presentation. A subject's response to the open line and the bipolar anchors does affect where he/she marks the line. To accommodate for these limitations, subjects were asked to mark the line vertically at any point between the two anchors that represented their breathlessness. Another limitation of the VAS is how the line is measured. The vertical line is normally measured from the lower anchor but variability in the 100 mm length of the scale line (horizontal) has been problematic (Douglas, Carrieri-Kohlman, Gormley, & Stuhlbarg, 1992). Copying can either lengthen or shorten the line; to account for these differences in scaling it is essential to measure the line after copying. (Carrieri-Kohlman, 1992). For VAS data to be comparable across studies it is necessary that the 100 mm scale remain consistent. To ensure reproducibility of VAS, it is essential that investigators clearly define the sensation, e.g. effort of breathing, they are asking subjects to rate, thereby preventing subjects from quantifying different sensations (Mador & Kufel, 1992).

The significant advantages of the VAS are the openness of the scale, it's ease of use, and it's inexpensiveness. The visual analogue scale, unlike the Borg scale, allows subjects to adjust their own interval size. Mador and Kufel (1982)

compared the perception of dyspnea using both a Borg and a VAS and noted that the VAS scores had almost twice the resolution of the Borg scale (slope of the relationship of VAS to Borg = 1.90). This increased resolution of the VAS may allow investigators to obtain more subtle differences in the measurement of sensory perception. To limit measurement errors in the current study, the investigator instructed subjects to mark a straight, vertical line to intersect with the horizontal line of the VAS. All of the VAS scales were measured after copying to ensure that they were exactly 100 mm in length; the same copy machine was used each time thus limiting variability between the types of equipment.

**Word Descriptor Questionnaire: Reliability and Validity**

The use of word descriptors as a means to examine the sensation of breathlessness was first undertaken by Simon and colleagues in 1990. Previously, breathlessness was considered a single sensation and not an experience that might encompass multiple sensations. Simon, et al., (1990) examined the qualitative differences among the sensations of breathlessness experienced by subjects with cardiopulmonary disease. A total of 53 subjects with a variety of cardiopulmonary diseases participated; they all experienced breathlessness. Because the subjects had a shared sensation of breathlessness but with different etiologies, these investigators were able to identify qualitative differences in breathlessness (Simon, et al., 1990; Mahler, et al., 1996). They did so by using a 19 Word Cluster Descriptor questionnaire that described the sensation(s) of breathlessness. Simon, et al., (1990) demonstrated that the specificity of the experience of breathlessness is different for different disease processes. The test-retest reliability of the 19 Word Descriptors was verified by Mahler and colleagues in 1996. The ability to correlate specific word descriptors with a

particular pathophysiology simplifies treatment and intervention. For example, "I feel out of breath" is associated with CHF whereas for asthma "my chest feels tight" reflects breathlessness.

We do not know what words or descriptors are associated with breathlessness for an African American with asthma. To explore if word descriptors differ between African American and Caucasian patients with asthma, this investigator devised an open word descriptor. This measurement tool will need reliability and validity testing in the future, but from this exploratory questionnaire a Word Descriptor Cluster did evolve to quantify the sensation of breathlessness for asthmatic African Americans. This ethnic word descriptor will allow for specificity of symptom treatment; the language of breathlessness may be culturally distinct, and this needs to be determined.

**Bronchodilator Question**

A lowered perception of breathlessness has been associated with poor control and under treatment of asthma (Boulet, et al., 1994; Roisman, et., 1995). The inability to perceive progressive airway obstruction in turn limits an asthmatic's decision to take the inhaled beta agonist. A risk factor of dying from asthma is the failure of asthma patients to seek help or the lack of appreciation on their part regarding the severity of the symptoms (Boulet, et al., 1991; Kikuchi, et al., 1994). This investigator had prior experience with young asthmatics who were experiencing significant airway obstruction (documented by a reduced FEV1) and who stated that they felt their symptoms did not require any treatment. This reaction occurred numerous times with different asthma subjects. The bronchodilator use question may explain if asthma subjects can perceive the severity of their symptoms and associate their symptoms with the need to use

their short acting beta agonist inhaler. According to Woods and Catanzaro (1988), it is essential that the wording of a question be understandable, clear, and unbiased. Therefore, the bronchodilator question was purposely phrased to provide a dichotomous (yes/no) response: "If you felt this way at home would you take your inhaler?".

## Procedures

### General Study Procedures

Subjects were asked to withhold inhaled bronchodilators for eight hours prior to testing. This is a standard approach used to obtain accurate baseline data (Cockcroft, et al., 1995). Those subjects who were unable to withhold their inhaler for eight hours were re-scheduled. Prior to the visit, subjects were asked to withhold caffeine and alcohol for eight hours; antihistamines or theophylline medications were withheld for 24 hours.

After arrival in the asthma research laboratory, each subject sat comfortably in a chair for ten minutes before baseline vital signs were obtained. While waiting, subjects were asked to fill out an asthma symptom/demographic questionnaire. Written consent was obtained. Pregnancy testing was performed on those women of child bearing potential. Before baseline pulmonary function testing (PFT), subjects were asked to rate their sensation of breathlessness on a Borg and a Visual Analog Scale (VAS); they were also asked to describe in their own words, in writing, any sensations (with respect to their breathing) that they were having at that time. This verified both a subject's disease status as well as their study eligibility. Allergen skin testing was performed as previously discussed.

**Pulmonary Function Testing**

Baseline PFT was performed using a Collins Eagle II system water-seal 8-liter spirometer (Quincy, MA). Three maneuvers or more were performed until three reproducible maneuvers within 5% of each other were obtained (ATS, 1987). The best maneuver was selected and served as the baseline value (ATS, 1987). Pulmonary function parameters that were measured were forced expiratory volume in 1 second (FEV1), forced expiratory capacity (FVC), peak expiratory flow rate (PEFR), and forced expiratory flows 25-75% (FEF 25-75%). Predicted values were calculated from a computerized program based on age, height, gender, and ethnicity (Morgan, 1980). Pulmonary function equipment was calibrated daily, using standardized procedures, prior to all visits. A systematic error, a threat to validity, could have resulted if the pulmonary function equipment had not been calibrated correctly.

**Bronchoconstriction Challenge/ Methacholine Provocation Test**

Methacholine chloride was administered using a standardized procedure (Cockcroft, 1995; Drazen, et al., 1996). A DSM-2 Micro-Dosimeter (S & M Instruments, Doylestown, PA) was used to nebulize the methacholine. Aerosols were nebulized by a Devilbiss Health Care, 646 nebulizer, Somerset. Compressed oxygen, regulated to generate 20 psi, was used to drive the nebulizer. While wearing a noseclip, subjects were instructed to inspire from functional residual capacity (FRC) up to total lung capacity (TLC) for a total of five inhalations of each solution. A short pause occurred between each inspiratory effort. While inhaling the solution, they were instructed to hold the nebulizer below the

reservoir to avoid warming the solution. Two mls of each concentration, at room temperature, were nebulized. Each nebulizer was calibrated, and the mean nebulizer output was 5.6 μ l/ per breath. A buffered 0.09% Sodium Chloride was inhaled initially. The FEV1 was measured 3 minutes after completion of the fifth inhalation of a methacholine concentration. Doubled concentrations of methacholine from 0.078 to 10 mg/ml were then inhaled in a similar fashion at 5 minute intervals. Measurement of the FEV1 was repeated 3 minutes after completion of each concentration of the methacholine. The percent reduction in the FEV1 was calculated from the highest value after saline inhalation, diluent, to the highest value once PC30 was reached. The test was stopped when the FEV1 had fallen by 30% or more. The PC30 was obtained by interpolation from the log-dose curve. During the methacholine challenge, before spirometric measurements (baseline), subjects were asked to rate their breathlessness on a Borg scale and a VAS; they were asked to describe, in their own words, on the word descriptor, any sensation that they were experiencing. These measurements were obtained two minutes after inhaling each methacholine concentration.

**Measurement Procedure for the Borg Scale**

After a subject's vital signs and health history were obtained the following instructions on use of the Borg scale were provided (Appendix B). Subjects were asked to fill out the Borg scale first. They were shown the Borg scale with the top portion of the form blank; the study parameters including a subject's initials, date, and time were added later. Subjects were informed that this information would be filled out by the investigator after they completed the form. The following script was read to them:

**Script:** During the challenge your breathing may change. Two minutes after each dose I will ask you to rate the sensation of breathlessness that you feel. You may feel this sensation as unpleasant or as distress, and it may be similar to the sensation you experience when your asthma is worse. Please draw a line under the words or numbers that best explain the sensation you are feeling at this time.

Subjects were asked to select either the verbal descriptor or a numerical value that represented their sensation of breathlessness (described above). In addition, they were informed they could select the numerical values of 6 or 8 even though the verbal descriptors for these two values were blank. A script was provided on a large flash card, and they were asked to refer to the script prior to marking the scale; a black pen was provided. Subjects were asked to rate their perception of breathlessness before the initial spirometry and two minutes after completing each concentration of the methacholine. A new Borg scale was provided each time. A timer was placed on the desk, in their view and when the timer reached two minutes they were instructed to begin rating their breathlessness. The investigator spoke to the subjects during this time period only to remind them when the two minutes were up. Once they had completed a Borg scale it was handed to the investigator who turned the form face down to limit interviewer bias. If subjects asked the investigator what their previous mark was, they were asked to read the script again. Subjects were not aware of what concentration of methacholine they were receiving; they were informed only that increasing doses of the solution would be nebulized during the course of the challenge. During the challenge the investigator noted any evident respiratory symptoms (e.g., audible wheezing) on the data form. A subject's heart rate was monitored

periodically throughout the challenge; a pre and post challenge blood pressure was recorded. These exact same procedures and instructions were used during the bronchodilator challenge. (Appendix B)

**Measurement Procedure for Visual Analogue Scale**

After completion of the Borg scale the following instructions on the use of the VAS scale were provided (Appendix B). They were shown the VAS scale with the top portion of the form blank; the study parameters including the subject's initials, date, and time were added later. Subjects were informed that this information would be filled out by the investigator after they completed the form. The following script was read to them:

**Script:** During the challenge your breathing may change. Two minutes after each dose I will ask you to rate the sensation of breathlessness that you feel. You may feel this sensation as unpleasant or as distress, and it may be similar to the sensation you experience when your asthma is worse. Please draw a vertical line between the two anchors that best represents your breathlessness at this time.

Each subject was instructed to mark a straight vertical line, such that its position was relative to the two extreme anchor words. The lower anchor word was not breathless and the upper anchor word was extremely breathless (Appendix B). This line reflected the perception of breathlessness (see above script). A black pen was provided. They were told they could use the entire line to mark their sensation of breathlessness. A demonstration of how to mark the

line was provided. Subjects were asked to rate their perception of breathlessness before the initial spirometry and two minutes after completing each concentration of the methacholine. A new VAS scale was provided each time. A timer was placed on the desk in their view, and when the timer reached two minutes they were instructed to begin rating their breathlessness. The investigator spoke only to the subjects during this time period to remind them when the two minutes were up. Once they had completed a VAS scale it was handed to the investigator who turned the form face down to limit interviewer bias. If a subject asked the investigator what their previous mark was, they were asked to read the script again. Subjects were not aware of what concentration of methacholine they were receiving; they were informed only that increasing doses of the solution would be nebulized during the course of the challenge. During the challenge the investigator noted any evident respiratory symptoms (e.g., audible wheezing) on the data form. A subject's heart rate was monitored periodically throughout the challenge; a pre and post challenge blood pressure was recorded. These exact same procedure and instructions were used during the bronchodilator challenge. (Appendix B)

**Measurement Procedures for Word Descriptors**

After completion of both the Borg and VAS scales the following instructions on use of the Word Descriptor instrument was provided (Appendix B). Subjects were shown the Word Descriptor with the top portion of the form blank; study parameters including the subject's initials, date, and time were added later. Subjects were informed that this information would be filled out by the investigator after they completed the form. The following script was read to them:

**Script:** After each dose of the inhaled solution, I will ask you to describe in your own words the sensation you are feeling at this time. You may use as many words as is necessary to explain the sensation(s) you are experiencing. There are no correct answers. I am interested in the word or words that best describe the sensation you are feeling in regards to your breathing. I am interested in your personal description of the sensation you are feeling at this point in time.

The word descriptor form was totally blank except for lines and the heading words. Each subject was provided verbal examples of word descriptors, e.g., "difficulty out", "tight", "shallow", "concentration", "heavy", "pressure", "can't get air in", and "work and deep". They were not allowed to see these descriptors after the initial instructions. Subjects were encouraged to use as many words as needed to describe their sensation of breathlessness. Subjects were asked to describe their perception of breathlessness before the initial spirometry and two minutes after completing each concentration of the methacholine. A new word descriptor form was provided each time; they were provided a pen to use. A timer was placed on the desk in their view and when the timer reached two minutes they were instructed to begin to describe their breathlessness. The investigator spoke only to the subjects during this time period to remind them when the two minutes were up. Once they had completed a word descriptor it was handed to the investigator who turned the form face down to limit interviewer bias. If subjects asked the investigator what their previous words were, they were asked to read the script again. Subjects were not aware of what concentration of methacholine they were receiving; they were informed only that

increasing doses of the solution would be nebulized during the course of the challenge. During the challenge the investigator noted any evident respiratory symptoms (e.g., audible wheezing) on the data form. A subject's heart rate was monitored periodically throughout the challenge; a pre and post challenge blood pressure was recorded. These exact same procedure and instructions were use during the bronchodilator challenge. (Appendix B)

**Measurement Procedure for Bronchodilator Question**

The bronchodilator question was asked when a subject's FEV1 was reduced by 15%, 20%, and 30% of the diluent FEV1. The calculation for the bronchodilator (BD) question was a simple percentage of the FEV1 obtained after the diluent (buffered 0.9% sodium chloride solution) concentration of methacholine. The percentiles of the diluent FEV1 were calculated for each subject and recorded on the BD questionnaire. Subjects were blinded to the fact that the question was being asked in conjunction with a specific reduction in their FEV1.

**Script:** If you felt this way at home would you take your inhaler?

Each subject's response was recorded verbatim on the BD questionnaire including the specific FEV1 value. Subjects were not queried about their response nor where they asked to expand or explain their response to the investigator. (Appendix B)

**Bronchodilator Challenge**

After spirometric confirmation of the PC30, subjects were asked to rate their breathlessness using the Borg and VAS and to fill out the word descriptor as previously described. Two puffs (180 mcg) of albuterol was delivered through a 750 ml spacing device (Aerochamber). Prior to the first dose of albuterol, subjects were instructed to place their lips around the mouthpiece tightly. To actuate a dose of albuterol into the chamber they were instructed to depress down once, firmly and quickly, on the canister. Then they were asked to take in a slow inspiratory effort to total inspiratory capacity and to hold their breath for 10 seconds at the end of inspiration. A demonstration of this technique was provided. The second puff of albuterol was delivered using the same procedure. Two minutes after the second puff of albuterol subjects were asked to rate their breathlessness on the Borg and VAS and to describe their sensations on the word descriptor. Spirometric measurements were obtained fifteen minutes after the second puff of albuterol was administered. This sequence of measurement of breathlessness continued until maximal bronchodilation was achieved.

The following procedure was used for the post methacholine spirometric measurements. Three maneuvers or more, within 5% or each other, were obtained; the highest of the three maneuvers was selected. The bronchodilator challenge continued until ≤ 5% improvement (calculated) in the FEV1 was present. The maximal bronchodilator dose was recorded as the last dose (mcg) that a subject received where ≤ 5% improvement in the FEV1 occurred. Maximal bronchodilator responsiveness was defined as no improvement or ≤ 5% change in the FEV1. The maximum dose of albuterol delivered was eight or a total 1080 mcg (Noseda, et al., 1993; Gold, 1994).

Administering the bronchodilator by a spacing device limited technique bias and ensured uniformity of dosing between the groups. Subjects were monitored for symptoms of increased sympathetic nervous system response due to cumulative doses of the inhaled beta agonist. They were observed for nervousness, agitation, or exaggerated hand tremor. (Noseda, et al., 1993). Each subject's heart and respiratory rate were monitored during the BD challenge; if tachycardia, a heart rate > 120 bpm, occurred the test was stopped. BP was taken at baseline and upon completion of the challenge.

## Data Management

### Introduction

In any study of two groups it is important that the two groups be comparable. Only then can the variance in the data be attributed to true differences between the groups. The dependent variable of interest in this study is perception of breathlessness between the two groups. The use of the Student's T Test is appropriate for interval type data collected in this study. Several assumptions must be met in order to use the T test for group comparisons. First, the dependent variable must be at least interval data and the group means must be normally distributed. Second is the assumption of independence; each subject must belong to only one group and contribute to only one score in the data. Third, the two groups must have similar variances (homogeneous) (Munro & Page, 1993). When the two groups are homogeneous Type II errors are limited; that is, incorrectly accepting the null hypothesis when it should be rejected. Also, if the standard deviation, variance, is smaller between the two groups than

difference in means may indicate that the two groups (populations) are clearly distinct. For this type of data, the T test would not be an appropriate choice.

The two samples were defined by race, African American and Caucasian. The sample population was recruited from a large geographical area. Each subject had an equal chance of responding to the newspaper study advertisement. One concern with newspaper advertisement is that only those individuals with a telephone or access to the newspaper can respond. There is not an easy solution to this recruitment bias. One approach included advertising in all of the regional newspapers. By recruiting subjects from this large geographical area it is hoped that the sample is representative. The study sample groups were of equal size, 16 per group, which contributed to group comparability. Group membership was by ethnicity (independence). Descriptive statistics on age, gender, severity of asthma (mild intermittent, moderate persistent), pulmonary function test, and PC30 indicated the two groups were quite comparable. Classification of Asthma Severity was according to the following guidelines:

**Table 2: Asthma Severity Scale**

| | |
|---|---|
| 1. Asthma symptoms ≤ 2 times a week | mild intermittent |
| 2. Asthma symptoms > 2 times a week | mild persistent |
| 3. Daily asthma symptoms | moderate |
| 4. Continuous asthma symptoms | severe |

NAEP, 1997

For the purpose of this data analysis, mild intermittent asthma was defined as FEV1 ≥ 80%; moderate persistent asthma was defined as FEV1 ≥ 70% and ≤ 80%.

## Data Management and Quality Control Procedures

The data was obtained in a clinical laboratory setting. All of the data, bronchoconstrictor and bronchodilator challenges, Borg, VAS, BD question, and word descriptors were entered into a customized database. Prior to data entry, coding of all outcome variables including coding for missing data, and data cleaning was devised. Computer derived scores were verified for accuracy by comparison with each handscored subject data. Discrepancies between the totals from the handscored subject data and computer derived scores were analyzed; data was corrected based on the primary source (subject) document. Continuous monitoring of study forms and data throughout the study promoted error-free data.

### Data Analyses Procedures

To assess for differences between the two ethnic groups a two sample T Test was used. The T test was used to compare the differences in group means for all of the study variables. A paired T test was used to determine group differences, by race, in the FEV1, Borg, and VAS scores. A Chi Square test was conducted on all of the word descriptors collected during all of the study points. Word descriptors occurring 40% of the time, four or more times, formed a word cluster for that ethnic group (Norman & Streiner, 1994).

A repeated measures ANOVA was used to determine the effect of race on the change in FEV1 and change in the Borg and VAS scores. A multivariate analysis was conducted to determine the linear associations and interactions of race upon the change in FEV1, the dose of methacholine at PC30, the change, over time, in the Borg and VAS scores, and the dose of beta agonist between groups.

Pulmonary function and PC30 data between groups were compared by means and standard deviations (SD). Low perception of breathlessness was defined as a PC30 more than 1 SD under the mean; high perception was defined as a PC30 more than 1 SD above the mean perception score of the group.

Statistical analyses were conducted using an Apple Macintosh Power Mac 7100/80 with SPSS, release 6.1, software licensed to the investigator.

## Human Subjects Assurance

This dissertation study received Institutional Review Board (IRB) approval from the University of California, San Francisco on June 5, 1996. No unique subject identifiers are included in the data set and study participants are identified only by their initials and by a two-digit identification number. Informed consent was obtained from each participant prior to study participation. The IRB approval letter is included in Appendix A.

# Chapter Four: Study Results

## Sample

The eligibility criteria for subjects were FEV1 ≥ 70% of predicted and a response to Mch, PC30, to ≤ 8 mg/ml. Subjects were omitted that did not meet these criteria. Eight subjects met the eligibility criteria but did not have a positive PC30 to ≤ 8 mg/ml and they were excluded. Six of the eight subjects excluded were African Americans and all were naive subjects to the Mch challenge. All of the pulmonary function data presented has been normalized to account for race and size. The number of subjects available for this analysis was 32 or 16 in each group.

Demographic characteristics (Table 3) were compared between the two groups. Subjects excluded from participation due to a negative PC30 were not included in the demographic comparisons. The two ethnic groups were quite comparable (by Chi Square) in baseline FEV1, FEV1 % predicted, age, level of education, smoking history, and allergen skin testing. The type of beta agonist agent was similar between the two groups with the majority (81-87%) of all subjects reporting use of albuterol only for symptom control. Only two subjects, both Caucasians, reported using an over-the-counter bronchodilator for symptom control. The two groups did not differ significantly in bronchodilator use and nocturnal awakenings using Chi Square analysis. Although differences were not significant African American subjects were more likely to wake up at night (more than twice a week) because of their asthma symptoms than Caucasians.

**Table 3: Subject Characteristics and Demographics**

| | Caucasian | African American | Total |
|---|---|---|---|
| Number of subjects | 16 | 16 | 32 |
| Age, yr | 37.4 | 31.8 | 34.5 ± 9.7 |
| (m/f) | 33.8/40.1 | 30/32.4 | |
| (mean ± SEM) | | | |
| Sex (m/f) | 7/9 | 4/12 | 9/21 |
| Percentage by sex (f) | 56.3 % | 75 % | 65.6% |
| Education, yr (m/f) | 14/14 | 13.5/13.1 | 13.6 yrs ± 2.6 |
| (mean ± SEM) | | | |
| Atopy (mean ± SEM) | | | |
| > 4 skin allergy response | 75.0 % | 62.5 % | 68.8 % |
| > 2 skin allergy response | 25.0 % | 37.5 % | 31.3 % |
| Nocturnal Awakenings | | | |
| > 2 times a week | 6.3 % | 31.3 % | 18.8 % |
| 1-2 times a month | 25.0 % | 37.5 % | 31.3 % |
| occasionally | 43.8 % | 12.5 % | 28.1 % |
| none | 25.0 % | 18.8 % | 21.9 % |
| Type of Bronchodilator (BD) | | | |
| albuterol | 81.2 % | 87.5 % | 84.4 % |
| alupent | 6.3 % | 12.5 % | 9.4 % |
| over the counter BD | 12.5 % | 0 % | 6.3 % |
| Smoking History | | | |
| none | 75.0 % | 75.0 % | 75 |
| ≥ 1-5 yr | 6.3 % | 12.5 % | 9.4 % |
| > 5 but ≤ 10 yr | 18.8 % | 14.3 % | 15.6 % |
| Baseline FEV1 (liters) | 3.25 | 2.85 | 3.05 ±2.5 |
| (mean ± SEM) | | | |
| Baseline FEV1 % predicted | 98.3 % | 95.7 % | 97.2 ± 17 |
| (± SEM) | | | |
| No. of subjects with neg. Mch | 3 | 5 | 8 * |

1. FEV1 = forced expiratory volume in 1 second
2. BD = bronchodilator
3. Nocturnal awakenings = asthma symptoms that disrupt sleep patterns
4. * Eight subjects were excluded due to a PC30 ≥ 8 mg/ml (3 Caucasian; 5 African Americans)

## Data Analysis: Study Objective One

**The first study objective was:**

> To compare and contrast the perception of breathlessness between Caucasian and African American patients with asthma at the provocative dose of methacholine that causes a 30% fall in the baseline FEV1.

### Introduction

Initially, an independent, two-tailed T test was conducted on all of the data set variables to test for differences in the group means. A paired T test with split case or a one-way ANOVA were conducted on specific variables to determine the influence of race on the above study outcomes. The mean breathlessness scores from both the Borg and VAS and the change in FEV1 lacked observed significance. The results of these tests are reported in Table 6.

To determine if the pattern of change over time was different between the two ethnic groups a model was developed to determine the relationship between VAS scores and (1) the Mch dose and (2) the change in the FEV1 not taking into account race (Table 6). This analysis was followed by a within-subjects RM ANOVA that was blocked by race to explain the presence or absence of group differences (Table 4). The results of the Repeated Measures ANOVA (table 4) indicate no significant contribution of race, percent change in FEV1, or the dose of Mch at PC30 to the VAS score. To explore the unique contribution of the study variables to change in breathlessness measured by the VAS, a hierarchial multiple regression was conducted and those results were not significant. The results of (table 4) indicate no significant contribution of race, percent change in FEV1, or any other variable to the VAS score.

**Table 4: Repeated Measures Anova**

**Changes in VAS* scores: Effect of race with Mch dose and Δ FEV1****

| Between-Subjects Effects | SS | df | F | p value |
|---|---|---|---|---|
| Within+residual | 349.49 | 30 | | |
| Race | 46.36 | 1 | 3.98 | .05 |
| | | | | |
| Effect of Δ in FEV1 | | | | |
| Within+residal | 245.10 | 30 | | |
| change in FEV1 overtime | 39.87 | 1 | 4.88 | .03 |
| Race by change in FEV1 | 27.73 | 1 | 3.39 | .07 |
| | | | | |
| Effect of Mch dose | | | | |
| Within+residual | 6.76 | 30 | | |
| Mch dose at PC30 | 1.15 | 1 | 5.10 | .03 |
| Race by Mch dose | .50 | 1 | 2.23 | .15 |
| | | | | |
| Effect of change FEV1 and Mch dose at PC30 | | | | |
| Within+residual | 9.60 | 30 | | |
| Δ FEV1 by Mch dose at PC30 | 21.07 | 1 | 65.85 | .000 |
| Race by Δ FEV1 by Mch dose | 1.30 | 1 | 4.95 | .05 |

* DV = VAS scores (product variable of VAS at baseline and change at PC30)
** Δ FEV1 = percent change in FEV1 from diluent dose to FEV1 at PC30

## VAS and Borg Results

The mean VAS scores (Table 5) for the study sample were comparable at baseline pulmonary function test (PFT). The mean baseline VAS for the Caucasian group was 11.00 mm and for the African American group was 14.25 mm (Table 5). To determine if group differences in the VAS scores could be explained by race a one-way ANOVA was conducted. Race did explain this variation in the VAS scores between the two groups at baseline ($F = 4.39$, df 1, $p < 0.04$).

The baseline FEV1 for the African American group was 2.85 L compared to 3.25 L for the Caucasian group (Table 6). To determine if differences in the VAS prior to PFT were related to the baseline FEV1 of each group a paired sample T

test was conducted. The VAS scores prior to PFT and the baseline FEV1 were inversely related ($p < 0.001$) ($r = -0.87$). The lower baseline FEV1 of the African American group indicated smaller lung volumes and smaller airway caliber as described by others (Schwartz, Katz, Fegley, Tockman, 1988; Cotes, 1979). Analysis of VAS and Borg scores with the FEV1% predicted will be conducted later. The mean VAS and Borg scores of the study sample were not significantly different at any measurement interval during the bronchoconstrictor challenge; Table 6 summarizes the results.

Variability in the data set was present. A paired T Test was conducted to determine if race explained any of the variability. One group difference was present. The two groups differed by VAS scores prior to PFT and at VAS PC30 (Paired T test = $p < 0.000$). The VAS scores at PC30 did not differ between the two groups (Table 6).

The difference in the mean Borg score at the diluent dose for the African American and Caucasian groups was not significant ($p < 0.20$) (Table 5). In addition, no group differences in the mean Borg scores at baseline and at PC30 were present (Table 5). The T test significance levels for the mean Borg scores between groups were large, at baseline ($p < 0.63$) and at PC30 ($p < 0.52$), indicating equal variances or that the variability in Borg scores were similar in each group. This finding is not unexpected since the verbal descriptors on the

**Table 5: Range of Scores in VAS & Borg Scales**

| Group | VAS Scores Range | | | Borg Scores Range | | |
|---|---|---|---|---|---|---|
| | Baseline | PC30 | T test | Baseline | PC30 | T test |
| Caucasian | 11.00 to 52.90 | | NS | .90 to 4.75 | | NS |
| African American | 14.25 to 63.00 | | NS | 1.09 to 5.25 | | NS |

**Table 6: Breathlessness Scores during Bronchoconstrictor (methacholine) Challenge**

| Variables | Caucasian n = 16 | | African American n = 16 | | t-value two tail Significance | Probability of Group Difference |
|---|---|---|---|---|---|---|
| | mean | ±SD | mean | ± SD | t | p |
| Borg at Baseline | .90 | .98 | 1.09 | 1.20 | -.48 | .20 |
| VAS at Baseline | 11.00 | 14.00 | 14.00 | 14.25 | - .65 | .24 |
| Borg at Diluent | 1.00 | .71 | 1.44 | 1.14 | -1.31 | .20 |
| VAS at Diluent | 13.00 | 11.70 | 17.60 | 16.50 | -.92 | .36 |
| Borg at PC15 | 2.90 | 1.70 | 3.00 | 1.03 | -.19 | .85 |
| VAS at PC15 | 33.19 | 18.50 | 33.80 | 16.20 | -.09 | .92 |
| Borg at PC20 | 3.56 | 2.00 | 3.88 | 1.46 | -.51 | .62 |
| VAS at PC20 | 39.75 | 23.20 | 46.10 | 22.30 | -.79 | .43 |
| Borg at PC30 | 4.75 | 2.20 | 5.25 | 2.10 | -.65 | .52 |
| VAS at PC30 | 52.90 | 25.40 | 63.00 | 19.20 | -1.26 | .21 |
| Pulmonary Function Results | | | | | | |
| FEV1 baseline | 3.25 | .85 | 2.85 | .50 | 1.64 | .11 |
| FEV1 at Diluent | 3.21 | .82 | 2.86 | .49 | 1.46 | .15 |
| FEV1 at PC30 (liter) | 2.13 | .70 | 1.94 | .39 | .99 | .17 |
| Dose of Mch @ PC30 | 5.19 | 4.12 | 2.89 | 2.71 | 1.87 | .073* |
| Calc Mch dose @ PC30 | 3.78 | 3.16 | 2.44 | 2.20 | 1.40 | .17 |

Level of Significance is listed if $p < .07$; SD = standard deviation

1. FEV1 = Forced Expiratory Volume in 1 second
2. PC30 = Provocative dose of methacholine that induced a 30% fall in the FEV1
3. Mch = Methacholine
4. Dose of Mch = mean mg/ml of methacholine that induced a 30% fall in the FEV1
5. Calculated Mch dose @ PC30 = log linear conversion of methacholine dose
6. Diluent = buffered 0.09% Sodium Chloride solution

Borg scale may impose a threshold of sensation intensity (i.e., limit a subject from marking up to a higher numerical value) (Muza, et al., 1990). In contrast, because the VAS is not restricted by verbal descriptor, the openness of the VAS scale encourages subjects to use the entire range of the scale. The range in the scores of the VAS and Borg between the two study groups is depicted in Table 5.

**Pulmonary Function Changes**

The mean baseline FEV1 for the Caucasian group was 3.25 L(SD ± .85) in comparison to the African American group which had a mean FEV1 of 2.85 L (SD ± .49) (T test = P< 0.11). The African Americans subjects had smaller lung volumes at baseline that Caucasians. The baseline FEV1 % predicted for the two groups were comparable; the mean FEV1% predicted for Caucasians were 98.3 % and 95.7 % for African Americans. The mean FEV1 at PC30 for the Caucasian group was 2.13 L (SD ± .70) compared to a mean FEV1 at PC30 for the African America group of 1.94 L (SD ± .94). The mean Mch dose for the Caucasian group was 5.19 mg/ml (SD ± 4.12); in contrast, the African American group required a mean Mch dose of 2.89 mg/ml ( SD ± 2.71).

Because African American have smaller lungs and a smaller airway caliber than Caucasians, it is likely that African Americans required a smaller Mch dose at PC30, since a smaller dose of Mch is required induce a 30% change (Schwartz, et al., 1988; Cotes, 1979). In addition, to the smaller lung volumes of the African American subjects this group also contained more women. An analysis of the data using the FEV % predicted will be conducted in the future.

An association was present between the dose of Mch required to induce a PC30 ($F_{1,30}$,<.07). The African American group required a lower dose of Mch for

a comparable PC30 (see Table 6). Howerver, the difference in the mean dose (Table 6) of Mch between the two groups was not significant.

The relationships between the change in VAS, Borg, and FEV1 with race are presented in Table 4. The specific variables of interest were: (1) the change in VAS scores from Baseline/control to PC30; (2) the change in the FEV1 from baseline/control to PC30; (3) the dose (mg/ml) of Mch at PC30; and (4) the interaction of race.

To determine the interaction of race a Multivariate test of significance was conducted on the following variables: FEV1 diluent, VAS scores at baseline, % change in the FEV1 (from control to PC30), dose of Mch at PC30, FEV1 at PC30, and VAS scores at diluent. ANOVA RM, is a more robust measure, and is useful to determine if the two ethnic groups varied from each other (within-group variation) or varied from each other (between-group variation) and to control for race. Between the groups, race partially explained the dose of Mch ($F = 2.68$, df 3, $P < 0.11$). The multivariate comparison suggested that an interaction of race may affect the dose of Mch at PC30. This assumption was investigated by adding an interaction for race and Mch dose to the regression model. Between the groups race was somewhat predictive of the dose of Mch required ($F = 2.54$, df 1, $p < 0.05$). The overall model explained 33% of the variance and the product variables (mchdose/race) explained 43% of the variance. A weak linear fit of Mch dose with race was present ($F = 3.49$, df 1, $P < 0.07$). There was an inverse linear fit of FEV1 at diluent and dose of Mch with the FEV1 at PC30 (product variable ) was $F = 14.94$, df 3, ( $p < 0.001$). The interactions between race and the changes in FEV1 from baseline to PC30 were partially explained. Group differences were explained by race as the intervening variable. In the future, data analysis using FEV1% predicted will be conducted; it is unlikely group differences exist since the FEV% predicted did not differ between subjects.

## Data Analysis: Study Objective Two

**The second objective was as follows:**

> To compare the word descriptors of breathlessness between Caucasian and African American subjects at PC30.

### Chi Square Tests

The language of breathlessness has not been described previously based on ethnicity. The purpose of the open word descriptor questionnaire (a blank space was provided for subjects to write down their word descriptors) was to allow subjects to describe in their own words their personal perception of breathlessness. This goal was achieved. The word descriptors represent the unique language of the study subjects, and their personal interpretation of breathlessness. The language descriptors represent the distinct language of breathlessness (Table 7) for African American and Caucasian subjects.

### Sorting of Word Descriptors

Since a large number of word descriptors were obtained, only those descriptors with an observed frequency > 25% in Table 7 are discussed. Several descriptors that did not meet the observed frequency criteria are discussed briefly due to the unique quality of the descriptor. These words were reported either in written text or verbalized by a subject during the procedure; verbalized symptoms were recorded by the investigator during the bronchconstrictor challenge.

To facilitate analysis, the word descriptors collected during the diluent dose and at PC30 of the methacholine challenge were sorted and combined by this investigator with other word(s) that appeared to represent similar sensation(s). The word clusterings, or categories, are listed in Table 7. Each word cluster represents a shared symptom experience derived from the individual word descriptors. From the initial word clustering, a total of 26 word descriptors were obtained from the diluent word descriptor questionnaires and 28 word clusters were derived from the word descriptor questionnaires at PC30. The data will be presented as sample data but, more importantly, specific to ethnicity. (Table 7)

**Word Descriptors at Diluent**

Word descriptors were collected after each dose of methacholine but the focus of the analysis is on the word descriptors at diluent and at PC30. Analysis of all of the word descriptors will be conducted in a future analysis prior to the development of a word descriptor questionnaire specific to African Americans. Eighteen of the 26 word descriptors collected at the diluent dose are presented in Table 7. Several word descriptors are not included in Table 7 because (1) the particular word may have been recorded by one or two subjects only, and (2) the terminology of the word descriptor provides insight into the unique sensory experience of these two ethnic groups.

The word descriptor "tight at the base of the throat" had an observed frequency of 43.75% in the African American group and the test was significant at $p < 0.05$ (Table 7). This descriptor was used by 8 (out of 16) African American subjects and by 2 (out of 16) Caucasian subjects. "Tight at the base of throat" illustrates the distinct influence of ethnicity upon the language of breathlessness. Even though, at diluent, only one word descriptor was found to be different

**Table 7: Word Descriptors during Bronchoconstrictor Challenge: Diluent**

| Word Descriptor | Caucasian n = 16 percentage | N | African American n = 16 percentage | N | Total frequency | Chi Square $X^2$ | p value |
|---|---|---|---|---|---|---|---|
| Diluent | | | | | | | |
| Tight base of throat | 6.3 | (1) | 43.8 | (8) | 9 | 3.86 | .04* |
| Itchy[1] | 12.5 | (2) | 18.8 | (3) | 5 | NS | .62 |
| Cough | 18.8 | (3) | 18.8 | (3) | 6 | NS | 1.00 |
| Chest irritation[2] | 6.3 | (1) | 25.0 | (4) | 5 | NS | .14 |
| Wheeze | 12.5 | (2) | 6.3 | (1) | 3 | NS | .54 |
| Stressed breathing[3] | 12.5 | (2) | 12.5 | (2) | 4 | NS | 1.00 |
| Phlegm[4] | 6.3 | (1) | 18.8 | (3) | 4 | NS | 28 |
| Shallow breath | 12.5 | (2) | 12.5 | (2) | 4 | NS | 1.00 |
| Difficult concentration | 6.3 | (1) | 12.5 | (2) | 3 | NS | .54 |
| Tight throat | 12.5 | (2) | 25.0 | (4) | 6 | NS | .36 |
| Throat congestion | 25.0 | (4) | 18.8 | (3) | 7 | NS | .67 |
| Tired & anxious | 18.8 | (3) | 12.5 | (2) | 5 | NS | .63 |
| Easy breath | 12.5 | (2) | 18.8 | (3) | 5 | NS | .63 |
| Chest tight | 6.3 | (1) | 12.5 | (2) | 3 | NS | .54 |
| Need deeper breath[5] | 25.0 | (4) | 6.3 | (1) | 5 | NS | .14 |
| Breath not clear[6] | 6.3 | (1) | 6.3 | (1) | 2 | NS | 1.00 |
| Nasal congestion | 18.8 | (3) | 37.5 | (6) | 9 | NS | .23 |
| Congested Chest | 12.5 | (2) | 6.3 | (1) | 3 | NS | .54 |

Chi Square: Pearson p values * = significant results $p < 0.05$
Expanded Descriptor Key:
1. Itchy = itchy sensation in throat
2. Chest irritation also spongy breathing
3. Stressed breathing also aware of breathing
4. Phlegm = phlegm in throat; need to clear throat of phlegm
5. Need deeper breath = in and out breath
6. Breath not clear = breathing not quite clear

between the two groups, ten distinct words were identified from diluent word descriptor questionnaire. Those words are: "stressed breathing, shallow breath, need a deeper breath, throat congestion, tight throat, easy breath, chest irritation, itchy, nasal congestion, and phlegm".

The word descriptor "nasal congestion" had the highest observed frequency between both groups; it was used a total of nine times. Although the word descriptor "nasal congestion" was not significant for either group, the frequency that it was reported suggests that it may be a clinically significant descriptor. For example, the word descriptor "nasal congestion" may represent an early physiological change perceived by asthma patients during an acute episode; this sensory perception information can result in changes to the educational content of self management programs.

"Cough" was reported by three members of each group; thus, "cough" was independent of race. Additional word descriptors that were independent of race include "itchy", "chest irritation", "tired and anxious", and "easy breath". The final two word descriptors represent the individual nature of the language of breathlessness and are "stressed breathing" and "shallow breath". All of the above word descriptors are unusual and further future testing will determine if chance alone played a role in their use by subjects.

**Word Descriptors at PC30**

A total of 28 distinct word descriptors was used by the study sample to describe the perception of breathlessness at PC30 (Table 8). From the initial 28 word descriptors a clustering or group of 25 word descriptors was derived (Table 8). Word descriptors were clustered based on a similarity of phrasing that suggested a shared perception by the study sample. Several word descriptors

were not clustered due to the uniqueness of the word itself or the inability to match a word with another word descriptor. Those ten word descriptors were equally distributed, five in each group, between the two groups. Study results for the African American group are presented first. All the study results are listed in Table 8; only those word descriptors in each group that are significant will be discussed.

**Word Descriptors: African American Group**

The Chi Square results were significant for five descriptors specific to the African American group. These word descriptors suggest that symptoms are perceived to be more in the upper airway such as "tight throat", "voice tight", "tough breath", and "itchy throat". Thirteen of the African American subjects used "tight throat", "voice tight" and "tough breath" were each used by seven African Americans, and "itchy throat" was used by four of the subjects. The lack of any word descriptors frequently associated (i.e., wheeze, chest tightness) with an acute asthma attack is striking. Moreover, these word descriptors suggestive of upper airway symptoms were not reported by any of the Caucasian subjects. The word descriptors collected at PC30 are listed in Table 8.

**Word Descriptors: Caucasian Group**

The Chi Square results were significant for five descriptors specific to the Caucasian group. The significant word descriptors used by the Caucasian group suggest more lower chest wall symptoms, e.g., "deep breath" and "hurts to breathe". The significant reported by the Caucasian group were "deep breath", "lightheaded ", "out of air", "aware of breathing ", and "hurts to

**Table 8: Word Descriptors during Bronchoconstrictor Challenge: PC30**

| Word Descriptor | Caucasian n =16 percentage | N | African American n = 16 percentage | N | Total frequency | Chi Square $X^2$ | p value |
|---|---|---|---|---|---|---|---|
| PC30 | | | | | | | |
| Heavy chest | 12.5 | (2) | 25.0 | (4) | 6 | NS | .36 |
| Wheeze | 37.5 | (6) | 25.0 | (4) | 10 | NS | .44 |
| Tired/irritable | 12.5 | (2) | 6.3 | (1) | 3 | NS | .54 |
| Concentration[1] | 25.0 | (4) | 37.5 | (6) | 10 | NS | .44 |
| Air in out[2] | 25.0 | (4) | 18.8 | (3) | 7 | NS | .66 |
| Tight throat | 12.5 | (2) | 81.3 | (13) | 16 | 12.5 | .0004* |
| Throat congestion | 18.8 | (3) | 37.5 | (6) | 9 | NS | .23 |
| Chest pressure | 6.3 | (1) | 00.0 | (0) | 1 | NS | .30 |
| Phlegm | 12.5 | (2) | 25.0 | (4) | 6 | NS | .36 |
| Scared-agitated | 00.0 | (0) | 37.5 | (6) | 6 | 7.38 | .006* |
| Chest Tight | 12.5 | (2) | 00.0 | (0) | 2 | NS | .14 |
| Voice Tight[3] | 12.5 | (2) | 43.8 | (7) | 9 | 3.86 | .04* |
| Dry nose-throat | 6.3 | (1) | 6.3 | (1) | 2 | NS | 1.00 |
| Shortness of breath | 6.3 | (1) | 00.0 | (0) | 1 | NS | 1.00 |
| Deep breath | 37.5 | (6) | 6.3 | (1) | 7 | 4.57 | .03* |
| Lightheaded | 25.0 | (4) | 00.0 | (0) | 4 | 4.57 | .03* |
| Ears ringing | 12.5 | (2) | 18.8 | (3) | 5 | NS | .62 |
| Tough Breath[4] | 12.5 | (2) | 43.8 | (7) | 9 | 4.57 | .04* |
| Coughing | 12.5 | (2) | 37.5 | (6) | 8 | NS | .10 |
| Out of air | 31.3 | (5) | 00.0 | (0) | 5 | 6.0 | .01* |
| Itchy throat | 00.0 | (0) | 25.0 | (4) | 4 | 4.57 | .03* |
| Warmth-face | 00.0 | (0) | 12.5 | (2) | 2 | NS | .14 |
| Shallow breath | 12.5 | (2) | 6.3 | (1) | 3 | NS | .54 |
| Aware breathing | 25.0 | (4) | 00.0 | (0) | 4 | 4.57 | .03* |
| Hurts - breath | 18.8 | (3) | 00.0 | (0) | 3 | 3.31 | .06* |

Chi Square: Pearson p values; $p < 0.05$ reported

1. Concentration = difficulty concentrating
2. Air in and out = difficulty getting air in and out
3. Voice tight = difficult to speak; voice deeper
4. Tough breath = strained breathing

breathe". More importantly, none of the African American subjects used any of these word descriptors reported by the Caucasian group. The one exception was "deep breath" which was used by one African American subject. The difference between the two groups in the perception of breathlessness by anatomical location was an unexpected finding. Table 8 provides a complete list of all the descriptors collected only at PC30.

## Data Analysis: Study Objective Three

**The third objective tested was:**

> To compare and contrast the perception of bronchodilation by Caucasian and African American patients by a change in breathlessness.

The perception of bronchodilation was measured by the Borg and VAS and determined by changes in the FEV1 and in FEV1 percent predicted. Maximal bronchodilation was achieved when less than a 5% improvement in the FEV1 was noted from one bronchodilator dosage to the next; if the percent improvement in the FEV1 was greater than 5 % then another bronchodilator dose was given. An independent T test (two tailed) was used to compare the breathlessness scores between the two groups. A paired T test with split cases, to account for race, was conducted on the Borg, VAS, FEV1, FEV1 % outcome variables. The pulmonary function data (FEV1) was collected 15 minutes post bronchodilator. All of the bronchodilator data (Borg, VAS, and FEV1) are presented in Table 9.

**Changes in the FEV1**

The mean FEV1 before the first dose of the bronchodilator (after PC30) was 2.13 L ± .70 for the Caucasian group and 1.94 L ± .39 for the African American group. Group differences in baseline (before bronchodilator) FEV1 were not present. The mean FEV1 was significantly different after 6 puffs of albuterol, 3.47 L ± .95 for the Caucasian group as compared to 2.42 L ± 1.29 for the African American group (T test = $p < 0.01$). Race did not explain this group difference ($F = 1.71$, df 3; $p < 0.19$). When the percent predicted FEV1 values were compared between the two groups, the difference in BD responsiveness at 6 puffs was not present. The mean FEV1 % predicted for the Caucasian group was 100.2 % and the African American group had a mean percent predicted of 97.2%. Table 9 lists these findings and figure 1 provides a graphic display of group differences to Max-BD.

To determine if lack of improvement (change) in the FEV1 was influenced by race a multivariate regression was conducted . An interaction term for race and beta agonist was added to the regression model for each dose (puffs) of the beta agonist. The interaction term "race" was a significant predictor of the change in FEV1 after 6 puffs ($F = 5.27$, df 3, $p < 0.02$). The interaction was strong even after controlling for variability in the data. What is interesting about these results is that the overall mean FEV1 for the African American group decreased from 2.88 L after 4 puffs of albuterol to 2.42 L after 6 puffs, a 15.9% reduction. For the African American group neither the VAS nor Borg scores increased during this study interval. The word descriptor "breath worse" collected after 6 puffs from the African American group indicated several subjects actually perceived their breathing as being worse. Only two subjects, one from each group, required 8 puffs of albuterol. Two of the study subjects were maximally bronchodilated (≤ a

5% improvement in the FEV1) after 4 puffs of albuterol. This resulted in a smaller sample size at the 6 puffs measurement period.

**Borg and VAS Results**

The mean Borg score before the first dose of bronchodilator was 4.75 for the Caucasian group and 5.25 for the African American group (Table 9). The mean VAS score before the first dose of the bronchodilator was 47.19 mm for the Caucasian group and 66.50 mm for the African American group (T test = $p < 0.04$). The VAS scores for the African American group were higher than the Caucasians before the first dose of bronchodilator than at PC30 (T test = $p < 0.02$).

This was the only significant group difference in the bronchodilator VAS and Borg scores (Table 9). Of clinical importance, the mean Borg score after 2 puffs of albuterol was 2.12 for the Caucasian group compared to 3.41 for the African American group (T test = $p < 0.08$). This difference in scores suggests that the two groups may perceive bronchodilation differently or that the Borg scale was not a sensitive in measuring perception changes associated with bronchodilation.

Another trend in the data related to the mean VAS score after 2 puffs of albuterol. The VAS score was 25.75 mm for the Caucasian group and 39.75 mm for the African American group ($p < 0.11$). These study results generate an important question about the possibility of ethnic differences in bronchodilator response. (Table 9)

The mean Borg scores for the study sample were quite comparable. For example, the mean Borg score after 6 puffs of albuterol was .53 for the Caucasian group and .85 for the African American group. In contrast, the mean VAS score also taken after 6 puffs of albuterol was 7.44 mm for the Caucasian group compared to 14.46 mm for the African American group (Table 9). These results

**Table 9: Breathlessness Scores during Bronchodilator Challenge**

| Variable | Caucasian n = 16 | | African American n = 16 | | t value two tail Significance | Probability of Group Difference |
|---|---|---|---|---|---|---|
| | mean | ± SD | mean | ± SD | t | p |
| Pulmonary Function Results | | | | | | |
| FEV1 after PC30 before BD[1] | 2.13 | .70 | 1.94 | .39 | 1.52 | .14 |
| FEV1 after 2 puffs BD[2] | 3.06 | .86 | 2.66 | .49 | 1.64 | .11 |
| FEV1 after 4 puffs BD | 3.37 | .91 | 2.88 | .48 | 1.90 | .06* |
| FEV1 after 6 puffs BD | 3.47 | .95 | 2.42 | 1.29 | 2.61 | .01* |
| FEV1 after 8 puffs BD* | 2.53 | .00 | 2.9 | .00 | | ** |
| FEV1 % Predicted | | | | | | |
| Baseline % predicted | 62.1 | 8.32 | 62.0 | 7.74 | | |
| 2 puffs % predicted | 86.6 | 9.54 | 88.2 | 13.4 | | |
| 4 puffs % predicted | 97.1 | 10.0 | 96.5 | 13.0 | | |
| 6 puffs % predicted | 100.2 | 10.1 | 97.2 | 13.4 | | |
| Breathlessness Scores | | | | | | |
| Borg prior to BD[3] | 4.28 | 2.57 | 5.78 | 2.60 | -1.64 | .11 |
| VAS prior to BD[4] | 47.19 | 28.45 | 66.50 | 23.44 | -2.10 | .04* |
| Borg after 2 puffs BD | 2.12 | 1.49 | 3.41 | 2.40 | -1.81 | .08 |
| VAS after 2 puffs BD | 25.75 | 18.34 | 39.75 | 24.67 | -1.80 | .08 |
| Borg after 4 puffs BD | 1.13 | .96 | 1.28 | 1.06 | -.43 | .67 |
| VAS after 4 puffs BD | 15.19 | 12.07 | 21.75 | 15.72 | -1.32 | .19 |
| Borg after 6 puffs BD | .53 | .50 | .85 | .83 | -1.27 | 22 |
| VAS after 6 puffs BD | 7.44 | 6.57 | 14.46 | 16.70 | -1.43 | 17 |
| Borg after 8 puffs BD[5] | .00 | .00 | .05 | .00 | | |
| VAS after 8 puffs BD[5] | 3.00 | .00 | 42.00 | .00 | | |

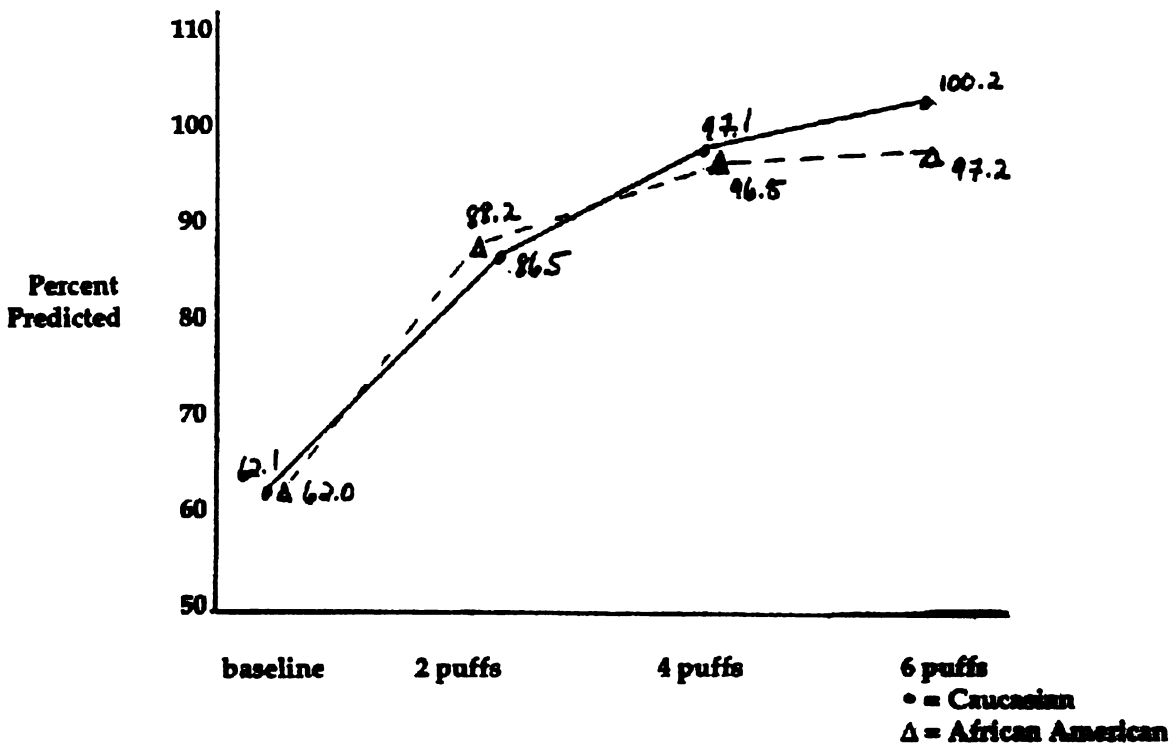
Level of Significance listed if $p < 0.08$; SD = standard deviation

1. FEV1 = Forced Expiratory Volume in 1 second; reported in liters
2. BD = bronchodilator (albuterol)
3. Borg = score obtained after PC30 but prior to first BD dose
4. VAS = score reported in mm/100 mm scale
5. Only two subjects required ≥ 8 puffs of BD (one in each ethnic group)
6. FEV1 obtained 15 minutes post BD
7. ** mean and SD not available: only two subjects at this dose

from two different measures of breathlessness suggest, even with a smaller sample (n = 14 in the African American group) that group differences may have been present in the data ($p < 0.17$). African Americans have smaller lung volumes than Caucasians; taking into account these differences African Americans did not respond differently to beta agonist. This investigator clinically observed in this

**Figure 1**

**Bronchodilator Response by Percent Predicted of FEV1**



subset of African Americans that their breathing was more labored after 6 puffs of albuterol. Supporting this clinical observation is the fact that three African American subjects used the word descriptor "breath worse" after 6 puffs of albuterol.

The fact that the mean FEV1 actually decreased for the African American group after 6 puffs of albuterol is of clinical interest. These changes probably result form the overall smaller lung volumes of African Americans; this was verified when the BD response by groups was compared using FEV1 % predicted which demonstrated no group differences (Schwartz, 1988, Cotes, 1979). Only two subjects, one from each group, required 8 puffs of albuterol for maximal bronchodilation. How these two groups respond to the inhaled beta agonist requires further study in view of the fact that the word descriptors suggest worsening of airflow for some of the African American subjects. During an acute asthma episode the usual therapeutic recommendation is to have a patient increase the number of puffs of the beta agonist inhaler. If a subset of African American asthma patients actually experiences airflow obstruction after a specific dose of beta agonist then they are at a greater risk of a fatal episode. All of the bronchodilator challenge data are presented in Table 9.

## Data Analysis: Study Objective Four

**The fourth objective tested was:**

> To compare and contrast the word descriptors at the dose of an inhaled beta agonist the two ethnic groups perceive bronchodilation.

**Word Descriptors : Baseline, 2, 4, 6, puffs (albuterol)**

The exact same data management procedures were used for the word descriptors collected during the methacholine and the bronchodilator challenges. The results of the word descriptors are presented by the number of puffs of the bronchodilator subjects received before they filled out the word descriptor questionnaire. Non-significant words refer to word descriptors that lacked statistical significance.

**Word Descriptors at Baseline (before first dose of Albuterol )**

The baseline word descriptors were collected from all subjects after a spirometry had confirmed their PC30 but before the first 2 puffs of the bronchodilator (albuterol) were given. Sixteen different word descriptors were identified and they are listed according to significance. All of these word descriptors are listed in Table 10. Tests of significance are reported by p values and the $X^2$ values for the significant word descriptors are provided in Table 10. Nine word descriptors specific to African Americans and one word descriptor specific to the Caucasian group were significant. Three non-significant word descriptors specific to the Caucasian group will be discussed.

**African American Group**

The Chi Square results were significant for nine word descriptors specific to the African American group (Table 10). These word descriptors suggest that symptoms are perceived to be more in the upper airway and these results are in total agreement with the word descriptor results from the bronchoconstrictor

challenge. What is remarkable is the lack of any descriptors reflecting lower chest wall discomfort. The one descriptor "voice change" was different from the data collected during the Mch challenge. This word descriptor included the terms: "difficult speech, forced speech, voice low, hard to speak, tired voice". This investigator noted a definite tonal change in the voices of some of the subjects.

This information about the voice change was recorded on the spirometry data by this investigator. The word descriptor "stomach pressure" was unusual. After the challenge (subjects had verbalized during the challenge that their stomach hurt) was completed the subjects were asked about this word descriptor and the terms "pain, upset stomach, hurts" were frequently provided. It is unclear if stomach discomfort occurs during acute asthma episodes or if this word descriptor is unrelated the airflow obstruction. The significant word descriptors are: "out of air, congested throat, itchy nose, nose congestion, tight throat, speech change, stomach pressure, voice tight, and tough breath". (Table 10)

**Word Descriptors: Caucasian Group**

The Chi Square results were significant for only one word descriptor "heavy chest" that was specific to the Caucasian group. Two of the three word descriptors for the Caucasian group that were not significant also suggest that symptoms are felt more in the chest wall. These word descriptors also agree with word descriptors from the Mch challenge. The descriptors are: "chest pressure" and "back hurt". The agreement across the data in the differences between the two ethnic groups in where (anatomical location) they perceive the sensory experience of breathlessness is consistent and impressive. Analyzing the word descriptor data by upper airway and chest symptom descriptors would validate this finding; this analysis will be conducted later. (Table 10)

**Table 10: Word Descriptors during Bronchodilator Challenge: Baseline ***

| Word Descriptor | Caucasian n =16 percentage | n | African American n = 16 percentage | n | Total frequency | Chi Square $X^2$ | P Value |
|---|---|---|---|---|---|---|---|
| Significant Words | | | | | | | |
| Air in out[1] | 00.0 | (0) | 43.8 | (7) | 7 | 8.96 | .002 |
| Congestion throat[2] | 12.5 | (2) | 68.8 | (11) | 13 | 10.49 | .001 |
| Heavy Chest | 43.8 | (7) | 18.8 | (3) | 10 | 2.76 | .090 |
| Itchy nose[3] | 00.0 | (0) | 18.8 | (3) | 3 | 3.31 | .060 |
| Nose congestion | 6.3 | (1) | 37.5 | (6) | 7 | 4.57 | .030 |
| Tight throat | 6.3 | (1) | 50.0 | (8) | 9 | 7.57 | .005 |
| Speech change[4] | 6.3 | (1) | 37.5 | (6) | 7 | 4.57 | .030 |
| Stomach pressure[5] | 00.0 | (0) | 18.8 | (3) | 3 | 3.31 | .060 |
| Voice Tight[6] | 6.3 | (1) | 50.0 | (7) | 8 | 6.00 | .010 |
| Tough Breath[7] | 6.3 | (1) | 37.5 | (6) | 7 | 5.57 | .030 |
| Other Words Used | | | | | | | |
| Back hurt | 25.0 | (4) | 12.5 | (2) | 6 | NS | .37 |
| Chest pressure | 37.5 | (6) | 12.5 | (2) | 9 | NS | .69 |
| Cough | 37.5 | (6) | 12.5 | (2) | 8 | NS | .10 |
| Ears hurt | 6.3 | (1) | 12.5 | (2) | 3 | NS | .54 |
| Lightheaded | 25.0 | (4) | 31.3 | (5) | 9 | NS | .69 |
| Wheeze | 18.8 | (3) | 18.8 | (3) | 6 | NS | NS |

Chi Square: Pearson p values; $p < 0.05$ reported

1. Air in and out = air stops going in, slow breath
2. Congestion throat = phlegm, clear, mucus, having to "spit out" mucus
3. Itchy nose = nose, throat, and face itching (forehead itchy x 1)
4. Speech change = voice deeper, different tone, effort to speak
5. Stomach pressure = stomach hurts, pain in stomach, stomach upset
6. Voice tight = difficult to speak; discomfort
7. Tough breath = strained breathing, lump, breathing through a lump

* Baseline values = Words reported after PC30 but before the first dose of a bronchodilator

**Word Descriptors after 2 Puffs**

A total of 30 distinct word descriptors were used by the two groups to describe their perception of breathlessness after 2 puffs of albuterol. (Table 11) From the initial 30 word descriptors a clustering of 21 word descriptors resulted. (Table 11) Eight word descriptors were identified, five word descriptors were significant for the African American group and three were significant for the Caucasian group. The word descriptors are listed in Table 11.

**Word Descriptors: African American Group**

The Chi Square results were significant for five word descriptors for the African American group and the word descriptors are: "air in out", "itchy", "tight throat", tight at base of throat", and voice tight". The word descriptors for the African American group continues to suggest that symptoms are perceived to be more in the upper airway. Table 11

**Word Descriptors: Caucasian Group**

The Chi Square results were significant for three word descriptors specific to the Caucasian group and those word descriptors are: " chest tight", "cough", and "ears hurt". The word descriptors of "cough" and "ears hurt" have not been previously observed in this group. The term "ears hurt" represents a distinct language for this Caucasian group. It is worth noting that none of the word descriptors used by Caucasians were reported by the African American group. Table 11 provides a complete list of all the word descriptors collected after 2 puffs of albuterol.

**Table 11: Word Descriptors during Bronchodilator Challenge: Two Puffs**

| Word Descriptor | Caucasian n =16 percentage | n | African American n = 16 percentage | n | Total frequency | Chi Square $X^2$ | P Value |
|---|---|---|---|---|---|---|---|
| Significant Words | | | | | | | |
| Air in out | 6.3 | (1) | 50.0 | (8) | 9 | 7.57 | .005 |
| Chest tight | 43.8 | (7) | 00.0 | (0) | 7 | 8.96 | .002 |
| Ears hurt[1] | 31.3 | (5) | 00. | (0) | 5 | 5.92 | .01 |
| Itchy[2] | 6.3 | (1) | 37.5 | (5) | 7 | 4.57 | .03 |
| Cough | 31.3 | (5) | 00.0 | (0) | 5 | 5.92 | .01 |
| Tight throat | 00.0 | (0) | 56.3 | (9) | 9 | 7.57 | .005 |
| Base of throat[3] | 00.0 | (0) | 18.8 | (3) | 3 | 3.31 | .06 |
| Voice Tight[4] | 6.3 | (1) | 56.3 | (9) | 10 | 9.31 | .002 |
| Other Words Used | | | | | | | |
| Airway clear | 18.8 | (3) | 37.5 | (5) | 9 | NS | .23 |
| Back pressures[5] | 18.8 | (3) | 12.5 | (2) | 5 | NS | .62 |
| Phlegm[6] | 43.8 | (7) | 37.5 | (5) | 13 | NS | .71 |
| Frustrated-upset | 18.8 | (3) | 18.8 | (3) | 6 | NS | NS |
| Headache | 31.3 | (5) | 31.3 | (5) | 10 | NS | NS |
| Long exhale[7] | 18.8 | (3) | 18.8 | (3) | 6 | NS | NS |
| Nasal congestion | 37.5 | (5) | 18.8 | (3) | 9 | NS | .28 |
| Stomach discomfort | 6.3 | (1) | 12.5 | (2) | 3 | NS | .54 |
| Substernal tight[8] | 6.3 | (1) | 00.0 | (0) | 1 | NS | .30 |
| Need take easy[8] | 18.8 | (3) | 25.0 | (4) | 7 | NS | .66 |
| Warm-sweaty | 12.5 | (2) | 6.3 | (1) | 3 | NS | .54 |
| Wheeze | 6.3 | (1) | 12.5 | (2 | 3 | NS | .54 |
| Concentration[9] | 6.3 | (1) | 18.8 | (3) | 4 | NS | .28 |

Chi Square: Pearson p values; $p < 0.05$ reported

1. Ears hurts = pain in ears, plugged, ringing, congested
2. Itchy = itchy nose and throat
3. Base of throat = discomfort, uncomfortable sensation at base of throat
4. Voice tight = difficult to speak; discomfort, hurts to speak, "force speech"
5. Back pressure = hurts, mid-back, pain in back
6. Phlegm = mucus in nose or throat
7. Substernal tight = tight across chest, middle chest hurts
8. Concentration = difficult , hard to write, hard to think, can't remember

**Word Descriptors after 4 puffs**

A total of 25 distinct word descriptors was used by the two groups to describe their perception of breathlessness after 4 puffs of albuterol (Table 12) From the initial 25 word descriptors a clustering of 15 word descriptors resulted (Table 12). Seven word descriptors were identified, five word descriptors were significant for the African American group and two were significant for the Caucasian group. All of the word descriptors are listed in Table 12.

**Word Descriptors: African American Group**

The five word descriptors specific to the African American group are: "ears congested", "tight throat", "tight at base of throat", "nose congestion", and "phlegm in throat". Word descriptors that were not significant but are worth noting are: "easy breath" , "difficulty concentrating" and "nose hurts ". The word descriptor "difficult concentrating" was also noted during Mch challenge. It is important to note that the word descriptors suggest upper airway symptoms and this finding is consistent with the word descriptors collected during the Mch challenge. Table 12 lists all of the word descriptors collected at 4 puffs.

**Word Descriptors: Caucasian Group**

The Chi Square results were significant for two word descriptors specific to the Caucasian group and they are: "chest tight" and "sweaty-warm". The word descriptor "sweaty -warm" probably represents a side effect from SNS stimulation resulting from the beta agonist therapy. All of the word descriptors collected after 4 puffs of albuterol are listed on table 12.

**Table 12: Word Descriptors during Bronchodilator Challenge: Four Puffs**

| Word Descriptor | Caucasian n =16 percentage | n | African American n = 16 percentage | n | Total frequency | Chi Square $X^2$ | P Value |
|---|---|---|---|---|---|---|---|
| Significant Words | | | | | | | |
| Chest tight | 31.3 | (5) | 00.0 | (0) | 5 | 5.92 | .01 |
| Ears Congested[1] | 6.3 | (1) | 37.5 | (6) | 7 | 4.57 | .03 |
| Tight throat | 12.5 | (2) | 43.8 | (7) | 9 | 7.57 | .009 |
| Tight base throat[2] | 00.0 | (0) | 37.5 | (6) | 6 | 3.31 | .01 |
| Nose congested | 6.3 | (1) | 31.3 | (5) | 6 | 3.28 | .07 |
| Sweating-warm | 18.8 | (3) | 00.0 | (0) | 3 | 3.31 | .06 |
| Phlegm throat[3] | 18.8 | (3) | 62.5 | (10) | 13 | 6.34 | .01 |
| Other Words Used | | | | | | | |
| Easy breath[4] | 43.8 | (7) | 43.8 | (7) | 14 | NS | NS |
| Headache | 25.0 | (4) | 18.8 | (3) | 7 | NS | .67 |
| Dry throat | 18.8 | (3) | 12.5 | (2) | 3 | NS | .54 |
| Cough | 12.5 | (2) | 6.3 | (1) | 3 | NS | .54 |
| Anxious -nervous[5] | 12.5 | (2) | 12.5 | (2) | 4 | NS | NS |
| Concentration[6] | 31.3 | (5) | 37.5 | (5) | 9 | NS | .69 |
| Tired[8] | 25.0 | (4) | 18.8 | (3) | 7 | NS | .66 |
| Nose hurts[9] | 31.3 | (4) | 50.0 | (8) | 13 | NS | .28 |

Chi Square: Pearson p values; $p < 0.05$ reported

1. Ears congested = plugged, difficult to hear, pain in ears, blocked
2. Tight at base throat = tight, discomfort, uncomfortable sensation at base of throat
3. Phlegm = mucus in nose, throat, sticking in throat, dripping down throat
4. Easy breath = breath goes in easier, clearer breath, almost normal
5. Anxious- nervous = jittery, restless, shakey
6. Concentration = difficult , hard to write, hard to think, can't remember
7. Tired = need to rest, take a nap
8. Nose hurts = pain in nose, dry, can't breathe through nose, dry

**Table 13: Word Descriptors during Bronchodilator Challenge: Six Puffs**

| Word Descriptor | Caucasian n =16 percentage | n | African American n = 16 percentage | n | Total frequency | Chi Square $X^2$ | P Value |
|---|---|---|---|---|---|---|---|
| Significant Words | | | | | | | |
| Breath worse[1] | 00.0 | (0) | 18.8 | (3) | 3 | 3.31 | .06* |
| Hard Concentrate[2] | 6.3 | (1) | 43.8 | (7) | 8 | 5.60 | .002 |
| Ears hurt[3] | 00.0 | (0) | 37.5 | (6) | 6 | 4.57 | .006 |
| Nasal congestion | 18.8 | (3) | 37.5 | (7) | 9 | 7.57 | .009 |
| Tight base throat | 00.0 | (0) | 62.5 | (10) | 10 | 6.34 | .01 |
| Nose congested | 6.3 | (1) | 31.3 | (5) | 6 | 3.28 | .07 |
| Speech-voice[4] | 6.3 | (1) | 37.5 | (6) | 7 | 4.57 | .03 |
| Other Words Used | | | | | | | |
| Anxious -nervous[5] | 12.5 | (2) | 12.5 | (2) | 4 | NS | NS |
| Cough | 12.5 | (2) | 12.5 | (2) | 4 | NS | NS |
| Need deep breath[6] | 25.0 | (4) | 12.5 | (2) | 6 | NS | .36 |
| Normal breath[7] | 50.0 | (8) | 25.0 | (4) | 12 | NS | .14 |
| Headache | 12.5 | (2) | 12.5 | (2) | 4 | NS | NS |
| Phlegm | 18.8 | (3) | 12.5 | (2) | 5 | NS | .63 |
| Shaky | 25.0 | (4) | 6.3 | (1) | 9 | NS | .69 |
| Throat congestion | 25.0 | (4) | 50.0 | (8) | 12 | NS | .14 |

Chi Square: Pearson p values; $p < 0.05$ reported

1. Breath worse = harder to get air in, breath stops
2. Hard Concentration = fuzzy , hard to think, can't remember, confused
3. Ears hurt = pain in ears, difficult to hear, , blocked
4. Speak-voice = voice tight, hard to speak, work to speak
5. Anxious- nervous = jittery, restless, shaky
6. Need deep breath = want to take a deeper breath, air doesn't go in, not fully open
7. Normal breath = air goes in easy, usual breath

**Word Descriptors at 6 Puffs**

From the initial 20 word descriptors described after 6 puffs of albuterol a clustering of 15 word descriptors resulted. (Table 13) The Chi Square results were significant for seven word descriptors all of which were significant for the African American group whereas none were significant for the Caucasian group.

**Word Descriptors: African American Group**

The seven significant word descriptors specific to the African American group are: "breath worse", "hard to concentrate", "ears hurt", "nasal congestion", "tight at base of throat", "nose hurts", and "speech-voice". Several new word descriptors "move up" and became significant; they are "concentration", "breath worse", "speech-voice" . Whether or not an association was present between the increased doses of the beta agonist and the descriptors was not explored. Several non-significant words worth mentioning are: "easy breath", "headache" , "concentration" , "cough" and "nose hurts". Other non-significant word descriptors of interest are: "need a deep breath" , "normal breath", "headache", and "throat congestion ". Moreover, three of the African American subjects described "normal breath". Two subjects used the word descriptor "need a deeper breath" and these same African American subjects also had a decrease in their FEV1 after 6 puffs of albuterol. (Table 13)

**Word Descriptors: Caucasian Group**

It is important to note that 8 (out of the 16) of the Caucasian subjects associated "normal breath" with maximal bronchodilation compared to only three African Americans. This was, in fact, an accurate perception on their part

and the word descriptors agreed with the measurement of their FEV1 after 6 puffs of albuterol. Although no word descriptors were significant for the Caucasian group at 6 puffs, four of the word descriptors of clinical interest are: "normal breath" , "need a deep breath", "phlegm" , and "throat congestion".

## Data Analysis: Study Objective Five

**The fifth objective tested was:**

> To compare the response to the bronchodilator question at PC15, PC20, and PC30 between these two ethnic groups

### Bronchodilator Question

The Chi Square test was used to test for differences in the proportion of yes/no responses to the bronchodilator question between the two groups. The results were not significant at either PC15, PC20, or PC30 (Table 14). The observed frequency of yes/no responses was equally distributed between the two groups; group differences were not ascertained. The number no responses to the BD question at PC 15 was 11 (out of 16) for the Caucasian group and 12 (out of 16) for the African American group. The number of no responses to the BD question at PC 20 was 7 (out of 16) for the Caucasian group and 11 (out of 16) for the African American group. The number of no response to the BD question at PC30 were identical in both groups or 44 % of the subjects in each group reported they would not use their bronchodilator. Stated differently, 7 out of the 16 subjects in each group would not have used their bronchodilator for symptom control if they were at home experiencing similar levels of breathlessness. The minimum reduction in a subjects FEV1 was 30% but in reality a greater than 30% reduction in the FEV1 occurred in many subjects. Even with major airflow

## Table 14: Chi Square Test for Bronchodilator Question

**BDQUES BD question response at PC30 by RACE black/white**

| BDQUES | RACE 1.00 white | RACE 2.00 black | Row Total |
|---|---|---|---|
| 1.00 no use of MDI | 7<br>50.0<br>43.8 | 7<br>50.0<br>43.8 | 14<br>43.8 |
| 2.00 yes would use MD | 9<br>50.0<br>56.3 | 9<br>50.0<br>56.3 | 18<br>56.3 |
| Column Total | 16<br>50.0 | 16<br>50.0 | 32<br>100.0 |

X2, df 1= .000
p value = 1.000

**PC20BD PC20 BD question response by RACE black/white**

| PC20BD | RACE 1.00 white | RACE 2.00 black | Row Total |
|---|---|---|---|
| 1.00 no would not use | 10<br>47.6<br>62.5 | 11<br>52.4<br>68.8 | 21<br>65.6 |
| 2.00 yes would take M | 6<br>54.5<br>37.5 | 5<br>45.5<br>31.3 | 11<br>34.4 |
| Column Total | 16<br>50.0 | 16<br>50.0 | 32<br>100.0 |

X2,df 1= .138
p value = .71

**PC15BD PC15 Bd response question by RACE black/white**

| PC15BD | race 1.00 white | race 2.00 black | Row Total |
|---|---|---|---|
| 1.00 no not use MDI | 11<br>47.8<br>68.8 | 12<br>52.2<br>75.0 | 23<br>71.9 |
| 2.00 yes would use MD | 5<br>55.6<br>31.3 | 4<br>44.4<br>25.0 | 9<br>28.1 |
| Column Total | 16<br>50.0 | 16<br>50.0 | 32<br>100.0 |

X2,df 1 = .155
p value = .69

obstruction half of each group would not have used their inhaler if at home; this finding is clinically alarming and indicates the need for patient education. Correlating the response of the bronchodilator question with each subjects level of lung function could identify factors that influence a subjects decision whether or not to take a dose of their inhaled beta agonist. Understanding what influences asthma patients to decide to use an inhaler is clinically important to determine. The need for education on self management strategies is clearly evident. But more importantly, assisting asthma patients to associate or identify which of their symptoms require treatment with a beta agonist. Word descriptors specific to ethnicity can be extremely valuable to this educational process.

# Chapter Five:
# Discussion and Conclusions

## Implications of Study Findings

This is the first study that has compared differences between African American and Caucasian asthma patients in the perception of breathlessness during induced airflow obstruction. The study results did not demonstrate a difference in the perception of induced breathlessness as measured by the Borg and VAS scales, nor was there any difference in how the two groups perceived airflow obstruction; and both groups responded equally well to medication that causes bronchodilation. But the study did demonstrate differences in the word descriptors that African Americans use to describe their airflow obstruction when compared to Caucasians. Descriptions of upper airway sensations, such as "tight throat" were far more common reports among the African American subjects in this study than among Caucasian subjects. Because these descriptors are not typical symptom descriptors, e.g., "wheezing", health care professionals often ignore or do not associate the descriptors with airflow obstruction. The reasons for these ethnic differences concerning where symptoms are sensed are not known, but it is possible that the mechanisms of airflow obstruction and the sensations associated are different or are medicated through different neurologic pathways. However, because word descriptors from African Americans with asthma have not been previously reported, this study's findings are both valuable and clinically important.

The findings of this study can be generalized to other African American and Caucasian asthma patients.

**Word Descriptors**

Word descriptors reflect the language of breathlessness, and as health professionals we must ask the correct symptom questions to determine the appropriate interventions. The five significant word descriptors for the African American group collected at PC30 , "tight throat", "scared-agitated", "voice tight", "tough breath", and "itchy throat" are radically different from the traditional symptoms associated with acute asthma episodes (shortness of breath, chest tightness, and wheezing). Whether or not these word descriptors can be applied to all African Americans with asthma requires further study with a larger sample. However, these findings do provide the basis for a word cluster questionnaire to be tested in a future study.

Several of the word descriptors collected from the African American group are worthy of discussion. "Tight throat" was used by 13 of the 16 African American subjects to describe their sensation of breathlessness at PC30. This investigator has heard this sensation described by other African American subjects unrelated to this study. When several non-study subjects were queried about this word descriptor, they clearly perceived the sensation in their throat rather than in their chest, across the chest, or even as chest tightness. Two of the African American study subjects used only the words "itchy throat" to describe their breathlessness at PC30. After the two subjects completed their participation, they were asked if they had experienced other symptoms at PC30 and both responded in the negative.

"Itchy" is not a word normally associated with fairly reduced airflow; thus, it is reasonable that this symptom would be disregarded by a health care provider as representing airflow obstruction. However, the use of such a descriptor is

important since some African American patients are undertreated for their asthma symptoms because they do not use traditional words, e.g., "wheezing", to describe their symptoms (Haire-Joshu, et al., 1993, Crain, et al., 1994). In view of the increased mortality from asthma for African Americans, the language of breathlessness must be clarified and understood.

In general, word descriptors from the African American group reflect more upper airway—throat, voice, and itchy throat—symptoms. The nature of the word descriptors from the African American subjects is very different from what studies of white cohorts have reported (Simon, et al., 1990; Janson-Bjerklie, et al., 1986). In the current study, the five significant descriptors for the Caucasian subjects were "deep breath", "out of air", "aware of breathing", "lightheaded", and "hurts to breathe". These word descriptors likely reflect chest discomfort or the sensation of effort; and these findings are in agreement with other studies of white cohorts (Elliott, et al., 1991; Simon, et al., 1990; Janson-Bjerklie, et al., 1986; Mahler, et al., 1996). Elliott and colleagues (1991), for instance, found that certain word descriptors, e.g., "aware of breathing", "need to take a deep breath", and "not enough air" reflected mechanical or chest sensations. In normal volunteers, Simon and colleagues (1989) noted that "being out of air" and "breath stops" were used to describe chest tightness.

The word descriptors from the bronchodilator challenge were consistent with the descriptors collected after the Mch challenge. African Americans consistently used word descriptors that reflected upper airway symptoms while Caucasians used descriptors reflective of chest wall sensations. The consistency of these within group findings were surprising. The findings indicate that ethnicity does affect the language of breathlessness. Moreover the anatomical location, e.g., upper airway for the African American group, concerning where airflow obstruction was sensed by these two ethnic groups was quite different.

As a result, it is essential to examine further ethnic differences in the language of breathlessness. It is known that ethnicity affects symptom interpretation and symptom reporting and that both influence health seeking behavior (Di Pede, et al., 1991; Haire-Joshu, et al., 1993).

**Borg and VAS**

There was one significant breathlessness score. The African American subjects rated their breathlessness significantly higher on the VAS before the first dose of bronchodilator when compared to the Caucasian subjects. It is possible that, for some subjects, performing the spirometry maneuver may have increased their perception of breathlessness. Overall, the study findings did not show a wide variability in the perception scores—Borg and VAS scores—between the groups. This lack of variability has also been noted in other studies (Boulet, et al., 1994; Brand, et al., 1990). Brand and colleagues (1990) also found no change in the Borg scale before and after a challenge in some subjects whom they termed asymptomatic hyperresponders. All of the subjects in the current study sample had mild disease. Mild disease is associated with variable or infrequent airflow obstruction, and infrequent symptoms have been shown to affect (decrease) the perception of bronchoconstriction (Brand, et al., 1990). A strong linear relationship was present between the Borg and VAS measurements at the control dose of Mch, and this linear relationship suggests that both of these tools were measuring the same thing.

In addition, there was minimal variability of the Borg scores between and within groups. This was not an unexpected finding since the verbal descriptors on the Borg scale are known to impose a threshold of sensation intensity (Muza, et al., 1990). For example, the mean Borg score at PC30 for the African American

group was 5.25 or "severe"; 10 represented the maximal possible score for breathlessness. Thus, for a 30 % reduction in airflow, African American subjects rated their breathlessness by using only half of the Borg scale (mean score was 5.25). The Borg scale accurately measures dyspnea intensity or magnitude but whether or not the perception of breathlessness is sensed by a person as intensity has not been studied (Mahler & Harver, 1992). The Borg scores varied little from baseline to PC30; the lack of variability suggests that either breathlessness was not being measured or that the tool lacked sensitivity in measuring the changes in perception of breathlessness.

The variability of the VAS scores between and within the two groups suggests that this tool is a more sensitive measure for assessing changes in the perception of breathlessness (Boulet, et al., 1994). This point is illustrated by the findings from the current study since some of the VAS scores were greater than 90 mm. In view of the fact that 100 mm is the maximal possible measurement, 90 mm indicates that the entire scale was used by subjects to rate their breathlessness. The openness of the scale and the lack of words may have allowed the two ethnic groups more control over how they chose to rate their sensations (Mador & Kufel, 1982; Carrieri-Kohlman, et al., 1992). Another factor known to limit perception is the scoring of breathlessness by subjects immediately after a bronchoprovocative dose (Cournoyer, et. al., 1993; Burdon, et al., 1982).

The Borg and VAS scores at PC30 were highly correlated suggesting that both tools were measuring changes in the perception of airflow obstruction. If the subjects had more than one challenge procedure, the second challenge could have confirmed the reliability of the VAS and Borg measurements. Multiple challenges also would have avoided the one point in time limitation of this study. For example, a worsening of asthma symptoms (e.g., allergies) could have

influenced whether or not a subject had higher or lower perception scores on a particular day.

Finally, whether or not prior experiences with a bronchoconstrictor challenge influenced how subjects rated their breathlessness was not evaluated. Nineteen of the thirty-two subjects were naive subjects to the bronchoconstrictor challenge. Analyzing the data for this factor is a possibility, and doing so would partially answer the question of whether or not prior challenge experiences influenced how a subject scored his or her breathlessness. In conclusion, the VAS, in particular, appeared to be a sensitive tool for measuring the perception of breathlessness.

**Bronchoconstrictor Challenge**

An important difference resulting from the study is that the African American subjects required significantly smaller doses of methacholine to induce a 30% reduction in their FEV1. This is undoubtedly due to the smaller lung size as reflected by the lower baseline FEV1 of the African American subjects. In turn, the smaller airway caliber of African Americans means that these subjects would reach PC30 more quickly and at a lower dose of Mch. To determine whether physiological differences contributed to the lower FEV1 at PC30, the data was analyzed using the FEV1 % predicted for each group. The mean FEV1 % predicted at PC30 were comparable, 62.2 % for the Caucasian group and 62% for the African American group. Future analysis of this component is planned.

In both groups, the actual FEV1 measurements were reduced greater than 30% since the mean FEV1 % predicted for both groups was 62%. By using a PC30 subjects may have rated their breathlessness higher because of the marked reduction in their airflow. For example, the 30% reduction in airflow (PC30) may

have exaggerated the symptoms experienced by both groups. When the scores of VAS at PC20 were compared to the scores of VAS at PC30 a greater group difference was present. The difference in the VAS scores suggests that the 30% reduction in airflow may have increased symptoms equally (PC20 to PC30) in both groups. In future studies, the upper limits of the FEV1 percent predicted (114% was the upper limit in this sample) should be controlled and the use of a PC20 should be considered.

The word descriptors collected at PC30 indicate that some degree of hypoxia may have been occurring. Subjects described having difficulty concentrating (thinking); many subjects had difficulty writing, and their actual handwriting became illegible during this time period. After bronchodilation the legibility in handwriting returned. In future studies, investigators should strongly consider monitoring oxygen saturation during the Mch challenge by using pulse oximetry.

**Bronchodilator Challenge**

The changes in FEV1 after the bronchodilator challenge provided discrete findings that are of clinical importance. When the Borg and VAS scores after 4 puffs and 6 puffs of albuterol were compared, the scores for African Americans actually decreased. The lower Borg and VAS scores may indicate an inability on the part of some of the African American subjects to accurately judge when their airways are open. Other investigators have noted a worsening of lung function for African Americans with frequent use (e.g., four times a day) of an inhaled beta agonist (Noseda, et al., 1994). Three African American subjects (two were male) used the word descriptor "breath worse" after 6 puffs of albuterol which suggests that they perceived their airflow obstruction as being worse. However, the FEV1 % predicted did not demonstrate any group differences. Four African

American subjects described their breathing as "normal breath" even though their actual FEV1 % predicted and FEV1 were reduced from their previous readings. Whether or not the word descriptors reflect a lowered perception or a physiological response to bronchodilation was not examined.

Cardiovascular studies have noted an altered responsiveness (decrease) of the beta adrenergic receptors in normotensive African American men (Johnson, et al., 1995). If one of the study groups had received a larger dose of the bronchodilator this could explain why some of the African American subjects felt worse and had a reduction in their airflows after 6 puffs of albuterol. An aerochamber was used to deliver the bronchodilator, thereby ensuring that a uniform dose of drug was delivered each time. Even though objective measures, FEV1 % predicted and FEV1, indicated that the groups were not different, the fact that African American subjects described their breathing as being worse after 6 puffs of albuterol is of clinical concern and should not be disregarded. How gender affects the response to an inhaled beta agonist was also not assessed. Whether or not inducing bronchoconstriction prior to the bronchodilator challenge influenced the breathlessness scores is not known.

Three study subjects, including two African American men, were maximally bronchodilated after 4 puffs. Only four African American men participated in the study, and one required 8 puffs of albuterol to achieve maximal bronchodilation. For the Caucasian group a greater decrement in the VAS scores occurred with increasing doses of the inhaled beta agonist, but this finding was not significant and would be expected.

**Bronchodilator Question**

At PC30, 50% of the subjects in each group said they would not have used their inhaler if they were at home. After the subjects so responded they were then asked "what would you do? " Half of the sixteen subjects stated they would "take a nap" whereas other subjects stated they would "go relax" or "drink coffee". This is an alarming finding and suggests the need for intensive education of asthmatic persons of any level of severity. However, for successful self management to result asthma patients must first understand which of their symptoms indicate the need for beta agonist treatment. By identifying ethnically sensitive word descriptors to describe symptoms, the educational process has greater potential for success. In addition, earlier treatment of symptoms may reduce the frequency of ER visits for both groups, but particularly for African Americans with asthma.

Having subjects respond to an open-ended question could have resulted in different responses since the question was asked of subjects after they had performed a spirometry maneuver (to document PC15, etc.). Asking the question at this particular time could have biased their answers towards the affirmative. Because of the increased mortality associated with African American asthma patients, however, this subject deserves further examination. The lack of symptom recognition, or acceptance, illustrates the confusion associated with both the perception of airflow obstruction and the language of breathlessness.

**Limitations**

The study sample was recruited from a large geographical area that is diverse economically, socially, and ethnically. Sample selection bias could have resulted

since subjects were recruited from local newspapers; people who lacked access to a newspaper were thus prevented from participation. Another possible selection threat was that individuals were not assigned to a group randomly but were assigned instead based on their ethnicity; this could have resulted in non-equivalent study groups. However, analysis of the sample demographics indicates that the two groups were comparable on all factors except one; that factor, nocturnal awakenings, was reported with greater frequency in the African American group. This demographic information was not verified by PEF monitoring since it was not a part of the study design.

Factors that are known to limit perception include age, duration of asthma, speed of bronchoconstriction, changes in lung volumes, and anxiety level (Burdon, et al., 1982; Boulet, et al., 1994). Burdon, et al., (1982) and Brand, et al., (1992) demonstrated an association between a lowered perception of breathlessness and temporal adaptation in adult asthma patients (over 60 years). However, age is unlikely to have affected the findings of the current study since the mean age of the two groups was 34.5 ± 9.7 years (Boulet, et al., 1994). The second factor, duration of asthma, could have biased the outcomes since the degree of concern a person assigns to a symptom is associated with how long they have had asthma. All of the subjects had mild disease, and mild disease is characterized by symptoms that "come and go"; however, information on the duration of asthma was not collected as part of the study design. Finally, anxiety was not assessed as part of the study design, though several subjects in both groups used word descriptors at PC30 and after 4 puffs of albuterol suggestive of anxiety. Expressions of anxiety by subjects experiencing significant airflow obstruction (PC30) are not unreasonable. This is not to suggest that anxiety was not present but rather that the measurement tools were not designed to measure anxiety. As noted above, one additional factor, nocturnal awakenings, was

reported by African American subjects with greater frequency. Nocturnal awakenings may indicate poor control of asthma symptoms or increased asthma severity (Janson-Bjerklie, et al., 1992; Storms, et al., 1989). To rule out nocturnal awakenings as a confounder, more definitive and complete data on the frequency of symptoms associated with nocturnal awakenings is required.

Some asthma subjects are highly intolerant to very mild levels of airflow obstruction whereas others tolerate very high levels. The idea that symptoms are tolerated or accepted as normal has been noted in studies of African American children with asthma (Crain, et al., 1994). It would be important to determine if the same symptom acceptance is true for adults and, if so, if this factor would affect their perception of bronchoconstriction. The asthma severity/risk index tool does measure this aspect of symptom perception (Janson-Bjerklie, et al., 1992) and utilizing this tool in a future study has merit.

Another important limitation is that some subjects were not naive subjects to the provocation test. One approach to assess if prior exposure to the challenge procedure affected the perception of breathlessness or the use of word descriptors would be to analyze the data for this factor. Conversely, recruiting only naive subjects to participate in a bronchoconstrictor study would be difficult. Subjects with varied exposure to the challenge procedure are commonly found in studies of this type (Boulet, et al., 1994; Turcotte, et al., 1993).

## Implications for Nursing

This study has wide application to nursing because the symptom experience is an integrative and essential component of clinical nursing practice. Currently, many people with asthma are at risk of dying from acute asthma exacerbation due to undertreatement of the disease. African Americans, in particular,

experience more frequent life threatening episodes related to asthma, and mortality from asthma is higher for them than for any other ethnic group; and the prevalence of asthma among African Americans is increasing. Though ethnicity alone is not a contributing factor to the incidence of asthma-related deaths, the findings reported here suggest that differences between African Americans and Caucasians in the clinical presentation of symptoms are significant despite experiencing the same intensity of breathlessness. For these reasons it is imperative to determine and understand if there are any ethnic differences in the perception and language of breathlessness. Clinicians need to be aware that the report of upper airway symptoms in African American people with asthma may be a very typical presentation of acute airflow obstruction.

The FEV1 measurements provide an objective measure of the differences in the perception of breathlessness between the two ethnic groups. Primarily, it is a subject's personal assessment and perception of a symptom, in this case breathlessness, that influences his/her health seeking behavior and, more importantly, management strategies. A patient's personal interpretation, perception, and assessment of a symptom, e.g., breathlessness, determines how he/she manages and controls his/her symptoms. An understanding of how ethnic differences influence both the perception of breathlessness and the reporting of symptoms should result in the development of more appropriate and ethnically sensitive clinical approaches to symptom management and more intensive attempts at appropriate diagnosis and treatment of acute airflow obstruction. To effectively help African Americans manage their asthma symptoms, we will need to begin by revamping present educational content about symptom management.

This study provides valuable and insightful new information regarding ethnic differences in the language of breathlessness. Taking this information and applying it to clinical practice is the next step.

## Future Research

Future research plans include exploring further ethnic differences in the perception of breathlessness. This study, in many ways, has served as a pilot study; the study outcomes will determine changes in the study design and in approaches to the measurement of breathlessness. The word descriptors identified in the study findings emphasize that ethnic differences in the language of breathlessness do exist. The word descriptors that were significant will form a word descriptor questionnaire specific to African Americans with asthma. This word descriptor questionnaire will then serve as a measurement tool for future study. Hopefully, through testing, a valid and reliable word descriptor questionnaire applicable to African Americans with asthma will result. The desired outcome is to both influence and promote the need for ethnically sensitive approaches to asthma management.

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# Appendix A:
# Human Research Documents

- CHR Approval Letter

- UCSF Consent to Act as a Research Subject

COMMITTEE ON HUMAN RESEARCH
OFFICE OF RESEARCH AFFAIRS, Box 0962
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

# CHR APPROVAL LETTER

TO: Susan Janson, D.N.Sc., R.N.
Box 0608

Grace Hardie, M.S., R.N.
School of Nursing
N611Y

RE: Perception of Symptoms During Induced Bronchoconstriction among African-American and Caucasian Asthmatics

The Committee on Human Research, the UCSF Institutional Review Board holding Department of Health and Human Services Multiple Assurance #M-1169, has reviewed and approved this application to involve humans as research subjects.

**APPROVAL NUMBER:** H7664-12785-01. This number is a UCSF CHR number and should be used on all consent forms, correspondence and patient charts.

**APPROVAL DATE:** June 5, 1996. **Full Committee Review**

**EXPIRATION DATE:** June 1, 1997. If the project is to continue, it must be renewed *by the expiration date*. See reverse sid · · · details.

**ADVERSE REACTIONS/COMPLICATIONS:** All problems having to do with subject safety must be reported to the CHR within ten worl· g days.

**MODIFICATIONS:** All protocol changes involving subjects must have prior CHR approval.

**QUESTIONS:** Please contact the office of the Committee on Human Research at (415) 476-1814 or campus mail stop, Box 0962.

Sincerely,

Reese T. Jones, M.D.
Chairman
Committee on Human Research

cc: Drug Information and Analysis Service

Project # 96012785

# University of California, San Francisco
## Consent to Act as A Research Subject

JUN 5 1996

**Perception of Symptoms during Induced Bronchoconstriction among African-American and Caucasian Asthmatics**

Purpose: Susan Janson, DNSc, ANP, RN , principal investigator, from the School of Nursing and Grace Hardie, Ph. D (Cand.), MS, RN are conducting a research study to learn if the perception of bronchoconstriction (such as breathing difficulty or airway tightness) is different and if the sensation of asthma symptoms are described differently by African-Americans and Caucasians. I am asked to participate in this study because I have mild asthma and I am currently taking an inhaler for my asthma symptoms.

Procedures: If I agree to participate the following procedures will occur:

(1) Spirometry
(2) Methacholine Challenge
(3) Bronchodilator Challenge
(4) Allergy Skin Test [if needed]
(5) Borg Scale and Visual Analog Scale to measure my breathing
(6) Word Descriptor Questionnaire

To participate in this research study, women of childbearing potential must not be pregnant and must be using a medically acceptable form of birth control during study participation. Pregnancy during the course of the study will be reason for ending participation.

## Protocol

I will have only one visit and this visit will take about two to three hours. I will be asked not to use my inhaler for 8 hours and to avoid caffeine ( such as coffee, cola, and tea) and alcohol for 8 hours before my appointment time. If I am taking an antihistamine (such as actifed or sudafed) or a theophylline medication (such as theodur, theolair or slophylline) I cannot take them for 24 hours before my appointment. If I believe I must use my medication (s) before my visit I will call and reschedule my appointment.

### A. Procedures:

After arriving in the lung function laboratory I will rest for ten minutes; during that time my blood pressure, heart rate, and pulse rate will be taken. I will be asked to fill out an asthma symptom and health history questionnaire. This is a six page questionnaire that will ask questions on how my asthma interferes with my daily activities. This form will take fifteen minutes to fill out.

If I am female, I will be asked for a urine sample for a pregnancy test.

I will have a allergy skin test during this visit, if needed. I will have fourteen drops of dissolved extract of common allergens (such as grasses, pollen, and trees) placed on my forearm (s) and my skin will be lightly pricked with a sterile disposable needle. Fifteen minutes later my skin will be inspected for localized redness and swelling and this information will be recorded.

During this visit I will have a routine test of my breathing function called a spirometry. During the spirometry I will be asked to wear a noseclip and to breathe out forcefully into an instrument that will measure the amount of air that I can blow out in one breath. I may be excluded from study participation after the spirometry if the results of my breathing function test does not meet the eligibility criteria. This procedure will take about five to ten minutes.

After the spirometry, I will have a methacholine challenge test. This test measures the sensitivity of my airways (bronchial tubes) by determining how much they narrow after I breathe in gradually increasing doses of a methacholine aerosol, a drug that causes narrowing of the airways. With each methacholine dose, I will be asked to inhale five times and three minutes after the fifth dose I will have the spirometry repeated. This sequence will be repeated at five minute intervals until it is determined what dose of methacholine causes my breathing function to decrease 30% from my original lung function. Immediately, upon reaching a 30% decrease in my breathing function, I will receive two puffs (180 mg) of albuterol and I will have my spirometery rechecked in fifteen minutes to ensure that my lung function has returned to normal. I will receive an additional two puffs (180 mg) of albuterol if my lung function has not returned to normal. This procedure will take about forty five to sixty minutes.

I will have a bronchodilator challenge. This test measures how well my airways (bronchial tubes) open up after I am given increasing doses of a bronchodilator medication (albuterol). This is a drug that is commonly used to open up or dilate the airways of the lung. I will be given 2 puffs of albuterol through a small spacing tube that holds the medication; this tube will allow me to breath the medication in slowly and deeply. Fifteen minutes later I will have my spirometry checked. This sequence will be repeated every 15 minutes until my airways do not open up or dilate any further. That is, there is not any further improvement in the amount of air that I can blow out in one second. I will have my pulse rate and respiratory rate checked routinely during this test. This procedure will take about forty five to sixty minutes.

During both the methacholine and bronchodilator challenge I will be asked to mark the change in my breathing on two different forms. I will also be asked to describe in my own words the sensation (s) of my asthma symptoms during each of the challenge procedures.

## Risks and Discomforts

<u>Allergen Skin Test:</u> This is a common test for allergy and carries the risks of itching and burning at the skin site, and the discomfort of the needle prick. In extremely rare cases exposure of allergic people to allergen can result in "anaphylaxis", a serious

combination of medical problems including severe asthma resulting in shortness of breath, hives, swelling of the skin or tongue, and a fall in blood pressure. In very rare instances anaphylactic reactions can result in death. This is extremely unlikely if treatment is started promptly. Facilities and medications are available for treatment in the laboratory and a physician is nearby when the skin test is performed.

Withholding of the Inhaler and Other Medication (s) prior to the study visit: This may cause an increase in my asthma symptoms such as chest tightness, shortness of breath, or wheezing. If these symptom (s) make me uncomfortable then I should take my asthma medication (s). I will then call and reschedule the visit.

Spirometry: These forced maneuvers of blowing out air fast can be associated with a temporary cough or lightheadedness.

Inhalation of Methacholine: This may cause coughing, chest tightness, and shortness of breath. These symptoms usually go away over 10-15 minutes without treatment and can be reversed quickly by treatment with one or two puffs of an albuterol inhaler.

Inhaled Beta Agonist: Albuterol is a standard treatment for asthma and it may cause an increase in heart rate or tremors if taken in excess. Taken in the doses recommended for this study, albuterol is of little risk of serious side effects.

Confidentiality of Records: Participation in research may involve a loss of privacy. However, my records will be kept as confidential as possible and no individual identities will be used in any reports or publications resulting from this study. All records will be coded, and kept in locked files so that only study investigators have access to them.

Treatment and Compensation for Injury Policy: If I am injured as a result of being in this study, treatment will be available. The costs of such treatment may be covered by the University of California, depending on a number of factors. The University does not normally provide any form of compensation for injury. For further information about this, I may call the office of the Committee on Human Research at (415) 476-1814 or write: Committee on Human Research, Box 0962, UCSF, San Francisco, Ca. 94143.

Benefits: I will not directly benefit from taking part in this study. The knowledge I obtain may increase my understanding of asthma and may help me to develop self management strategies to better control my symptoms.

Reimbursement: I will receive $40.00 for my study participation. I must provide my name, address, and social security number so that the accounting office can issue a check. The check will be mailed to my home address and it will take four to six weeks to receive the check.

Costs: Neither I nor my insurance carrier will be charged for any costs relating to my participation in this study.

**Questions or Problems:** The information on this consent form was explained to me by Grace Hardie, Ph. (Cand.), MS, RN. I should report to Grace Hardie any problems I have that relate to this study. For questions related to this study I may call Grace Hardie, MS, RN at : (510) 451-6522 or 654-1620 or page her at: (510) 539-0488. Or I may call Dr. Susan Janson at : (415) 476-5282. To use the pager: first, I will dial in the area code of the pager followed by the pager number. Secondly, I will hear two 'beeps' then I will dial in my area code followed by my telephone number and then I will press the pound sign (#) on my telephone. After I hear the statement 'thank you for calling' I may hang up my telephone receiver. It will take several minutes for my page to go through to the actual pager. Before leaving the laboratory, I will receive a demonstration on how to dial the pager number and how to leave a message/ phone number on the pager .

**Consent:** Participation in research is voluntary. I have been given a copy of the Experimental Subject's Bill of Rights and this consent form to keep. I may decline to enter this study or I may withdraw from it any time without jeopardizing my status as a student, patient, or employee of the University of California, San Francisco.

Date:_____Subject's Signature:_____

Date:_____Person Obtaining Consent:_____

# Appendix B:
# Study Instruments

- Borg Scale
- Visual Analogue Scale
- Word Descriptor
- Bronchodilator Use Question

# Perception of Symptoms

Subject ID:_____ Date:_____

Subject's Initials:_____ Procedure:_____

Time procedure began:_____am/pm Dose:_____

Time of questionnaire:_____am/pm Responded at:_____

## Modified Borg Scale

| | |
|---|---|
| 0 | Nothing at all |
| 0.5 | Very, very, slight (just noticeable) |
| 1 | Very slight |
| 2 | Slight |
| 3 | Moderate |
| 4 | Somewhat severe |
| 5 | Severe |
| 6 | |
| 7 | Very Severe |
| 8 | |
| 9 | Very, very severe |
| 10 | Maximal |

Subject ID:_____ Date:_____

Procedure:_____ Time procedure began:_____am/pm

Dose:_____ Minutes after dose:_____

Time of questionnaire:_____am/pm Responded at:_____

## Perception of Symptoms

not breathlesss |_____| extremely breathless

# Word Descriptors of Symptoms

**Subject ID:**_____ **Date:**_____

**Subject's Initials:**_____ **Procedure:**_____

**Time procedure began:**_____**am/pm** **Dose:**_____

**Time of questionnaire:**_____**am/pm** **Responded at:**_____

After each dose of the inhaled solution, I will ask you to describe in your own words the sensation you are feeling at this time. You may use as many words as is necessary to explain the sensation (s) you are experiencing. There are no correct answers. I am interested in the word or words that best describe (s) the sensation you are feeling in regards to your breathing. I am interested in **your personal description** of the sensation you are feeling at this point in time.

**Your Words:**

_____

_____

_____

_____

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_____

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_____

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_____

GH/ 10.1.96

## Question at Maximal Bronchoconstriction

**Subject ID:**_____ **Date:**_____
**Subject's Initials:**_____ **Time:**_____
**Mch Dose:PC15**_____**PC20**_____**PC30**_____

**<u>When the subject reaches PC15; PC20; PC30:</u>**

**If you felt this way at home would you take your inhaler?**

**Response:**

**PC15**_____

**PC20**_____

**PC30**_____

GH/ 7.28.96

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For reference

Not to be taken from the room.

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