ADVERSE RESPIRATORY HEALTH EFFECTS OF COMPETITIVE SWIMMING: THE PREVALENCE OF SYMPTOMS, ILLNESSES, AND BRONCHIAL RESPONSIVENESS TO METHACHOLINE AND EXERCISE

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ABSTRACT

Indoor swimming pools, with their high ambient temperatures and relative humidity, contain a number of volatile chemicals that are known irritants, sensitizing agents, and possible carcinogens. While swimming may improve fitness and reduce morbidity associated with asthma, there is both anecdotal and scientific information to suggest that there are health-related problems associated with swimming in chemically-treated pool water. Competitive swimmers are especially susceptible to the adverse effects of chemically-treated pool water because of the number of hours they spend training in this environment and the increase in ventilation that occurs with exercise. While case reports of respiratory and other health-related problems are common, there have been no epidemiological studies that have surveyed competitive swimmers about the prevalence of health-related problems or the prevalence and severity of clinical symptoms.

The purpose of this study was to determine the prevalence of respiratory and other health-related symptoms, illnesses, and allergies among competitive swimmers using a questionnaire, and to establish whether the symptoms were associated with swimming-related exposure. In order to determine how these symptoms and illnesses manifest themselves clinically, a group of lower mainland swimmers and non-swimmers also completed pulmonary functions studies, a methacholine challenge test, and exercise studies in the laboratory and swimming pool.

Our results show that competitive swimmers have a high prevalence of asthma that, in national and international level swimmers, appears to have developed after they began competitive swimming. There was also a high prevalence of exercise-related respiratory symptoms that were strongly associated with swimming-related exposure. Nearly all of the competitive swimmers had normal pulmonary function tests, however, 60% of the swimmers

were found to have increased non-specific bronchial responsiveness (BHR) to methacholine. There was no difference in the prevalence of BHR among swimmers with or without asthma and/or exercise-related symptoms, however, the prevalence of BHR was significantly higher in swimmers than in non-swimmers. The prevalence of exercise-induced asthma (EIA) was higher running or cycling in the laboratory than during tethered swimming in the pool. There was no difference in the prevalence of EIA among swimmers and non-swimmers during the laboratory testing.

These results suggest that swimming related exposure, as determined by the amount of time spent swimming or the distance covered during training sessions in the swimming pool, increases non-specific bronchial responsiveness without affecting baseline pulmonary function or short-term exercise responses. Longer exposures may lead to the development of upper and lower respiratory tract symptoms, and the adoption of a restrictive breathing pattern in susceptible individuals. We propose that differences in the clinical presentation of these competitive swimmers may be dependent on the presence of atopy, underlying respiratory illnesses such as asthma, the pre-existing level of bronchial responsiveness, and the extent of the swimming-related exposure. It is possible that chronic, low level exposure to the chemicals used to disinfect swimming pool water may, ultimately, be responsible for our clinical and exercise-related findings.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ANOVA	analysis of variance
ATPS	ambient temperature and pressure saturated with water vapour
β	beta
BAL	broncho-alveolar lavage
BC	British Columbia
BHR	bronchial hyperresponsiveness
BTPS	body temperature and pressure saturated with water vapour
CA	California
CCK	cholecystokinin
CO_2	carbon dioxide
COPD	chronic obstructive pulmonary disease
EIA	exercise-induced asthma
CCl_4	carbon tetrachloride
CCl_3CH_3	1,1,1-trichloroethane
CCl_2CHCl	trichloroethylene
CCl_2CCl_2	tetrachloroethylene
$CHBr_3$	bromoform
CH_2BrCl	bromochloromethane
$CHBrCl_2$	bromodichloromethane
$CHBr_2Cl$	chlorodibromomethane
$CHCl_3$	chloroform
CH_2Cl_2	dichloromethane

CH_2ClCH_2Cl	1,2-dichloroethane
cm	centimetres
°C	degrees celsius
ECG	electrocardiography
f	respiratory frequency
FEF_{25-75}	mid maximum expiratory flow rate
FEV_1	forced expiratory volume in 1 second
FVC	forced vital capacity
gm	gram
HOCl	hypochlorous acid
HR	heart rate
HRF	histamine releasing factor
IgE	immunoglobulin E
IgG	immunoglobulin G
IgM	immunoglobulin M
IL	Illinois
IL	interleukin
kg	kilograms
L	litres
L/sec	litres per second
LT	leukotrienne
log	logarithm
MET_{dose}	final cumulative dose of methacholine

$\bar{x}$	mean
mg	milligram
μg	micrograms
min	minute
mL	millilitre
MMC	metabolic measurement cart
MN	Minnesota
MO	Missouri
N_2	nitrogen
NANC	non-adrenergic, non-cholinergic
NC	North Carolina
NCFA	neutrophil chemotactic factor of anaphylaxis
NH_2Cl	chloramide
$NHCl_2$	chlorimide
NC	North Carolina
NCl_3	chlorine azide
No.	number
NO_2	nitrogen dioxide
O_2	oxygen
O_3	ozone
OCl^-	hypochlorite ion
ON	Ontario
PAF	platelet activating factor

PC_{20}	provoking concentration of methacholine causing a 20% fall in FEV_1
PG	prostaglandin
ppm	parts per million
PQ	Quebec
prob	probability
R	respiratory exchange ratio
RADS	reactive airways dysfunction syndrome
RHL	respiratory heat loss
ΣT	total time
SO_2	sulfur dioxide
SEM	standard error of the mean
SVC	slow vital capacity
SD	standard deviation
Tx	thromboxane
UBC	University of British Columbia
UK	United Kingdom
US	United States
USEPA	United States Environmental Protection Agency
$\dot{V}CO_2$	carbon dioxide production
$\dot{V}E$	minute ventilation
VIP	vasoactive intestinal peptide
$\dot{V}_{max}$	maximum expiratory flow rate
$\dot{V}O_2$	oxygen consumption

$\dot{V}O_2max$	maximal oxygen consumption
V_T	tidal volume
WA	Washington
WI	Wisconsin

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The task of completing a doctoral thesis is not an easy one. When you attempt to complete an interdisciplinary thesis in an applied faculty it is even more difficult. The best advice I could give anyone who intends to complete such a thesis is to research their topic thoroughly and choose their research chairman and committee members judiciously! I am extremely grateful for the time and effort that my committee members were able to give me. In-spite of their hectic academic and clinical schedules, they always had time to discuss my thesis with me and resolve any problems that I had.

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GENERAL INTRODUCTION

As we near the end of the 20th century, we are becoming increasingly aware of how environmental issues affect our health. This concern has evolved to include our working environment and its potential for fostering occupational illnesses. The evidence is persuasive that the workplace environment is responsible for occupational illnesses such as pneumoconioses (asbestosis, silicosis, berylliosis and other dust diseases of the lung), asthma, and a variety of neurologic and psychological illnesses (Landrigan and Baker, 1991; Rom, 1983; Rutstein et al., 1983).

Occupational illnesses are underdiagnosed and many are incorrectly attributed to other causes (Landrigan and Baker, 1991). This reflects the fact that many work-related illnesses are not clinically distinct from diseases due to other causes (Goldman and Peters, 1981), and because there is usually a long latency between exposure to the causative agent and the appearance of symptoms or the illness (Rosenstock and Landrigan, 1986). As a result of these concerns, the focus of epidemiological research is shifting from the avoidance of disease among highly exposed individuals toward the protection of the general population from an unacceptable burden of disease at much lower exposures (Samet and Utell, 1991). In addition, the development of more sensitive methods for identifying causative agents is now allowing researchers to also focus on environmental exposures which may be associated with work-related illnesses.

The study of environmental illnesses is now extended to include the milieu in which we pursue our recreational interests. We know that outdoor activities in cities with high levels of photochemical air pollution can be problematic and incite respiratory problems. However, the possibility of occupational-like illnesses occurring in indoor recreational facilities is relatively new and merits our scientific interest and intervention.

One of the diseases with "environmental" causation is asthma. When asthma is diagnosed, particularly in the young, physicians frequently advise against participating in certain forms of exercise in order to reduce the risk of the patient developing the symptoms associated with exercise-induced asthma (EIA). There are numerous scientific articles which have reported the beneficial effects of swimming in subjects with asthma. Training in the swimming pool has been shown to improve the fitness level of asthmatics (Fitch et al., 1976; Schnall et al., 1982) and to reduce the frequency of asthma attacks, airway resistance, frequency of wheezing, need for medication, visits to the emergency room of a hospital, and absenteeism from school (Huang et al., 1989). While swim training may improve fitness and reduce morbidity associated with asthma, there is both anecdotal and scientific information to suggest that there are health-related problems associated with swimming in chemically-treated pool water.

The indoor swimming pool environment, with its high ambient temperature and relative humidity, contains a number of volatile chemicals that are known irritants, sensitizing agents and possible carcinogens. Competitive swimmers are especially susceptible to the adverse effects of chemically-treated pool water because of the number of hours they spend swimming in this environment and the increased minute ventilation that occurs with exercise. While anecdotal reports of respiratory and other health-related problems are common, there have been no epidemiological studies that have surveyed competitive swimmers about the prevalence of respiratory and other health-related problems or the prevalence and severity of clinical symptoms. The first Chapter of this thesis provides a descriptive profile of competitive swimmers from Canada, the United States, and a number of Pacific Rim countries. Included in the profiles of these swimmers are the prevalence of respiratory and other health-related symptoms and illnesses, as well as information about their training.

The chemicals used to treat the pool water may cause irritation or sensitization of the airways. This may lead to the manifestation of respiratory symptoms and increased bronchial responsiveness during or after exercise in the swimming pool. In the second chapter, the prevalence of bronchial hyperresponsiveness among two groups of competitive swimmers, those who have asthma and/or pool-associated symptoms and those who have neither asthma nor pool-associated symptoms, is determined using a methacholine challenge test. The prevalence of bronchial hyperresponsiveness is also determined for a group of non-swimming, athletic control subjects in order to assess whether competitive swimmers have a higher prevalence of bronchial hyperresponsiveness than non-swimmers.

The anecdotal reports of respiratory and other health-related symptoms may be due to chemical treatment of the pool water, exercise, or both. In the presence of chemical irritants or sensitizing agents, an exercise broncho-provocation test in the swimming pool may be used to induce symptoms or changes in lung function that are not elicited during laboratory studies. In the third chapter, a standard clinical test is used to determine the prevalence of EIA in the laboratory and in the swimming pool among two groups of competitive swimmers, those who have asthma and/or pool-associated symptoms and those who have neither asthma nor pool-associated symptoms. The prevalence of EIA in the laboratory is also determined for a group of non-swimming, athletic control subjects. In addition, a 45 minute exercise broncho-provocation test will be used to evaluate the effects of continuous, low intensity swimming on post-exercise lung function in both groups of competitive swimmers.

Each of these studies was approved by the University of British Columbia's Clinical Screening Committee for Research and Other Studies Involving Human Subjects (Certificate C91-007).

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CHAPTER 1

The Prevalence of Respiratory Symptoms and Other Health-Related Problems in Competitive Swimmers

ABSTRACT

Respiratory illness associated with occupational or environmental exposures include a wide variety of conditions, ranging from acute reversible symptoms to chronic disabling lung disease. The indoor swimming pool environment, with its high ambient temperature and relative humidity, contains a number of volatile chemicals that are known irritants, sensitizing agents, and possible carcinogens. Competitive swimmers are especially susceptible to the adverse effects of chemically-treated pool water because of the number of hours they spend training in this environment and the increase in ventilation that occurs with exercise. While anecdotal reports of respiratory and other health-related problems are common, there have been no epidemiological studies that have surveyed competitive swimmers about the prevalence of respiratory and other health-related problems or the prevalence and severity of clinical symptoms.

The purpose of this study was to determine the prevalence of respiratory and other health-related symptoms, illnesses, and allergies among competitive swimmers from across Canada, the United States, and a number of Pacific Rim countries. In addition, we wanted to establish whether the respiratory symptoms were associated with a swimming-related exposure as determined by the amount of time spent swimming, or the distance covered, during training sessions in the swimming pool.

A total of 738 competitive swimmers completed the questionnaire which represents a participation rate of 65.8%. A high percentage (43.5%) of the swimmers had at least one chest illness that kept them from participating in their normal daily activities for 3 days or more during the past year. The overall prevalence of physician-diagnosed asthma among the competitive swimmers was 13.4%, but was as high as 20.6% in swimmers who participated at an international level. Many of the younger swimmers had their asthma diagnosed before they started competitive swimming, while the older, more accomplished swimmers had their asthma diagnosed after they started swimming. The prevalence of bronchitis (24.9%) and pneumonia (10.2%) is slightly higher, and hay fever (16.9%) slightly lower, than that reported for the general population. The most common allergies reported were to dust, pollen, animal hair, grasses, and molds, and the prevalence of allergies is similar to those reported for high performance athletes as well as the general population.

Almost all of the exercise-related symptoms were associated with the swimming-related exposure. We also identified a number of gender- and age-related differences for several of the exercise-related symptoms. Female swimmers were more likely to cough, feel congested, have difficulty breathing, and experience headaches. Older swimmers were more likely to feel congested, sneeze, wheeze, have chest tightness or a sore throat, difficulty breathing, and headaches. A majority of the swimmers with exercise-related symptoms reported that their symptoms were less severe, less noticeable, or absent if they spent several days away from the swimming pool.

Cigarette smoking is extremely uncommon among competitive swimmers and is significantly lower than that reported for the general population. Prescription medication is used by more than 21% of the swimmers, and the trend in medication use tends to support the high

prevalence of asthma, allergies, and respiratory symptoms, among the swimmers. The use of certain medications is also suggestive of a number of skin-related problems such as eczema, contact dermatitis, and psoriasis. Finally, nearly 74% of the swimmers smell a strong chemical odor in the swimming pool that they associate with respiratory and other health-related symptoms.

INTRODUCTION

Little is known about the effects of acute or chronic exposure to chemically-treated pool water on the short- and long-term health of swimming pool users. Competitive swimmers, tri-athletes, fitness swimmers, lifeguards, coaches, instructors and young children in swimming classes are examples of individuals who may be affected (Sutherland, 1992). Anecdotal reports of respiratory distress and irritation of the airways and lungs are common among competitive swimmers, although the prevalence of respiratory symptoms and illnesses has not been established for this group. Competitive swimmers often complain of upper respiratory tract and other health-related symptoms such as coughing, chest tightness, wheezing, dyspnea, headaches, nausea, lethargy and irritation of the eyes, nose and throat.

In some instances, competitive swimmers have stopped using swimming pool facilities because of medical problems associated with the indoor pool environment (Laverdure, 1991; Sutherland, 1992). Swimming-pool water is disinfected in the interests of public health, but it would appear that disinfection of the pool water with chlorine may be the cause of the respiratory symptoms (Mustchin and Pickering, 1979; Palin, 1974; Penny, 1983; Zwick et al., 1990).

Evidence suggests that exposure to chlorine, derivatives of chlorine, chloroform or chloramines causes edema of the mucous membranes of the respiratory tract and lung; alteration, degeneration and desquamation of the columnar epithelial cells; and severe inflammatory reactions (Kummer, 1975; Wood et al., 1987). The concentration of chloroform in alveolar air and blood samples of competitive swimmers has been found to vary directly with that found in the pool water and surrounding air, the number of swimmers in the pool, the length of time spent swimming and with the intensity of exercise (Aggazzotti et al., 1990;

Aggazzotti et al., 1993). Chloroform is not only a respiratory tract irritant, but is also a suspected carcinogen.

Frequent exposure to these irritants may make the airways more susceptible to allergens, cause bronchial hyperresponsiveness, and may lead to the development of asthma (Penny, 1983; Zwick et al., 1990). Competitive swimmers have been shown to have a higher prevalence of allergic diseases and sub-clinical sensitization to aeroallergens, disorders of the immune system and bronchial hyperresponsiveness in comparison with control subjects (Mustchin and Pickering, 1979; Zwick et al., 1990). The development of clinical symptoms and bronchial hyperresponsiveness may also be due to, or enhanced by, the presence of underlying respiratory disease (Mustchin and Pickering, 1979).

Rose (1992) has implicated extrinsic allergic alveolitis as a cause of swimming pool-related lung disease in a group of lifeguards who worked at an indoor swimming pool with poor air quality, a strong chloramine odor and numerous water sprays and fountains. The outbreak of extrinsic allergic alveolitis in these lifeguards was attributed to the presence of high levels of an endotoxin, a component of gram negative bacterial cell walls, in both air and water samples taken from the swimming pool.

Indoor swimming pools, with their high ambient temperatures and relative humidity, represent an environment where operational failures in water quality management or deficiencies in the ventilation system could cause a number of health-related problems. Recent innovations in aquatic recreation technology, increased use of existing facilities and the introduction of "energy efficient" ventilation systems complicate air and water quality management in these facilities.

As discussed above, disinfection of the pool water with chlorine generates the chemical irritants that are found in the water and air of indoor pools. Several other types of disinfection are available. They include bromination, ozonation, ionization of silver and copper atoms, ultraviolet radiation and the use of hydrogen peroxide, iodine and chlorine dioxide. However, none has yet proved to be as effective or economical as chlorination.

A number of chemicals are added to the pool water to control the pH, alkalinity, and water hardness. Swimmers add a number of contaminants to the pool water. These include sweat, urine, hair-spray, body lotion and other secretions. The chemicals used to treat the pool water mix with these contaminants and undergo a series of complex chemical reactions that result in the formation of simple and complex halogenated compounds and other organic and inorganic oxidation by-products.

Since swimmers breathe the air just above the surface of the water they are exposed to a number of chemicals that could cause irritation of the airways and lungs. All of these chemicals have the following properties: (1) high volatility; (2) chemical stability; and (3) a generation process that is compatible with the environmental conditions of the pool water (Shaw, 1987).

Active chlorine species are found in measurable concentrations in indoor pool environments (Scotte, 1984). At the pH found in pool water (7.2 to 7.8), chlorine is completely hydrolysed to hypochlorous acid (HOCl) and hypochlorite ion (OCl^-). Of these, chlorine gas is not volatile, HOCl has very low volatility and OCl^- is not volatile at all (Holzwarth et al., 1984). The relative distribution of HOCl and OCl^- in the water is very important because HOCl is 40 to 80 times more efficient as a disinfecting agent than OCl^- is (Metcalf and Eddy, 1979).

The addition of cyanuric acid as a stabilizing agent for free chlorine has been widely used in swimming pool disinfection since the mid 1950s (Feldstein et al., 1985). Cyanuric acid reacts with chlorine to form mono-, di- and trichloroisocyanurate depending on the pH of the water and the concentration of free chlorine. Cyanuric acid acts as a reservoir for free chlorine in solution; that is, as free chlorine is consumed, more free chlorine is released from chlorinated isocyanurates. Studies in swimming pools indicate that chlorinated isocyanurates are at least as effective as chlorine in bactericidal efficiency (Linda and Hollenback, 1978). Chlorinated isocyanurates are thought to generate HOCl.

The irritating effects of the indoor pool environment are attributed to the presence of chloramines (Jessen, 1986; Lahl et al., 1981; Metcalf and Eddy, 1979; Shaw, 1987). These include the inorganic compounds chloramide (NH_2Cl), chlorimide ($NHCl_2$), and chlorine azide (NCl_3). These compounds are formed by the chlorination of ammonia derived from the urine and sweat of swimming pool users, however, they contain very small amounts of free ammonia. NH_2Cl is stable only in the presence of an excess of ammonia, it has low volatility and it does not exist in the presence of free chlorine, so it is generally absent from pool water. $NHCl_2$ is extremely unstable at the pH of pool water and in the presence of free chlorine, it is slightly more volatile than NH_2Cl, but does not appear to persist in the atmosphere. NCl_3 is stable at low concentrations in water only in the presence of a large excess of free chlorine, is highly volatile, however, it does not appear to persist in the atmosphere (Shaw, 1987).

Chlorine is known to react with specific amino acids to form either formaldehyde or acetaldehyde (Hrudey et al., 1988,1989; Laverdure, 1991). Under conditions of high chlorine to amino acid ratios, nitriles can also be formed (Hrudey et al., 1988, 1989). Formaldehyde vapours are known to cause sore throats, nausea, and irritation of the respiratory tract and eyes.

Contact with the skin causes irritation and allergic sensitization (EPS, 1985). These symptoms may occur at airborne levels as low as 0.05 ppm in very sensitive individuals such as infants, children, the elderly and those with pre-existing allergies or respiratory illnesses. Chronic low-level exposure to formaldehyde may lead to the development of cancer (Turoski, 1985).

Aldehydes are highly reactive reducing agents: acetaldehyde forms covalent bonds with many biologically important organic molecules, destroying their function. At high concentrations, acetaldehyde appears to paralyse respiratory muscles and its general narcotic action prevents coughing. It is also known to cause irritation of the eyes and mucous membranes, skin and respiratory tract (USEPA, 1987). Prolonged exposure causes headaches, sore throats, a decrease in red blood cell mass, an increase in heart rate and a sustained increase in blood pressure (Mark et al., 1978).

Research by several investigators has demonstrated the presence of a number of halogenated hydrocarbons in pool water. These chemicals are both volatile and chemically stable. Their generation increases proportionally with the number of swimming pool users and the available chlorine. Many of these chemicals cause acute respiratory distress and irritation of the eyes, nose and throat (see Table 1). These chemicals are also known to be common industrial and office air contaminants and are found in chlorinated drinking water (Cotruvo and Wu, 1978; Otson et al., 1983).

Outbreaks of enteroviral infections, skin lesions and rashes, respiratory tract problems, fever, headaches and fatigue are also associated with the presence of micro-organisms in the pool water (Davis, 1985; Laverdure, 1991; Lenaway et al., 1989). These usually occur in hot tubs, whirlpools and spa pools that are heated to a temperature above 37°C, but may also occur in community and private swimming pools where the water temperature is well below 37°C

(Laverdure, 1991; Lenaway et al., 1989; Strauss et al., 1988). Several microbial indicators of inadequate disinfection of swimming pool water have been reported in the literature. Elevated levels of total coliforms, faecal coliform, faecal streptococci, total bacterial counts and yeasts are associated with increased risk for infection (Tosti et al., 1988). Others have suggested that elevated levels of pseudomonas aeruginosa, amoebae (Esterman et al., 1987) and mycobacterium marinum may be problematic as well (Fisher, 1988).

While anecdotal reports of respiratory and other health-related problems are common, there have been no epidemiological studies that have surveyed competitive swimmers about the prevalence of respiratory and other health-related problems or the prevalence and severity of clinical symptoms. The purpose of this study was to determine the lifetime prevalence of respiratory and other health-related symptoms, illnesses, and allergies in competitive swimmers from across Canada, the United States, and a number of Pacific Rim countries. In addition, we wanted to establish whether the respiratory symptoms were associated with a swimming-related exposure as determined by the amount of time spent swimming, or the distance covered, during training sessions in the swimming pool.

Table 1: Properties of volatile halogenated hydrocarbons found in swimming pool water. At values above 10^{-3} atm·m^3/mole, chemicals are readily volatilized from water. (Adapted from Laverdure, 1991; Shaw, 1987).

Compounds	Chemical Formula	Henry's Law Constant atm·m^3/mole @ 25°C	Health Effects in Air	B.C. Occupational Limits 8 h Exposure		15 min Exposure	
				ppm	mg/m^3	ppm	mg/m^3
Chloroform	$CHCl_3$	4.35×10^{-3}	eye and mucous membrane irritation	10	50		
Bromodichloromethane	$CHBrCl_2$	1.60×10^{-3}	eye and mucous membrane irritation	N/A	N/A	N/A	N/A
Chlorodibromomethane	$CHBr_2Cl$		eye and mucous membrane irritation	N/A	N/A	N/A	N/A
Bromoform	$CHBr_3$		eye irritation and lacrimation	0.5	5		
Bromochloromethane	CH_2BrCl		eye and mucous membrane irritation	200	1050	250	1300
Carbon Tetrachloride	CCl_4	3.04×10^{-2}	burning irritation of eyes and lacrimation	10	65	20	130
Dichloromethane	CH_2Cl_2	2.68×10^{-3}	respiratory tract irritation	200	700	250	870
1,2-Dichloroethane	CH_2ClCH_2Cl	9.77×10^{-4}	eye, nose and throat irritation	50	200	75	300
1,1,1-Trichloroethane	CCl_3CH_3	8.00×10^{-3}	eye irritation	350	1900	440	2380
Trichloroethylene	CCl_2CHCl	1.03×10^{-2}	eye and respiratory tract irritation	100	535	150	800
Tetrachloroethylene	CCl_2CCl_2	1.49×10^{-2}	burning irritation of eyes, lacrimation, nose and throat irritation	100	670	150	1000

N/A Not Available

METHODS

Subjects

Seven hundred and thirty-eight competitive swimmers completed the self-administered questionnaire between May 1991 and August 1992. The swimmers were recruited from the Lower Mainland and Fraser Valley regions of British Columbia (B.C.) and from three competitive venues: (1) the 1991 Canadian Summer National Swimming Championships in Vancouver, B.C.; (2) the 1991 Pan Pacific Swimming Championships in Edmonton, Alberta; and (3) national team training camps hosted by United States Swimming.

The swimmers from the Lower Mainland and Fraser Valley regions of B.C. were recruited from 17 competitive swim clubs registered with the B.C. Section of the Canadian Amateur Swimming Association. A list of these clubs, their coaches, addresses, and phone numbers was obtained from the B.C. Section Office and the coaches were initially informed about the study by letter. A follow-up telephone call was made two weeks later to solicit the cooperation of the coaches and meetings were arranged with the coaches, the swimmers and their parents. The questionnaire was administered to the swimmers at this time. Swimmers who were unable to attend the meetings were given instructions on how to complete the questionnaire and were asked to complete the questionnaire at home. The Age Group Swimmers were encouraged to complete the questionnaire with the help of a family member who might be more familiar with the swimmer's medical history. Three hundred and seventy-five swimmers completed the questionnaire. To study these 375 swimmers we distributed questionnaires to 680 eligible swimmers. This represents a participation rate of 66%.

Swimmers who attended the 1991 Canadian Summer National Swimming Championships in Vancouver, B.C. were asked to complete the questionnaire. Prior to the competition, the

High Performance Director for Swimming/Natation Canada, the national-governing body for competitive swimming in Canada, was contacted by letter to ask for his approval to conduct the survey. The coaches were approached prior to the competition to ask for their cooperation and meetings were arranged with the coaches and swimmers. The swimmers completed the questionnaire at these meetings which were held 2-3 days prior to the competition. Two hundred and fifty-one swimmers completed the questionnaire. To study these 251 swimmers we distributed questionnaires to 300 eligible swimmers. This represents a participation rate of 84%.

Swimmers who attended the 1991 Pan Pacific Swimming Championships in Edmonton, Alberta were also asked to complete the questionnaire. The High Performance Director for Swimming/Natation Canada and the Chairman of the Competition's Organizing Committee were contacted by letter to solicit their approval for conducting the survey. The national team coaches from the participating teams were contacted several days before the competition, informed about the purpose of the study, and meetings were arranged with the swimmers and coaches. The swimmers completed the questionnaire at these meetings which were held 2-3 days prior to the competition. Forty-six swimmers completed the questionnaire. To study these 46 swimmers we distributed questionnaires to 69 eligible swimmers. This represents a participation rate of 67%.

Swimmers who attended United States (U.S.) Swimming National Team Training Camps in Colorado Springs, Colorado and Indianapolis, Indiana were also asked to complete the questionnaire. The National Team Director and the Director of Sports Medicine Programs for U.S. Swimming were initially contacted by letter to inform them of the study and solicit their cooperation. We had originally planned to administer the questionnaire to the American swimmers at the Pan Pacific Championships in Edmonton, however, at that time it was decided

by the American coaches that it would be inappropriate to interfere with their swimmers' preparation for the competition. The National Team Director suggested that the questionnaire could be administered to the swimmers at two U.S. National Team Training Camps to be held in the fall of 1991. At each of these training camps, meetings were arranged with the swimmers and their coaches and the questionnaire was completed at that time. Sixty-six swimmers completed the questionnaire. To study these 66 swimmers we distributed questionnaires to 72 eligible swimmers. This represents a participation rate of 92%. The swimmers were informed about the purpose of the study and read and signed a consent form prior to completing the questionnaire.

The Questionnaire

The American Thoracic Society's Respiratory Disease Questionnaires for Adults and Children (Ferris, 1978) were modified and administered as a single questionnaire to the competitive swimmers. A copy of the questionnaire is included in this dissertation as APPENDIX A.

The identification section of the questionnaire included information about the swimmer's club or affiliation, his or her coach's name, and the level of competition that the swimmer participated. The level of competition was determined by the swimmer's age, the swimmer meeting a time standard to qualify for an individual event or events at a national championship, or if the swimmer participated on a national team at an international competition. The swimmers were placed into one of three categories depending on the performance criteria that they met. If the level of competition was determined by the swimmer's age, the swimmer was classified as an Age Group Swimmer. If the swimmer met a time standard and qualified to

swim at a national championship meet, the swimmer was classified as a National Qualifier. Finally, if the swimmer participated on a national team at an international competition, the swimmer was classified as an International Level Swimmer.

Information about the amount of exposure to chemically-treated pool water was elicited from a series of questions about the swimmers' experience as a competitive swimmer and the amount of training that he/she did. These questions included the training facility that the swimmer used, the number of years spent in competitive swimming, the number of workouts per day, the number of days of training per week, the number of weeks of training per year, the average number of metres of swimming per week, and the time and length of each training session. Whenever possible, the swimmer's coach was asked to review his or her training log to estimate these training parameters.

The number of chest illnesses that occurred in the past year and the average number of colds that the swimmer has each year were included in the questionnaire. In addition, respiratory symptoms such as coughing, congestion, the production of phlegm, sneezing, wheezing, chest tightness and difficulty breathing were reported during colds, apart from colds (allergies), during exercise other than swimming, and during swimming. Symptoms such as sore throats, sore eyes, headaches, and ear infections were also reported during similar conditions. For the purposes of this study, only the swimming-related symptoms will be reported.

Questions on respiratory illnesses such as asthma, bronchitis, croup, pneumonia, and hay fever, and allergies to dust, pollen, animals, grass, molds, tobacco smoke, air pollution, insect bites, food, and medication were included in the questionnaire. Each of these illnesses or allergies had to have been diagnosed by a physician in order to be considered to be present. The number of years that the swimmer had the illness or allergy was also included. Similar

questions about family members with these illnesses or allergies was also included in the questionnaire, but the results will not be discussed in this manuscript.

The smoking history of the swimmer and his or her family was included in the questionnaire. A swimmer was considered to be a smoker if he/she smoked more that 20 cigarettes in a lifetime. This criterion is significantly different than the criterion outlined by the American Thoracic Society (Ferris, 1978), but was instituted because of the younger age and athletic prowess of our subject population.

The use of prescription medication and, in particular, medication used in the treatment of respiratory problems was included in the questionnaire. A series of questions about symptoms that the swimmer associated with a strong chemical odor were asked. Once again, respiratory symptoms such as coughing, congestion, sneezing, wheezing, chest tightness and difficulty breathing, and other health-related symptoms such as sore throats, sore eyes, headaches, and nausea were included.

The rationale and justification for using each of the components of the Adult and Children's Questionnaires are described by Ferris (1978). A number of questions that were asked on the American Thoracic Society's Respiratory Disease Questionnaires for Adults and Children were omitted from our questionnaire. These include the name of the interviewer, the marital status, race, level of education and job history of the subject or his or her parents, and a number of questions related to the age of the youngest sibling or child, the number of children sharing a bedroom, and the number of rooms in the house, etc. Optional questions such as the type of home heating and fuels used, whether or not air conditions, humidifiers, and air filters are used in the house, the month of the year when respiratory symptoms are worse, or if there are pets living in the house were also omitted from our questionnaire.

Statistical Analysis

The mean, standard deviation, standard error of the mean, and the range of values were calculated for all of the descriptive variables. Chi-square analysis was used to determine the association between each of the symptoms of cough, congestion, sneezing, wheezing, chest tightness, difficulty breathing, sore throat, sore eyes, and headaches and the three categories of competitive swimmers (Age Group Swimmers, National Qualifiers, and International Level Swimmers). Initial analysis was completed using 2x3 contingency tables. If the overall association was statistically significant, 2x2 contingency tables were used to evaluate the association between each of the symptoms and individual categories of competitive swimmers.

Independent t-tests and chi-square analysis were used to determine whether there was an association between the swimmers' age, sex, and swimming-related exposure among swimmers with and without swimming-related symptoms. The exposure variables included the number of minutes of training per day, the number of days of training per week, the number of weeks of training per year, the number of years of competitive swimming, and the number of metres of swimming per week. In addition, two aggregate measures of exposure were created. Training volume was defined as the product of the number of metres of swimming per week and the number of weeks of training per year. The second variable, cumulative exposure, was defined as the product of the number of minutes of training per day, the number of days of training per week, the number of weeks of training per year, and the number of years of competitive swimming.

Stepwise logistic regression (SAS Institute, Inc., 1987) was used to determine the probability that asthma and each of the symptoms of cough, congestion, sneezing, wheezing, chest tightness, difficulty breathing, sore throat, sore eyes, and headache occurred as a function

of the swimmers' age, sex, category, and swimming-related exposure. In this context, exposure referred to the amount of time spent swimming, or the distance covered, during training sessions in the swimming pool.

Because multiple comparisons were made, we adopted the following convention for interpreting statistical significance: p values below 0.005 were considered statistically significant; values between 0.005 and 0.05 were considered to indicate associations that were of marginal statistical significance and worth further consideration; and values above 0.05 were considered statistically non-significant. All statistical analyses were completed using the SAS® Statistical Software Package (SAS Institute, Inc., Cary, NC).

RESULTS

Overview

A total of 738 competitive swimmers completed the questionnaire. Of these, 357 (48.4%) were male and 381 (51.6%) were female. The average age of the male swimmers was 15.10 ± 4.15 years and the average age of the female swimmers was 14.69 ± 3.60 years. Thirty-five swimmers, or 4.7% of those surveyed, were between the ages of 5-8 years, 187 (25.3%) were between the ages of 9-12 years, 231 (31.3%) were between the ages of 13-16 years, 215 (29.1%) were between the ages of 17-20 years, and 70 (9.6%) were 20 years of age or older.

There were a total of 348 Age Group Swimmers, 225 National Level Swimmers, and 165 International Level Swimmers. These numbers represent 47.2%, 30.5%, and 22.3% of the total number of swimmers who completed the questionnaire. A total of 626 swimmers, or 84.9% of those surveyed, were from Canada. Sixty-six (8.9%) were from the United States, 36 (4.9%) were from Australia, 7 (0.9%) were from New Zealand, 2 (0.3%) were from Indonesia, and 1 (0.1%) was from Hong Kong.

The swimmers who completed the questionnaire had a wide range of experience in competitive swimming. The swimmers had been involved in competitive swimming for 6.61 ± 3.95 years, trained an average of 5.34 ± 1.21 days per week, for 44.00 ± 4.51 weeks per year. The swimmers spent an average of 190.80 ± 79.61 minutes per day training. The average swimming distance covered during training was 36,665 ± 23,128 metres per week. Table 2 summarizes the descriptive characteristics and training parameters for the three groups of competitive swimmers.

The National Qualifiers and International Level Swimmers were older ($p < 0.0001$), had

been involved in competitive swimming longer ($p<0.0001$ and $p<0.0001$, respectively), and trained more weeks/year ($p<0.0001$ and $p<0.0001$, respectively), days/week ($p<0.0001$ and $p<0.0001$, respectively), and minutes/day ($p<0.0001$ and $p<0.0001$, respectively) than the Age Group Swimmers. The National Qualifiers and International Level Swimmers also had more practices/day ($p<0.0001$ and $p<0.0001$, respectively) and swam greater distances ($p<0.0001$ and $p<0.0001$, respectively) than the Age Group Swimmers. Similarly, the International Level Swimmers were involved in competitive swimming longer ($p<0.0001$) and swam greater distances ($p<0.0001$) than the National Level Swimmers.

Three hundred and twenty-one swimmers, or 43.5% of those surveyed, reported having a chest illness that kept them from participating in their normal daily activities for 3 days or more during the past year. Of those reporting being ill, there were an average of 2.52 ± 2.06 illnesses with only 1.01 ± 1.30 lasting more than 7 days. There was a strong overall association between the swimmer reporting a chest illness and his or her level of competitive swimming ($p<0.0001$). Age Group Swimmers were more likely to report chest illnesses than were National Qualifiers or International Level Swimmers ($p<0.0001$). The swimmers also reported having an average of 3.26 ± 2.06 colds each year. International Level Swimmers experienced fewer colds per year than did either Age Group Swimmers or National Qualifiers ($p<0.0001$). Table 3 summarizes the chest illnesses reported by the three groups of competitive swimmers.

Swimming-Related Symptoms

The number of swimmers who cough during exercise in the swimming pool was 206 (27.9%) while 186 (25.2%) cough after exercise in the swimming pool. Overall, 36.4% of the

swimmers cough during or after exercise in the swimming pool, while only 16.7% cough both during and after exercise in the swimming pool. Only 11.2% of those who cough during exercise in the swimming pool had to stop swimming because of the severity of the cough. Of those swimmers who cough during or after exercise in the swimming pool, 72.9% claim that their cough gets better if they have not exercised in the swimming pool for several days.

The number of swimmers who feel congested during exercise in the swimming pool was 126 (17.1%) while 113 (15.3%) feel congested after exercise in the swimming pool. Overall 22.8% of the swimmers feel congested during or after exercise in the swimming pool while only 9.6% feel congested both during and after exercise in the swimming pool. Only 12.7% of those who feel congested during exercise in the swimming pool had to stop swimming because of the severity of the congestion. Of those swimmers who feel congested during or after exercise in the swimming pool, 80.4% claim that their congestion is improved if they have not exercised in the swimming pool for several days.

The number of swimmers who sneeze during exercise in the swimming pool was 227 (30.8%) while 289 (39.2%) sneeze after exercise in the swimming pool. Overall, 45.0% of the swimmers sneeze during or after exercise in the swimming pool while only 24.9% sneeze both during and after exercise in the swimming pool. Only 3.1% of those who sneeze during exercise in the swimming pool had to stop swimming because of the severity of the sneeze.

The number of swimmers who wheeze during exercise in the swimming pool was 167 (22.6%) while 137 (18.6%) wheeze after exercise in the swimming pool. Overall, 26.3% of the swimmers wheeze during or after exercise in the swimming pool, while only 14.4% wheeze both during and after exercise in the swimming pool. Only 13.8% of those who wheeze during exercise in the swimming pool had to stop swimming because of the severity of the wheeze. Of

those swimmers who wheeze during or after exercise in the swimming pool, 90.7% claim that their wheeze is improved if they have not exercised in the swimming pool for several days.

The number of swimmers who experience chest tightness during exercise in the swimming pool was 156 (21.1%) while 118 (16.0%) experience chest tightness after exercise in the swimming pool. Overall, 24.8% of the swimmers have chest tightness during or after exercise in the swimming pool, while only 12.3% wheeze both during and after exercise in the swimming pool. Only 16.0% of those who have chest tightness during exercise in the swimming pool had to stop swimming because of the severity of the wheeze. Of those swimmers who wheeze during or after exercise in the swimming pool, 79.2% claim that their wheeze is improved if they have not exercised in the swimming pool for several days.

The number of swimmers who have difficulty breathing during exercise in the swimming pool was 266 (36.0%) while 156 (21.1%) have difficulty breathing after exercise in the swimming pool. Overall, 39.4% of the swimmers have difficulty breathing during or after exercise in the swimming pool, while only 17.8% have difficulty breathing both during and after exercise in the swimming pool. Only 41 swimmers or 15.4% of those who have difficulty breathing during exercise in the swimming pool had to stop swimming because of the severity of their symptoms. Of those swimmers who have difficulty breathing during or after exercise in the swimming pool, 66.7% claim that their breathing is improved if they have not exercised in the swimming pool for several days.

The number of swimmers who complain of a sore throat during exercise in the swimming pool was 153 (20.7%) while 162 (22.0%) complain or a sore throat after exercise in the swimming pool. Overall, 27.1% of the swimmers complain of a sore throat during or after exercise in the swimming pool, while only 15.6% complain of a sore throat both during and

after exercise in the swimming pool. Only 7.8% of those who complain of a sore throat during exercise in the swimming pool had to stop swimming because of their sore throat. Of those swimmers who complain of a sore throat during or after exercise in the swimming pool, 52.0% claim that their sore throat is improved if they have not exercised in the swimming pool for several days.

The number of swimmers who complain of sore eyes during exercise in the swimming pool was 186 (25.2%) while 243 (32.9%) complain of sore eyes after exercise in the swimming pool. Overall, 36.0% of the swimmers complain of sore eyes during or after exercise in the swimming pool, while only 22.1% complain of sore eyes both during and after exercise in the swimming pool. Only 7.5% of those who complain of sore eyes during exercise in the swimming pool had to stop swimming because of their sore eyes. Of those swimmers who complain of a sore eyes during or after exercise in the swimming pool, 75.2% claim that their sore eyes are improved if they have not exercised in the swimming pool for several days. There was a moderate overall association between the swimmer complaining of sore eyes during or after exercise in the swimming pool and his or her level of competitive swimming ($p<0.01$). Age Group Swimmers and National Qualifiers were more likely to complain of sore eyes during or after exercise in the swimming pool than were International Level Swimmers ($p<0.05$ and $p<0.01$, respectively).

The number of swimmers who complain of headaches during exercise in the swimming pool was 216 (29.3%), while a similar number complain of headaches after exercise in the swimming pool. Overall, 35.9% of the swimmers complain of headaches during or after exercise in the swimming pool, while only 22.6% complain of headaches both during and after exercise in the swimming pool. Only 57 swimmers or 26.4% of those who complain of

headaches during exercise in the swimming pool had to stop swimming because of their headache. Of those swimmers who complain of a headache during or after exercise in the swimming pool, 50.9% claim that their headache is improved if they have not exercised in the swimming pool for several days. A comparison of the swimming-related symptoms reported by the competitive swimmers is presented in Table 4.

Ear infections were reported by 551 swimmers or 74.7% of those surveyed. Among those swimmers who reported having an ear infection, the average number of ear infections was 2.24 ± 2.08 per year. National Qualifiers and International Level Swimmers were more likely to report ear infections than were Age Group Swimmers ($p<0.0001$ and $p<0.0001$, respectively).

The Relationship Between Symptoms and the Swimming-Related Exposure

Most of the swimming-related symptoms were associated with the swimmers' age, sex, level of competition, and swimming-related exposure. Older swimmers were more likely to cough, feel congested, sneeze, wheeze, and experience chest tightness, difficulty breathing, sore throats, and headaches. Female swimmers were more likely to cough, feel congested, and experience difficulty breathing and headaches. National Qualifiers were more likely to be congested ($p<0.001$ and $p<0.001$, respectively), wheeze ($p<0.001$ and $p<0.01$, respectively), and have chest tightness ($p<0.001$ and $p<0.05$, respectively), difficulty breathing ($p<0.001$ and $p<0.001$, respectively), and a sore throat ($p<0.001$ and $p<0.001$, respectively) than were either Age Group or International Level Swimmers. National Qualifiers were also more likely to cough and have headaches than were Age Group Swimmers ($p<0.001$ and $p<0.01$, respectively). Age Group Swimmers were less likely to sneeze than were either National

Qualifiers or International Level Swimmers ($p<0.001$ and $p<0.01$, respectively).

All of the swimming-related symptoms except for sore eyes, were strongly associated with the swimming-related exposure variables. This included not only the individual exposure variables such as the number of minutes, days, weeks, and years of swimming or the number of metres of swimming each week, but also the two aggregate measures of exposure which incorporated the individual exposure variables. A summary of the univariate analyses and logistic models is presented in Tables 5-8.

Respiratory Illnesses and Allergies

A number of physician-diagnosed respiratory illnesses were included in the medical history of the competitive swimmers. Asthma was reported by 99 swimmers or 13.4% of those responding to the questionnaire. This number included 10.6% of Age Group Swimmers, 12.4% of National Qualifiers, and 20.6% of International Level Swimmers. Older swimmers and swimmers who swam more weeks per year, more metres per week, and who had higher training volumes were more likely to report asthma. A summary of the univariate and logistic regression analyses relating asthma to the swimming-related exposure is presented in Tables 6 and 8, respectively. When the effect of age was removed from the logistic regression analysis, training volume became the most important variable associated with the presence of asthma ($p<0.0110$).

International Level Swimmers had a higher prevalence of asthma than did either the Age Group Swimmers or National Qualifiers ($p<0.01$ and $p<0.05$, respectively). Interestingly, of those swimmers who reported asthma, 35.1% of Age Group Swimmers, 78.6% of National Qualifiers, and 70.6% of International Level Swimmers had their asthma diagnosed by a physician after they began competitive swimming.

Bronchitis was reported by 184 swimmers or 24.9% of those surveyed. This number includes 22.4% of Age Group Swimmers, 26.2% of National Qualifiers, and 28.5% of International Level Swimmers. There was no significant association between the swimmer reporting bronchitis and his or her level of competitive swimming.

Pneumonia was reported by 75 swimmers or 10.2% of those surveyed. This number includes 8.3% of Age Group Swimmers, 13.3% of National Qualifiers, and 9.7% of International Level Swimmers. There was no significant association between the swimmer reporting pneumonia and his or her level of competitive swimming.

Hay Fever was reported by 125 swimmers or 16.9% of those responding to the questionnaire. This number includes 15.2% of Age Group Swimmers, 17.8% of National Qualifiers, and 19.4% of International Level Swimmers. Once again, there was no significant association between the swimmer reporting hay fever and his or her level of competitive swimming. A total of 179 swimmers, or 24.3% of those responding to the questionnaire, reported other physician-diagnosed respiratory illnesses such as croup, the flu, and mononucleosis. Table 9 summarizes the respiratory illnesses reported by the three groups of competitive swimmers.

A number of physician-diagnosed allergies were also reported by the competitive swimmers. Allergies to dust were reported by 154 swimmers or 20.9% of those who responded to the questionnaire. This number includes 20.1% of Age Group Swimmers, 22.2% of National Qualifiers, and 20.6% of International Level Swimmers. There was no significant association between the swimmer reporting allergies to dust and his or her level of competitive swimming.

Allergies to pollen were reported by 142 swimmers or 19.2% of those surveyed. This number includes 16.1% of Age Group Swimmers, 23.6% of National Qualifiers, and 20.6% of

International Level Swimmers. There was no association between the swimmer reporting allergies to pollen and his or her level of competitive swimming.

Allergies to animal hair were reported by 126 swimmers or 17.1% of those surveyed. This number includes 16.4% of Age Group Swimmers, 17.8% of National Qualifiers, and 17.6% of International Level Swimmers. There was no association between the swimmer reporting allergies to animal hair and his or her level of competitive swimming.

Allergies to grasses were reported by 126 swimmers or 17.1% of those surveyed. This number includes 16.1% of Age Group Swimmers, 17.8% of National Qualifiers, and 18.2% of International Level Swimmers. There was no association between the swimmer reporting allergies to grasses and his or her level of competitive swimming.

Allergies to molds were reported by 63 swimmers or 8.5% of those surveyed. This number includes 6.3% of Age Group Swimmers, 9.8% of National Qualifiers, and 11.5% of International Level Swimmers. Once again, there was no association between the swimmer reporting allergies to molds and his or her level of competitive swimming. A total of 349 swimmers, or 47.3% of those surveyed, reported other physician-diagnosed allergies. These include allergies to smoke (10.0%), insect bites (7.0%), food (10.3%), and medication (10.4%). Table 10 summarizes the allergies reported by the three groups of competitive swimmers.

Smoking History

Only 31 swimmers, or 4.2% of those who completed the questionnaire, have smoked more than 20 cigarettes in their lifetime. A majority (80.6%) of these swimmers were male. There was a moderate association between a swimmer smoking and his or her level of competitive swimming. National Qualifiers and International Level Swimmers were more likely

to smoke than were Age Group Swimmers ($p<0.01$ and $p<0.05$, respectively). National Qualifiers were also more likely to live with someone who smokes than were Age Group Swimmers ($p<0.01$). Table 11 summarizes the data that we collected on the smoking history of the swimmers.

Use of Medication

Prescription medication was used by 156 swimmers or 21.1% of those surveyed. This includes 14.1% of Age Group Swimmers, 24.4% of National Qualifiers, and 31.5% of International Level Swimmers. There was a strong association between the use of prescription medication and the swimmer's level of competition ($p<0.001$). National Qualifiers and International Level Swimmers were more likely to use prescription medication than were Age Group Swimmers ($p<0.01$ and $p<0.001$, respectively).

The most frequently prescribed medications were antibiotics (6.8% of the swimmers), β_2- agonists (5.0%), topical corticosteroids (4.2%), antihistamines (3.1%), non-steroidal anti-inflammatory drugs (2.7%), inhaled corticosteroids (1.9%), mast cell stabilizers (1.5%), anticholinergic drugs (0.4%), and theophylline (0.3%). In addition, refined petrolatums, acne therapeutics, ulcerative colitis therapeutics, anti-depressants, anti-viral agents, anti-fungal agents, anti-hypertensives, thyroid hormones, estrogens, and migraine therapeutics were also prescribed to the swimmers for medical reasons.

The sample cell sizes were too small to perform statistical analysis on the association between most of the prescription drugs and the three levels of competitive swimming, however, there was a marginal association between the use of β_2-agonists and the swimmer's level of competitive swimming ($p<0.05$). International level swimmers were more likely to use β_2

agonists than were Age Group Swimmers or National Qualifiers ($p<0.05$ and $p<0.05$, respectively). Table 12 summarizes the use of the more commonly prescribed drugs among the three groups of competitive swimmers.

Symptoms Associated with a Strong Chemical Odor

A total of 544 swimmers, or 73.8% of those who completed the questionnaire, have smelled a strong chemical odor in the swimming pool. This includes 64.1% of Age Group Swimmers, 87.1% of National Qualifiers, and 76.4% of International Level Swimmers. There was a strong overall association between smelling a strong chemical odor and the swimmer's level of competitive swimming ($p<0.001$). National Qualifiers and International Level Swimmers were more likely to smell a strong chemical odor in the swimming pool than were Age Group Swimmers ($p<0.001$ and $p<0.05$, respectively). Similarly, National Qualifiers were more likely to smell a strong chemical odor in the swimming pool than were International Level Swimmers ($p<0.01$).

The swimmers associated a number of symptoms with the strong chemical odor. These included coughing (40.9%), difficulty breathing (36.4%), sore eyes (26.3%), sneezing (25.2%), a sore throat (22.9%), headaches (22.0%), chest congestion (21.3%), chest tightness (21.0%), wheezing (20.9%), and nausea (11.7%). There was a strong overall association between the swimmer complaining of symptoms in the presence of a strong chemical odor and his or her level of competitive swimming. National Qualifiers and International Level Swimmers were more likely to cough, have difficulty breathing, sore eyes, a sore throat, headaches, chest congestion, chest tightness, wheezing, or nausea than were Age Group Swimmers. National Qualifiers were more likely to sneeze than were either International Level Swimmers or Age

Group Swimmers. There was no association between the swimmer becoming nauseated in the presence of a strong chemical odor and his or her level of competitive swimming.

The number of swimmers who have to stop swimming because of the severity of any of these symptoms was 136 or 18.4% of those surveyed. There was a strong overall association between the swimmer having to stop swimming and his or her level of competitive swimming ($p < 0.001$). National Qualifiers and International Level Swimmers were more likely to stop swimming than were Age Group Swimmers ($p < 0.001$ and $p < 0.001$, respectively). Table 13 summarizes the swimmer's beliefs about the symptoms they associate with a strong chemical odor in the swimming pool.

Table 2: A summary of the descriptive characteristics and training parameters for the three groups of competitive swimmers. The mean value and the standard deviation are reported. The percentage of male and female swimmers in each group is in parenthesis.

	Age Group Swimmers	National Qualifiers	International Level Swimmers	Level of Significance
No. of Subjects	348	225	165	
Mean Age (years)	11.93 ± 3.09	17.70 ± 2.40 *	18.23 ± 2.99 *	$p<0.0001$
No. of Male Swimmers	169 (48.6%)	112 (49.8%)	76 (46.1%)	
Mean Age (years)	11.68 ± 3.13	18.65 ± 2.37 *	19.50 ± 2.83 †	$p<0.0001$
No. of Female Swimmers	179 (51.4%)	113 (50.2%)	89 (53.9%)	
Mean Age (years)	12.16 ± 3.05	16.75 ± 2.03 *	17.15 ± 2.69 †	$p<0.0001$
Average no. of years of competitive swimming	3.80 ± 2.62	8.73 ± 2.94 *	9.67 ± 3.40 †	$p<0.0001$
Average no. of weeks/year of competitive swimming	41.37 ± 4.19	46.13 ± 2.97 *	46.65 ± 3.78 *	$p<0.0001$
Average no. of days/week of competitive swimming	4.59 ± 1.39	5.97 ± 0.27 *	6.05 ± 0.41 *	$p<0.0001$
Average no. of minutes/day of competitive swimming	131.15 ± 67.19	242.84 ± 46.07 *	245.64 ± 41.69 *	$p<0.0001$
Average no. of practices/day	1.30 ± 0.50	1.97 ± 0.24 *	1.95 ± 0.40 *	$p<0.0001$
Average no. of metres/week	17,449 ± 13,131	51,098 ± 13,301 *	57,515 ± 17,048 †	$p<0.0001$
Training Volume (kilometres/year)	741 ± 587	2,362 ± 676 *	2,695 ± 857 †	$p<0.0001$
Cumulative Exposure (hours)	2,325 ± 2,814	9,819 ± 4,043 *	11,152 ± 4,434 †	$p<0.0001$

Training Volume is defined as the product of the number of metres of swimming per week and the number of weeks of swimming per year.
Cumulative Exposure is defined as the product of the number of minutes of swimming per day, the number of days of swimming per week, the number of weeks of swimming per year, and the number of years of competitive swimming.

* The mean value for National Qualifiers and International Level Swimmers is significantly higher than the mean value for Age Group Swimmers.

† The mean value for International Level Swimmers is significantly higher than the mean value for National Qualifiers and Age Group Swimmers.

Table 3: A comparison of chest illnesses (pneumonia, bronchitis, asthma, and colds) that have kept competitive swimmers from participating in daily activities for 3 days or more during the past year. The mean value and the standard deviation are reported. The percentage of swimmers reporting illnesses in each group is in parenthesis.

	Age Group Swimmers	National Qualifiers	International Level Swimmers	Level of Significance
No. of Subjects Reporting Chest Illnesses	177 (50.9%)	85 (37.8%)	59 (35.8%)	$p<0.0001$ *
Average no. of illnesses	2.47 ± 2.08	2.51 ± 2.22	2.70 ± 1.78	N.S.
Average no. of illnesses > 7 days	0.94 ± 1.27	1.11 ± 1.45	1.06 ± 1.17	N.S.
Average no. of colds/year	3.41 ± 2.25	3.38 ± 2.05	2.76 ± 1.55 †	$p<0.0001$

* The level of significance indicates a strong overall association between the variable of interest and the level of competitive swimming.

† International Level Swimmers have fewer colds per year than either Age Group Swimmers or National Qualifiers.

N.S. Not Statistically Significant

Table 4: A comparison of respiratory and other health-related symptoms that occurred in three groups of competitive swimmers during or after exercise in the swimming pool. The mean value and standard deviation are reported. The percentage of swimmers reporting symptoms in each group is in parenthesis.

	Age Group Swimmers	National Qualifiers	International Level Swimmers	Level of Significance
No. of subjects who cough	109 (31.3%)	100 (44.4%)	60 (36.4%)	$p<0.01$ †
Average no. of years	2.11 ± 1.61	3.87 ± 2.83	3.89 ± 3.98	
No. of subjects who have congestion	65 (18.7%)	69 (30.7%)	34 (20.6%)	$p<0.01$ †
Average no. of years	2.07 ± 1.55	3.87 ± 2.57	4.66 ± 3.73	
No. of subjects who sneeze	126 (36.2%)	132 (58.7%)	74 (44.8%)	$p<0.001$ *
Average no. of years	3.52 ± 2.92	4.60 ± 2.83	6.34 ± 5.27	
No. of subjects who wheeze	60 (17.2%)	92 (40.9%)	42 (25.5%)	$p<0.001$ *
Average no. of years	2.65 ± 2.05	4.76 ± 3.16	5.00 ± 4.32	
No. of subjects who have chest tightness	63 (18.1%)	79 (35.1%)	41 (24.8%)	$p<0.001$ *
Average no. of years	2.71 ± 2.45	3.80 ± 2.63	5.40 ± 4.43	
No. of subjects who have difficulty breathing	92 (26.4%)	132 (58.7%)	67 (40.6%)	$p<0.001$ *
Average no. of years	2.80 ± 2.06	4.19 ± 2.89	4.71 ± 4.09	
No. of subjects who have a sore throat	67 (19.3%)	99 (44.0%)	34 (20.6%)	$p<0.001$ *
Average no. of years	2.28 ± 1.71	4.66 ± 3.43	4.52 ± 3.63	
No. of subjects who have sore eyes	129 (37.1%)	93 (41.3%)	44 (26.7%)	$p<0.01$ †
Average no. of years	3.63 ± 2.57	5.76 ± 3.93	5.22 ± 4.17	
No. of subjects who have headaches	105 (30.2%)	97 (43.1%)	63 (38.2%)	$p<0.01$ †
Average no. of years	2.37 ± 1.83	4.97 ± 3.58	4.28 ± 2.61	

* The level of significance indicates a strong overall association between the variable of interest and the level of competitive swimming.
† The level of significance indicates a marginal overall association between the variable of interest and the level of competitive swimming.

Table 5: Results of the univariate analysis that was used to determine whether there was a strong association between the swimmers' age, sex, and swimming-related exposure and the presence of swimming-related symptoms (Part I).

	Coughing	Congestion	Sneezing	Wheezing	Chest Tightness
Age (Older > Younger)	(↑) $p<0.0109$	(↑) $p<0.0017$	(↑) $p<0.0001$	(↑) $p<0.0001$	(↑) $p<0.0001$
Sex (Female > Male)	(↑) $p<0.001$	(↑) $p<0.007$	N.S.	N.S.	N.S.
Minutes of Training per Day	(↑) $p<0.0001$	(↑) $p<0.001$	(↑) $p<0.0001$	(↑) $p<0.0001$	(↑) $p<0.0001$
Days of Training per Week	(↑) $p<0.0001$	(↑) $p<0.0002$	(↑) $p<0.0001$	(↑) $p<0.0001$	(↑) $p<0.0001$
Weeks of Training per Year	(↑) $p<0.0007$	(↑) $p<0.0001$	(↑) $p<0.0001$	(↑) $p<0.0001$	(↑) $p<0.0001$
Years of Competitive Swimming	(↑) $p<0.0054$	(↑) $p<0.0081$	(↑) $p<0.0001$	(↑) $p<0.0001$	(↑) $p<0.0002$
Metres of Training per Week	(↑) $p<0.0002$	(↑) $p<0.0052$	(↑) $p<0.0001$	(↑) $p<0.0001$	(↑) $p<0.0001$
Training Volume *	(↑) $p<0.0002$	(↑) $p<0.0011$	(↑) $p<0.0001$	(↑) $p<0.0001$	(↑) $p<0.0001$
Cumulative Exposure †	(↑) $p<0.0025$	(↑) $p<0.0041$	(↑) $p<0.0001$	(↑) $p<0.0001$	(↑) $p<0.0001$

(↑) Increased prevalence of symptom associated with increased exposure

* Training Volume is defined as the product of the number of metres of swimming per week and the number of weeks of swimming per year.

† Cumulative Exposure is defined as the product of the number of minutes of swimming per day, the number of days of swimming per week, the number of weeks of swimming per year, and the number of years of competitive swimming.

N.S. Not Statistically Significant

Table 6: Results of the univariate analysis that was used to determine whether there was a strong association between the swimmers' age, sex, and swimming-related exposure and the presence of swimming-related symptoms or asthma (Part II).

	Difficulty Breathing	Sore Throat	Sore Eyes	Headaches	Asthma
Age (Older > Younger)	(↑) $p<0.0001$	(↑) $p<0.0001$	N.S.	(↑) $p<0.0002$	(↑) $p<0.001$
Sex (Female > Male)	(↑) $p<0.003$	N.S.	N.S.	(↑) $p<0.001$	N.S.
Minutes of Training per Day	(↑) $p<0.0001$	(↑) $p<0.0001$	N.S.	(↑) $p<0.0003$	N.S.
Days of Training per Week	(↑) $p<0.0001$	(↑) $p<0.0001$	N.S.	(↑) $p<0.0001$	N.S.
Weeks of Training per Year	(↑) $p<0.0001$	(↑) $p<0.0002$	N.S.	(↑) $p<0.0001$	(↑) $p<0.0437$
Years of Competitive Swimming	(↑) $p<0.0001$	(↑) $p<0.0001$	N.S.	(↑) $p<0.0089$	N.S.
Metres of Training per Week	(↑) $p<0.0001$	(↑) $p<0.0001$	N.S.	(↑) $p<0.0001$	(↑) $p<0.0289$
Training Volume *	(↑) $p<0.0001$	(↑) $p<0.0001$	N.S.	(↑) $p<0.0001$	(↑) $p<0.0204$
Cumulative Exposure †	(↑) $p<0.0001$	(↑) $p<0.0001$	N.S.	(↑) $p<0.0026$	N.S.

(↑) Increase prevalence of symptom associated with increased exposure

* Training Volume is defined as the product of the number of metres of swimming per week and the number of weeks of swimming per year.

† Cumulative Exposure is defined as the product of the number of minutes of swimming per day, the number of days of swimming per week, the number of weeks of swimming per year, and the number of years of competitive swimming.

N.S. Not Statistically Significant

Table 7: Results of the logistic regression analysis that was used to determine the probability that each of the swimming-related exposure variables occurred as a function of the swimmers' age, sex, level of swimming, and swimming-related exposure (Part I).

Symptom	Parameter	Estimate	Standard Error	Level of Significance	Odds Ratio
Coughing	Y-Intercept	2.3245	0.4267	$p<0.0001$	
	Number of Days per Week	0.3744	0.0749	$p<0.0001$	1.45
	Sex (Male)	-0.5428	0.1592	$p<0.0007$	0.58
Congestion	Y-Intercept	5.9048	1.1091	$p<0.0001$	
	Number of Weeks per Year	0.0845	0.0271	$p<0.0018$	1.09
	Sex (Male)	-0.4810	0.1847	$p<0.0092$	0.62
	International Level Swimmer	-0.5875	0.2345	$p<0.0122$	0.56
	Number of Days per Week	0.2301	0.1024	$p<0.0246$	1.26
Sneezing	Y-Intercept	4.3695	0.8463	$p<0.0001$	
	Number of Weeks per Year	0.0681	0.0213	$p<0.0014$	1.07
	National Level Swimmer	0.4633	0.1771	$p<0.0089$	1.59
	Number of Days per Week	0.1879	0.0804	$p<0.0183$	1.21
Wheezing	Y-Intercept	5.2668	1.0365	$p<0.0001$	
	National Level Swimmer	0.6681	0.1879	$p<0.0004$	1.95
	Number of Weeks per Year	0.0626	0.0253	$p<0.0135$	1.06
	Number of Days per Week	0.2214	0.1033	$p<0.0320$	1.25
Chest Tightness	Y-Intercept	7.1885	1.0989	$p<0.0001$	
	Number of Weeks per Year	0.1093	0.0258	$p<0.0001$	1.12
	Age (Years)	0.0869	0.0256	$p<0.0007$	1.09
	International Level Swimmer	-0.6601	0.2303	$p<0.0041$	0.52

Table 8: Results of the logistic regression analysis that was used to determine the probability that each of the swimming-related exposure variables or asthma occurred as a function of the swimmers' age, sex, level of swimming, and swimming-related exposure (Part II).

Symptom	Parameter	Estimate	Standard Error	Level of Significance	Odds Ratio
Difficulty Breathing	Y-Intercept	3.1567	0.4888	$p<0.0001$	
	National Level Swimmer	0.7074	0.1831	$p<0.0001$	2.03
	Number of Days per Week	0.3426	0.1001	$p<0.0006$	1.41
	Sex (Male)	-0.5796	0.1679	$p<0.0006$	0.56
	Age (Years)	0.0577	0.0269	$p<0.0319$	1.06
Sore Throat	Y-Intercept	2.9045	0.5126	$p<0.0001$	
	National Level Swimmer	0.9387	0.1856	$p<0.0001$	2.56
	Number of Days per Week	0.2866	0.0933	$p<0.0021$	1.33
Sore Eyes	Y-Intercept	1.2362	0.3071	$p<0.0001$	
	International Level Swimmer	-0.7423	0.2144	$p<0.0005$	0.48
	Age (Years)	0.0541	0.0205	$p<0.0084$	1.06
Headaches	Y-Intercept	2.5908	0.4435	$p<0.0001$	
	Number of Days per Week	0.4164	0.0776	$p<0.0001$	1.52
	Sex (Male)	-0.5521	0.1606	$p<0.0006$	0.58
Asthma	Y-Intercept	2.5149	0.5208	$p<0.0001$	
	Age (Years)	0.1449	0.0341	$p<0.0001$	1.16
	Number of Days per Week	-0.2982	0.1234	$p<0.0157$	0.74

Table 9: A comparison of the prevalence of physician-diagnosed respiratory illnesses among three groups of competitive swimmers. The percentage of swimmers from each group reporting respiratory illnesses is in parenthesis.

	Age Group Swimmers	National Qualifiers	International Level Swimmers	Level of Significance
No. of subjects with asthma	37 (10.6%)	28 (12.4%)	34 (20.6%)	$p<0.01$ †
No. of subjects with bronchitis	78 (22.4%)	59 (26.2%)	47 (28.5%)	N.S.
No. of subjects with pneumonia	29 (8.3%)	30 (13.3%)	16 (9.7%)	N.S.
No. of subjects with hay fever	53 (15.2%)	40 (17.8%)	32 (19.4%)	N.S.
No. of subjects with other illnesses	13 (3.7%)	20 (8.9%)	4 (2.4%)	N.S.

† The level of significance indicates a marginal overall association between the variable of interest and the level of competitive swimming.
N.S. Not Statistically Significant

Table 10: A comparison of the prevalence of physician-diagnosed allergies among three groups of competitive swimmers. The percentage of swimmers from each group reporting allergies is in parenthesis.

	Age Group Swimmers	National Qualifiers	International Level Swimmers	Level of Significance
No. of subjects with allergies to dust	70 (20.1%)	50 (22.2%)	34 (20.6%)	N.S.
No. of subjects with allergies to pollen	56 (16.1%)	53 (23.6%)	33 (20.6%)	N.S.
No. of subjects with allergies to animals	57 (16.4%)	40 (17.8%)	29 (17.6%)	N.S.
No. of subjects with allergies to grasses	56 (16.1%)	40 (17.8%)	30 (18.2%)	N.S.
No. of subjects with allergies to molds	22 (6.3%)	22 (9.8%)	19 (11.5%)	N.S.

N.S. Not Statistically Significant

Table 11: A description of the smoking history among three groups of competitive swimmers. Subjects were considered to be smokers if they smoked more than 20 cigarettes in their lifetime. The mean value and the standard deviation are reported. The percentage of swimmers from each group who smoke or live with someone who smokes is in parenthesis.

	Age Group Swimmers	National Qualifiers	International Level Swimmers	Level of Significance
No. of subjects who have smoked > 20 cigarettes	6 (1.7%)	16 (7.1%)	9 (5.5%)	$p<0.01$ †
Average no. of cigarettes smoked	2.50 ± 2.07	2.07 ± 2.97	4.75 ± 6.90	
Average age of subject when he/she started smoking	13.50 ± 2.35	15.21 ± 4.17	13.63 ± 2.88	
Average age of subject when he/she stopped smoking	13.83 ± 2.40	17.42 ± 3.37	16.71 ± 3.68	
No. of subjects who currently smoke	0 (0%)	2 (0.9%)	2 (1.2%)	
No. of subjects who live with someone who smokes	66 (19.0%)	64 (28.4%)	42 (25.5%)	$p<0.05$ †

† The level of significance indicates a marginal overall association between the variable of interest and the level of competitive swimming.

Table 12: A comparison of prescription drug use among three groups of competitive swimmers. The percentage of swimmers in each group who use prescription medication is in parenthesis.

	Age Group Swimmers	National Qualifiers	International Level Swimmers	Level of Significance
No. of subjects who take prescription medication	49 (14.1%)	55 (24.4%)	52 (31.5%)	$p<0.001$ *
Bronchodilators				
β_2-Agonists	13 (3.7%)	9 (4.0%)	15 (9.1%)	$p<0.05$ †
Theophylline	1 (0.3%)	1 (0.4%)		
Anticholinergics	1 (0.3%)	1 (0.4%)	1 (0.6%)	
Mast Cell Stabilizers	4 (1.1%)	1 (0.4%)	6 (3.6%)	
Inhaled Corticosteroids	5 (1.4%)	3 (1.3%)	6 (3.6%)	
Topical Corticosteroids	16 (4.6%)	12 (5.3%)	3 (1.8%)	
Antihistamines	5 (1.4%)	9 (4.0%)	9 (5.5%)	
Antibiotics	12 (3.4%)	17 (7.6%)	21 (12.7%)	
NSAIDs	6 (1.7%)	5 (2.2%)	9 (5.5%)	

* National Qualifiers and International Level Swimmers were more likely to use prescription medication than were Age Group Swimmers.

† International Level Swimmers were more likely to use β_2-Agonists than were Age Group Swimmers or National Qualifiers.

Table 13: A description of respiratory and other health-related symptoms that competitive swimmers associate with a strong chemical odor in the swimming pool. The percentage of swimmers reporting symptoms in each group is in parenthesis.

	Age Group Swimmers	National Qualifiers	International Level Swimmers	Level of Significance
No. of subjects who smell a strong chemical odor	223 (64.1%)	195 (87.1%)	126 (76.4%)	$p<0.001$ *
No. of subjects who cough	76 (21.8%)	136 (60.4%)	90 (54.5%)	$p<0.001$ *
No. of subjects who have congestion	37 (10.6%)	76 (33.8%)	44 (26.7%)	$p<0.001$ *
No. of subjects who sneeze	72 (20.7%)	75 (33.3%)	39 (23.6%)	$p<0.005$ †
No. of subjects who wheeze	37 (10.6%)	72 (32.0%)	45 (27.3%)	$p<0.001$ *
No. of subjects who have chest tightness	39 (11.2%)	69 (30.7%)	47 (28.5%)	$p<0.001$ *
No. of subjects who have difficulty breathing	69 (19.8%)	121 (53.8%)	79 (47.9%)	$p<0.001$ *
No. of subjects who have a sore throat	48 (13.8%)	75 (33.3%)	46 (27.9%)	$p<0.001$ *
No. of subjects who have sore eyes	70 (20.1%)	74 (32.9%)	50 (30.3%)	$p<0.001$ *
No. of subjects who have headaches	54 (15.5%)	64 (28.4%)	44 (26.7%)	$p<0.001$ *
No. of subjects who have nausea	34 (9.8%)	36 (16.0%)	16 (9.7%)	N.S.
No. of subjects with other complaints	14 (4.0%)	11 (4.9%)	7 (4.2%)	N.S.
No. of subjects who have to stop swimming	38 (17.0%)	57 (25.3%)	41 (24.8%)	$p<0.001$ *

* The level of significance indicates a strong overall association between the variable of interest and the level of competitive swimming.
† The level of significance indicates a marginal overall association between the variable of interest and the level of competitive swimming.
N.S. Not Statistically Significant

DISCUSSION

The purpose of this study was to determine the lifetime prevalence of respiratory and other health-related symptoms, illnesses, and allergies among competitive swimmers, and to establish whether the symptoms are associated with a swimming-related exposures determined by the amount of time spent swimming, or the distance covered, during training sessions in the swimming pool. Our results suggest that the prevalence of respiratory and other health-related symptoms, illnesses, and allergies are extremely common among competitive swimmers. In addition, we found that many of the symptoms were strongly associated with the amount of time spent swimming, or the distance covered, during training sessions in the swimming pool. We also identified significant gender- and age-related differences for several of the exercise-related symptoms. Although we have no objective information about the 34.2% of swimmers who did not respond to the questionnaire, it is possible that there is a selection bias within our sample population that has excluded swimmers who have no significant respiratory symptoms or illnesses.

One of the most impressive characteristics of these competitive swimmers is the amount of training that they do. Some of the swimmers have participated in competitive swimming for as many as 20 years, they train up to 6 hours daily, for as many as 52 weeks of the year. During the course a of week they may swim up to 100 kilometres and may, over the course of the competitive season, swim as many as 5,200 kilometres. This exposure data suggests that competitive swimmers are extremely susceptible to any adverse health effects of chemically-treated pool water.

A high percentage (43.5%) of the swimmers had a chest illness that kept them from participating in their normal daily activities for 3 days or more during the past year. In addition,

13.9% of the swimmers complained of a cough, and 22.9% of the swimmers produced phlegm, on most days for 3 months or more during the past year. Clinical data from studies by Jokl (1974) and Nieman and Nehlsen-Cannarella (1992) suggest that competitive athletes may have a higher prevalence of infectious illnesses than non-athletes. One of the reasons for this is that intense physical activity may depress non-specific cellular immunity and make the athlete more susceptible to infection (Lewicki et al., 1987).

Respiratory Illnesses and Allergies

The overall prevalence of asthma among the 738 competitive swimmers was 13.4%. This included 10.6% of the Age Group Swimmers, 12.4% of the National Qualifiers, and 20.6% of the International Level Swimmers. The extremely high prevalence of asthma among the International Level Swimmers was associated with the use of β_2-agonists among 9.1% of the swimmers in this group. It has been suggested that the prevalence of asthma may be affected by heredity, allergic conditions, and the environment (Gerstman et al., 1989). It ranges from as low as 1.8% in Scandinavian countries (Haahtela et al., 1990) to 14.3% or higher in the South Pacific (Liard et al., 1988). Data from the National Health and Nutrition Examination Survey showed that the lifetime prevalence of asthma among 3 to 17 year old American children and adolescents was 6.7% (Gergen et al., 1988). Helbling and Muller (1991) estimated the prevalence of asthma among German high performance athletes to be 7.1%. The prevalence of asthma among athletes on the 1976 and 1980 Australian Olympic Teams was 9.7% and 8.5%, respectively (Fitch, 1984).

An interesting finding in our study was that among those swimmers who reported asthma, 35.1% of Age Group Swimmers, 78.6% of National Qualifiers, and 70.6% of International

Level Swimmers had their asthma diagnosed after they began competitive swimming. One possible explanation for these results is that many of the younger swimmers were diagnosed with asthma and their physicians recommended swimming as a form of exercise that would be least likely to exacerbate their asthmatic symptoms. The National and International Level swimmers may have developed exercise-related symptoms during swimming which were suggestive of asthma, seen their physician, and had their asthma diagnosed after beginning swimming. In addition, it would be interesting to know how severe the asthma was in these competitive swimmers. It is possible that these swimmers have remained in competitive swimming because they have a mild form of asthma that may be seasonal or well-controlled by medication, and the presence of exercise-related symptoms does not severely effect their asthma or swimming performance. Those swimmers who had more severe forms of asthma may have been selected out of the sport because they had chronic asthma that was not well-controlled by medication or their symptoms may have limited their performance.

Among the other respiratory illnesses that we identified, the lifetime prevalence of bronchitis was 24.9%. This is significantly higher than the 0.8 to 1.3% reported for 12 to 74 year olds in the United States (Turkeltaub and Gergen, 1991) and the 9% reported for 35 to 66 year olds in Sweden (Lundback et al., 1993). The prevalence of pneumonia among the swimmers was 10.2% which is slightly lower than the 14.6% reported for a cohort of 905 patients by Heckerling et al. (1992). A history of hay fever was reported by 16.9% of the swimmers. This prevalence is significantly lower than the 42% reported for German high performance athletes (Helbling and Muller, 1991), and slightly higher than the 9% to 15% reported for Welsh schoolchildren (Burr et al., 1989) and the 10% reported for 15 to 70 year olds from Norway (Bakke et al., 1990).

The most common allergies among the competitive swimmers were to dust (20.9%), pollen (19.2%), animal hair (17.1%), grasses (17.1%), and molds (8.5%). It is estimated that as many as 20% to 30% of the population of developed countries may suffer from allergies (Peshkin, 1965). Fitch (1984) reported the prevalence of allergies among high performance athletes who participated on the 1976 and 1980 Australian Olympic Teams. Approximately 20.0% of the athletes on the 1976 team and 19.8% of the athletes on the 1980 team had allergies.

Ear infections were reported by 74.7% of the competitive swimmers. Otitis externa or "swimmer's ear" is quite common among athletes involved in aquatic sports (Strauss and Dierker, 1987; Weinberg, 1986). The moisture and the warm environment of the ear canal make it an ideal breeding ground for bacteria which generate debris and invade the lining of the canal. The most common bacteria associated with otitis externa are staphylococcus aureus, streptococcus pyogenes, pseudomonas aeruginosa, and proteus (Harrison, 1977).

Asthma, Exercise-Related Symptoms, and the Swimming-Related Exposure

Asthma was more likely to occur in swimmers who were older and had higher training volumes (a product of the number of weeks of training per year and the number of metres of training per week). Since International Level Swimmers were older and had a higher swimming-related exposure than either Age Group Swimmers or National Qualifiers, it is not surprising that they had a higher prevalence of asthma. It is interesting to note that the logistic regression analysis showed that swimmers with asthma were more likely to train fewer days per week than were swimmers without asthma. This would suggest that while asthmatic swimmers train fewer days per week, they must train greater distances during each day of training than non-asthmatic

swimmers do. In fact, this effect was confounded by the age of the swimmer. When age was removed from the logistic regression analysis, higher training volumes became the most important variable associated with asthma ($p < 0.011$).

The prevalence of exercise-related symptoms were common among the competitive swimmers. The symptoms of coughing, wheezing, chest tightness, and difficulty breathing are often associated with exercise-induced asthma (McKenzie, 1991; Mahler, 1993). Although International Level Swimmers had the highest prevalence of asthma (20.6%), National Qualifiers had a higher prevalence of exercise-related symptoms suggestive of asthma than did the International Level Swimmers. This may suggest that the association between asthma and exercise-related symptoms is not well supported in our study. However, swimmers who are National Qualifiers represent a wide range of age and abilities and there may, in fact, be minimal differences in the swimming-related exposure between the best National Qualifiers and the International Level Swimmers. Another possible explanation for the dissociation of asthma from exercise-related symptoms suggestive of asthma is that younger, more inexperienced swimmers may associate their symptoms with the intensity of exercise or the presence of a strong chemical odor in the swimming pool as opposed to the presence of an obstructive airways disease such as asthma. It is for this reason that they may be less concerned about their symptoms and less likely to make an appointment to see their family physician about their symptoms. The older, more experienced swimmers may realize that the exercise-related symptoms are not typical of high intensity training, but may be associated with respiratory problems. If this scenario is true, it is possible that we may have underestimated the prevalence of asthma among the National Qualifiers.

All of the symptoms, except for sore eyes, were strongly associated with the swimming-

related exposure. The exposure variables that we used included the average number of minutes of training each day, the number of days of training each week, the number of metres swum each week, the number of weeks of training each year, and the two composite measures of exposure, training volume and cumulative exposure. Since all of the individual exposure variables were strongly associated with the presence of exercise-related symptoms, and since the composite exposure variables were simply products of the individual exposure variables, the composite variables were also strongly associated with the presence of exercise-related symptoms.

We also identified age- and gender-related differences for several of the symptoms. Female swimmers were more likely to cough, feel congested, have difficulty breathing, and experience headaches than were male swimmers. In addition, older swimmers were more likely to cough, feel congested, sneeze, wheeze, have chest tightness, difficulty breathing, a sore throat, and experience headaches than were younger swimmers. When interpreting these data, it is important to remember that the reported prevalences are lifetime prevalences, so that as the swimmers get older their prevalences can only increase, they can not decrease.

The logistic regression analyses identified the variables that remained statistically important after adjusting for the effects of collinear or confounding variables. The effects of age became statistically non-significant when the data was stratified by using age group categories instead of age by itself. The swimmers' level of competition remained an important determinant on whether the swimmer presented with exercise-related symptoms. National Level Swimmers were more likely to sneeze, wheeze, or have difficulty breathing or a sore throat, while International Level Swimmers were more likely to feel congested, or have chest tightness or sore eyes.

Studies Comparing the Prevalence of Exercise-Related Symptoms

The most common symptom, sneezing, was reported by 45.0% of the swimmers. Sneezing is often associated with allergies, chronic rhinitis (Katz, 1984), or exercise-induced rhinitis (Silvers, 1992). Sneezing may also be induced by inhaling water through the nose and activating irritant receptors in the nasal cavity. Wheezing is the symptom that is most closely associated with asthma and, in many studies, questions about the prevalence of asthma and/or wheezing are often asked. The prevalence of wheezing (26.3%) among the competitive swimmers is significantly higher than that reported for the general population. In the Second National Health and Nutritional Examination Survey, the prevalence of frequent wheeze was estimated to be between 6.2% and 9.3% among white and black children in the United States (Schwartz et al., 1990). Sennhauser and Guntert (1992) estimated the prevalence of wheezing in children from Switzerland. The lifetime prevalence of wheezing was 16.5%, with only 34% of those reporting a history of asthma. The authors also showed that night-time symptoms of irritant cough, chest tightness, and wheezing were more frequent in children who lived in urban areas and in households with smokers.

Our results show that the prevalence of lower respiratory tract symptoms in competitive swimmers is significantly higher than that reported for football and basketball players. Weiler et al. (1986) reported the prevalence of exercise-related respiratory symptoms for college football and basketball players at the University of Iowa. The prevalence of symptoms for the football and basketball players were coughing (14% and 0%, respectively), wheezing (7% and 0%, respectively), chest tightness (9% and 12%, respectively), and dyspnea (6% and 0%). Following exposure to cold air, smoke, fumes, dust, or molds, the prevalence of chest symptoms

were reported by 35% and 38% of the football and basketball players, respectively.

The prevalence of sore eyes and sore throats among the competitive swimmers were 36.0% and 27.1%, respectively. Many of the chemicals used to disinfect the pool water are known irritants of the eyes, nose, and throat (Laverdure, 1991; Shaw, 1987). Exposure to these chemicals may be responsible for the swimmer's complaining of these symptoms. However, while there was a strong statistical association between a swimmer complaining of a sore throat and the swimming-related exposure, a similar association did not exist for sore eyes. An alternative reason for the high prevalence of sore eyes among the competitive swimmers involves the use of swimming goggles. Swimming goggles are almost universally worn by swimmers and the soft malleable foam padding in the goggles is composed of dibutylthiourea, an agent which is known to irritate the eyes and cause contact dermatitis (Alomar and Vilatella, 1985). The chemicals used to disinfect the pool water have also been shown to cause conjunctivitis in competitive swimmers (Weinberg, 1986).

In our study, 35.9% of the subjects complained of a headache during or after exercise in the swimming pool. Coughing, sneezing, sexual activity, and exercise are all known to cause benign exertional headaches (Diamond and Medina, 1982; Indo and Takahashi, 1990; Powell, 1982; Rasmussen and Olesen, 1992; Silbert et al., 1991). These headaches are characterized by severe, short-lived pain and are thought to have a vascular origin. Rasmussen and Olesen (1992) assessed the prevalence of headache disorders in a sample of 25-64 year olds. Their results suggest that approximately 1% of the general population suffer from benign exertional headaches. It has also been shown that exertional headaches are 4-5 times more common in men than in women (Rooke, 1968; Silbert et al, 1991). In our study, headaches were more common in female swimmers which suggests that the underlying mechanism that cause these headaches

may differ from benign exertional headaches. Three cases of sudden, severe headaches occurring in swimmers have been reported by Indo and Takahashi (1990). In all three cases neurological, radiological, and hematological findings were normal and the patients' outcomes were good. It is possible that the headaches experienced by competitive swimmers may have to do with entrainment of their breathing pattern to their stroke rate or, in some instances, to "breath-hold" training sets. In either case, exertional headaches may occur from the resulting hypercapnia.

The nature of the symptom and its severity were important determinants of whether the swimmer could continue to exercise or not. Only 3.1% of the swimmers who sneeze during exercise were compelled to stop swimming because of the nature and severity of their symptoms. This compares to 7.5% of the swimmers who have sore eyes, 7.8% who have sore throats, 11.2% who cough, 12.7% who develop congestion, 13.8% who wheeze, 15.4% who have difficulty breathing, 16.0% who have chest tightness, and 26.4% who have headaches.

There is a general belief among the swimmers that if they don't exercise in the swimming pool for several days, their symptoms will "get better". This term was explained to the swimmers as meaning that when resuming training following periods away from the swimming pool the symptom would be less severe, less noticeable, or absent. In those swimmers who reported exercise-related wheezing, 90.7% felt their symptoms were less severe, less noticeable, or absent following periods away from the swimming pool. A high percentage of swimmers who reported exercise-related congestion (80.4%), chest tightness (79.2%), sore eyes (75.2%), coughing (72.9%), difficulty breathing (66.7%), sore throat (52.0%), and headaches (50.9%) felt their symptoms were less severe, less noticeable, or absent following periods away from the swimming pool.

When we asked the swimmers whether they ever smelled a strong chemical odor in the swimming pool, 73.8% of the swimmers responded that they did. The most common exercise-related symptom associated with a strong chemical odor, coughing, was reported by 40.9% of the swimmers. Other symptom prevalences included difficulty breathing (36.4%), sore eyes (26.3%), sneezing (25.2%), sore throats (22.9%), headaches (22.0%), congestion (21.3%), chest tightness (21.0%), wheezing (20.9%), and nausea (11.7%). The nature and severity of the symptoms associated with this strong chemical odor were significant enough to cause 18.4% of the swimmers to stop swimming at one time or another. It is important to remember that these results only reflect the swimmer's beliefs about an association between a strong chemical odor and the development of respiratory symptoms.

Studies Comparing the Use of Medication and Tobacco Products

Prescription medication was used by 21.1% of the swimmers. Antibiotics (6.8%), β_2-agonists (5.0%), topical corticosteroids (4.2%), antihistamines (3.1%), non-steroidal anti-inflammatories (2.7%), inhaled corticosteroids (1.9%), mast cell stabilizers (1.5%), anticholinergic drugs (0.4%), and theophylline (0.3%) were the medications most commonly prescribed to the competitive swimmers. The trend in medication use tends to support the high prevalence of respiratory symptoms, asthma, and allergies among the competitive swimmers and is suggestive of a number of skin-related problems such as eczema, contact dermatitis, and psoriasis. The chemicals used to disinfect the pool water have also been shown to cause persistent swelling of the lips and generalized pruritus in swimmers (Parks and Camisa, 1986).

Only 4.2% of the competitive swimmers have smoked more than 20 cigarettes in their lifetime. Of these, nearly 81% were male. Dlin et al. (1991) estimated the prevalence of

smoking among Israeli male athletes to be 15.5%. Among foreign-born Canadians, the prevalence of smoking is 16% and among native-born Canadians, the prevalence of smoking is 25% (Millar, 1992). In the United States, a 1987 survey suggested that approximately 29% of the population were smokers, and the prevalence of smoking among 12-17 year old Australian students was estimated to be 27-30% (Hill et al., 1990).

CONCLUSIONS

In conclusion, this study shows that the prevalence of respiratory and other health-related symptoms, illnesses, and allergies are extremely common among competitive swimmers. The overall prevalence of physician-diagnosed asthma among the 738 competitive swimmers was 13.4%. This is significantly higher than the 7.1% to 9.7% reported for other competitive athletes. There was a significant difference in the prevalence rates of asthma among the three groups of competitive swimmers. The range of values include 10.6% of Age Group Swimmers, 12.4% of National Qualifiers, and 20.6% of International Level Swimmers. The extremely high prevalence of asthma among the International Level Swimmers is associated with the use of β2-agonists among 9.1% of the swimmers in this group.

There was a tendency for Age Group Swimmers to have their asthma diagnosed before they began competitive swimming, and National Qualifiers and International Level Swimmers to have their asthma diagnosed after they began competitive swimming. This suggests that the swimming-related exposure may be responsible for the development of respiratory symptoms that were severe enough for the National Qualifiers and International Level Swimmers to have a diagnosis of asthma made by their physician. We also question whether or not the swimming-related exposure precludes severe asthmatics from participating in competitive swimming because of uncontrolled symptoms, poor exercise tolerance, and/or poor performance.

Among the other respiratory illnesses that we identified, the prevalence of bronchitis (24.9%) and pneumonia (10.2%) were higher than that reported for the general population. The prevalence of hay fever (16.9%) is significantly lower than that reported for other high performance athletes, but is slightly higher than that reported for the general population. The most common allergies among the competitive swimmers were to dust (20.9%), pollen (19.2%),

animal hair (17.1%), grasses (17.1%), and molds (8.5%). These prevalences appear to be similar to those reported for high performance athletes as well as the general population.

A high percentage (43.5%) of the swimmers had at least one chest illness that kept them from participating in their normal daily activities for 3 days or more during the past year. The prevalence of swimming-related symptoms included sneezing (45.0%), difficulty breathing (39.4%), coughing (36.4%), sore eyes (36.0%), headaches (35.9%), sore throat (27.1%), wheezing (26.3%), chest tightness (24.8%), and chest congestion (22.8%) and suggest that both upper and lower respiratory tract irritation occurs as a result of the swimming-related exposure.

All of the symptoms, except for sore eyes, were strongly associated with the swimming-related exposure. Congestion, sneezing, wheezing, chest tightness, difficulty breathing, sore throats, and headaches were all associated with the average number of minutes spent training each day, the number of days spent training each week, the number of metres swum each week, and the number of weeks of training each year. The remaining symptom, coughing, was associated with the average number of minutes spent training each day, the number of days of training each week, and the number of metres swum each week. These results suggest that there is a dose-response relationship between the amount of training and the occurrence of symptoms.

We identified a number of gender- and age-related differences for several of the swimming-related symptoms. Female swimmers were more likely to cough, feel congested, have difficulty breathing, and experience headaches. Older swimmers were more likely to feel congested, sneeze, wheeze, have chest tightness, difficulty breathing, sore throats, and headaches. A majority of the swimmers with swimming-related symptoms reported that their symptoms were less severe, less noticeable, or absent if they spent several days away from the swimming pool.

Cigarette smoking is extremely uncommon among competitive swimmers. Only 4.2% of the swimmers reported smoking more than 20 cigarettes in their lifetime. The prevalence of smoking among the swimmers is significantly lower than that reported for the general population. Just over 21% of the competitive swimmers use prescription medication. The trend in medication use tends to support the high prevalence of respiratory symptoms, asthma, and allergy among the competitive swimmers and is suggestive of a number of skin-related problems such as eczema, contact dermatitis, and psoriasis.

And finally, nearly 74% of the swimmers smell a strong chemical odor in the swimming pool that they associate with respiratory and other health-related symptoms. While a majority of these symptoms were similar to the swimming-related symptoms that have previously been discussed, they tended to be less prevalent. However, the nature and severity of these symptoms were severe enough to cause 18.4% of the swimmers to stop swimming at one time or another.

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CHAPTER 2

The Prevalence of Increased Bronchial Responsiveness to Methacholine in a Select Group of Competitive Swimmers and Non-Swimmers

ABSTRACT

Non-specific bronchial hyperresponsiveness (BHR) is almost a universal finding in patients with obstructive airways diseases such as asthma. In the workplace, inhalation of agents that have known or suspected allergic properties may result in the development of a variant of asthma known as occupational asthma. Over 200 compounds have been reported to cause occupational asthma and, as in other obstructive airways diseases, almost all patients with symptomatic occupational asthma have BHR. Inhalation of respiratory irritants may also result in the development of occupational asthma. Because of its non-immunological etiology this form of asthma is known as irritant-induced occupational asthma.

A number of studies have shown that chronic, low level exposure to environmental irritants may cause a significant increase in BHR. These include a number of swimming-related studies that suggest chronic, low level exposure to the chemicals used to disinfect swimming pool water may be responsible for the development of asthma-like symptoms and BHR among competitive swimmers. Therefore, it was the purpose of this study to: (1) assess the prevalence of BHR in a group of 35 competitive swimmers from the lower mainland of British Columbia using a methacholine challenge test; and (2) determine whether there are differences in the prevalence of BHR among competitive swimmers with asthma or swimming-related symptoms (Case Group) and those who have neither asthma

nor swimming-related symptoms (Control Group), and to compare their results with a group of non-swimming athletes who have neither asthma nor swimming-related symptoms (Non-Swimming Control Group).

Our results show that the prevalence of BHR ($PC_{20} \leq 16$ mg/mL) among lower mainland competitive swimmers is 60.0%. When the sensitivity of the methacholine challenge test is decreased to include only those swimmers with a $PC_{20} \leq 8$ mg/mL, the prevalence of BHR is 34.3%. These values are significantly higher than the respective 12.5% and 0% prevalences that were observed for 16 non-swimming athletes in our study, and the 11-14% prevalence reported in several population-based studies. There was no difference in the prevalence of BHR between swimmers in the Case Group (61.1%) and swimmers in the Control Group (58.8%). When the sensitivity of the methacholine challenge test is decreased to include only those swimmers with a PC20 $\leq$ 8 mg/mL, 33.3% of the swimmers in the Case Group and 35.3% of the swimmers in the Control Group demonstrated BHR.

The clinical manifestations of this swimming-related exposure, whether it is related to the chemical treatment of the pool water, exercise, or both, may simply be to increase BHR and, in some individuals, cause swimming-related symptoms suggestive of asthma. What remains unknown is why some swimmers develop swimming-related symptoms suggestive of asthma and others do not. A possible explanation might be that swimmers with swimming-related symptoms may have been exposed to higher concentrations of pool chemicals than those swimmers without swimming-related symptoms, however, this theory remains speculative.

The most likely mechanism for the increased BHR in these competitive swimmers

is that chronic, low level exposure to the chemicals used to disinfect the pool water may cause damage to the epithelial layer of the swimmer's airways. This damage may result in increased exposure of afferent receptors, increased sensitivity of the receptors, and enhanced accessibility of bronchoconstrictor agents to bronchial smooth muscle and/or sensory nerve endings under the mucosa. The tracheo-bronchial irritant receptors and pulmonary C-fibers are likely involved in this physiological response which triggers an axon reflex resulting in the release of several neuropeptides that enhance smooth muscle contraction and inflammation of the airways.

While there is some clinical evidence from other studies to suggest that competitive swimmers may have increased sensitization to a number of common aero-allergens, we are extremely hopeful that chronic, low level exposure to chemically-treated pool water does not result in the severe pathological changes that occur to the airways of individuals with immunological- or irritant-induced occupational asthma.

INTRODUCTION

Non-specific bronchial responsiveness is the complex and poorly understood physiological response of the airways to non-antigenic stimuli. The measurement of non-specific bronchial responsiveness is widely used in the diagnosis of asthma and other obstructive airways diseases and the grading of their severity. It is also used in occupational and population-based studies to identify host characteristics and environmental exposures that increase the risk of developing chronic obstructive pulmonary disease (COPD). Bronchial responsiveness is not necessarily a static trait, but may be influenced by exposure to several modulating factors (Sparrow and Weiss, 1989). Spontaneous changes in bronchial responsiveness occur in asthmatic, as well as non-asthmatic subjects, however, asthmatics persistently have hyperresponsive airways. This suggests that asthma should be classified as a variable airways disease instead of a reversible airways disease (Vedal et al., 1988).

Increased bronchial responsiveness (BHR) is almost a universal finding in patients with asthma. Subjects with asthma develop bronchial narrowing to a greater extent in response to smaller quantities of pharmacological, physical, or chemical stimuli than do normal subjects (Hargreave et al., 1981). Methacholine and histamine are the pharmacological agents that are most commonly used to assess non-specific bronchial responsiveness. Breathing cold air or solutions containing non-isotonic aerosols, voluntary hyperventilation, and exercise are physical stimuli that can be used to assess non-specific bronchial responsiveness as well. The level of responsiveness to methacholine has been shown to correlate with the level of responsiveness to histamine (Aquilina, 1983), exercise (Ahmed and Danta, 1988;), and hyperventilation of cold air (Ahmed and Danta, 1988; Aquilina, 1983). The use of gases such as sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and

ozone (O_3), and specific challenge agents that are identified in the workplace are frequently being used in studies of occupational asthma.

The results of several studies suggest that the prevalence of BHR is between 11-14% in normal subjects (Burney et al., 1987; Cockcroft et al., 1992; Woolcock et al., 1987;); 47% of patients with cough and no other chest symptoms; 40% of patients with rhinitis and vague chest symptoms; and 22% of patients with rhinitis and no chest symptoms (Cockcroft et al, 1977; Makino, 1966). Increased bronchial responsiveness is also reported in cigarette smokers with normal lung function (Gerrard et al., 1980). The degree of airway responsiveness appears to be higher in children than in adults, and similar between males and females (Weiss et al., 1984).

The clinical presentation of asthma may include episodes of coughing, dyspnea, chest tightness, or wheezing. It may also involve an exaggerated diurnal variability in airway caliber that leads to nocturnal and early morning breathlessness and chest tightness (Ryan et al., 1982). While the severity of BHR in asthma has been shown to be related to the severity of the patient's symptoms (Ryan et al., 1982), it has been suggested by Kennedy (1992) that the absence of respiratory symptoms does not necessarily rule out BHR in all persons. Many studies have attempted to determine the underlying pathophysiology of BHR. It has become evident that one single factor is not responsible for hyperresponsiveness, but rather there is a complex interaction of several factors involved (Postma et al., 1989).

Because changes in bronchomotor tone in asthma may occur rapidly, it has been suggested that asthma, and in particular BHR, might be explained by an abnormality of autonomic control (Postma et al., 1989). Several different autonomic abnormalities have

been proposed in the pathogenesis of asthma, including enhanced cholinergic, alpha-adrenergic or non-cholinergic excitatory mechanisms, or reduced beta-adrenergic or non-cholinergic inhibitory mechanisms (Nadel and Barnes, 1984).

The autonomic nervous system plays an important role in the regulation of airway caliber in health and disease. In addition to regulation of airway smooth muscle tone, autonomic nerves may influence secretion of mucus from submucosal glands, transport of fluid across airway epithelium, permeability and blood flow in the bronchial circulation, and release of mediators from mast cells and other inflammatory cells. An important function of sensory nerves and their receptors is to protect the airway against inhalation of irritant and chemical particles. Apart from protective effects such as cough, airway irritation causes local defense reactions such as bronchoconstriction, vasodilatation, and increased vascular permeability, resulting in an increased reflex bronchoconstriction due to stimulation of sensory receptors by inflammatory mediators.

Most theories relating epithelial damage and airway hyperresponsiveness are based on the assumption that epithelial damage and loss result in increased exposure of afferent receptors, increased sensitivity of those receptors, and enhanced accessibility of bronchoconstrictor to smooth muscle and/or sensory nerve endings under the mucosa (Postma et al., 1989). Exposure of sensory nerves may bring on increased reflex bronchoconstriction via vagal, or local reflexes involving antidromic conduction along sensory afferent fibers (Barnes, 1986).

Slowly adapting stretch receptors are myelinated nerve terminals localized in the smooth muscle of the trachea and larger bronchi. It has been postulated that the bronchopulmonary stretch receptors provide information about the degree of inflation of the

lung and may regulate the rate and depth of breathing to achieve the optimal combination of mechanical work and/or inspiratory force. Slowly adapting receptors may be responsible for the bronchodilator response to lung inflation in humans, particularly after induced bronchoconstriction (Barnes, 1991).

Tracheo-bronchial irritant receptors are non-specialized nerve endings that are thought to terminate between the epithelial cells close to the mucosal surface of the airways. These fibers are rapidly adapting to a maintained stimulus and have an irregular spontaneous discharge. They are stimulated by large inflations or deflations of the lungs and by a large number of inhaled irritants such as ammonia, SO_2, O_3, and inflammatory mediators such as histamine, serotonin, and prostaglandin (PG) $F_{2\alpha}$. Stimulation of the irritant receptors causes cough, hyperpnea, increased mucus secretion, as well as vagally-mediated reflex bronchoconstriction and laryngeal constriction.

Pulmonary and bronchial C-fibers arise from a wide area of the lung and bronchial tree. These non-myelinated nerve endings are thought to be stimulated by pulmonary edema and congestion and by embolization of the pulmonary vascular bed. They are also stimulated by capsaicin, bradykinin, histamine, $PGF_{2\alpha}$, PGE_2, PGI_2, and SO_2. Stimulation causes rapid, shallow breathing, bronchoconstriction and increased airway secretion and are often associated with cardiovascular depressor effects.

There is some indirect evidence of an increase in central vagal drive in patients with asthma or COPD (Kallenbach et al., 1985; Postma et al., 1985). Activation of afferent and efferent pathways may also lead to increased vagal tone. Human airway smooth muscles are almost completely devoid of adrenergic nerves, however, endogenous circulating catecholamines play an important role in inhibiting cholinergic neurotransmission in the

airways (Danser et al., 1987). Impaired circulation of epinephrine is known to occur in asthmatic subjects and may play a role in BHR (Ind et al., 1985).

Since non-adrenergic, non-cholinergic (NANC) innervation is the sole inhibitory system from the large to small airways, it has been suggested that a defect of this system may contribute to BHR. There is increasing evidence to suggest that neuropeptides may be involved in NANC neurotransmission. VIP and a related peptide, peptide histidine methionine, are known to be potent relaxants of airway smooth muscle. VIP is a co-transmitter with acetylcholine in airway cholinergic nerves and may act as a "braking" mechanism to excessive cholinergic bronchoconstriction (Barnes, 1987). VIP also inhibits antigen-induced histamine release in the guinea-pig lung, suggesting that VIP-receptors may be present on mast cells (Undem et al., 1983).

Perhaps a more likely abnormality in the modulation of airway responsiveness is an increase in NANC excitatory mechanisms. NANC bronchoconstriction is due to release of neuropeptides from C-fiber endings (Lundberg et al., 1988). It has been proposed by Barnes (1986) that when these nerve endings are exposed to epithelial-cell-damaging inflammatory mediators an axon reflex might be triggered, resulting in smooth muscle contraction, microvascular leakage, and hypersecretion of mucus. Substance P, Neurokinin A and B, Neuropeptide K, and Calcitonin Gene-Related Peptide are all neuropeptides that enhance airway smooth muscle contraction and amplify neutrophil and eosinophil responses to chemotactic agents, thus magnifying the inflammatory response in the airways (Hua et al., 1985; Lundberg et al., 1983; Saria et al., 1988).

Recent studies have suggested that inflammation may play an important role in the development of BHR and the symptoms of chronic asthma (Barnes, 1989). Increased vascular leakage through the basement membrane of the endothelium is now thought to play

an important role in the regulation of airway inflammation (Laitinen et al., 1985). The mechanisms responsible appear to be independent of epithelial permeability (Hogg, 1981). The role of the epithelial barrier against physiologic, pathologic, and pharmacologic stimuli is becoming of interest to researchers because of two reasons: (1) permeability changes of the epithelium; and (2) mediator generation from the epithelium. In patients with asthma or COPD, an increase in epithelial permeability may be present.

Recently, epithelial cells have been identified as a possible source of mediators involved in smooth muscle contraction and inflammatory reactions. Epithelial cells may release epithelium-derived relaxing factor (Flavahan and Vanhoutte, 1985), a relaxing factor for airway smooth muscle. Epithelial cells are also able to produce LTB_4 which attracts neutrophils, contracts smooth muscle, and increases BHR in some species (Holtzman et al., 1983 and O'Byrne et al., 1985). Damage to the epithelium may increase sensitivity to acetylcholine, serotonin, and histamine (Flavahan et al., 1985).

The immunologic pathway that is classically implicated in asthma involves the release of mediators from mast cells. Mast cells are located throughout the bronchial tree, but are mainly located in the bronchial mucosa between the epithelium and basement membrane. IgE receptor-mediated stimulation results in the release of several vasoactive, spasmogenic, and chemotactic mediators including histamine, leukotriennes, prostaglandins, and platelet activating factor (PAF). It appears that the release of mast cell mediators is important in maintaining the early phase reactions of asthma (Deyzer et al., 1984), and attracting a number of inflammatory cells that are responsible for the late phase reactions (Wenzel et al., 1988).

Macrophages, eosinophils, and platelets also have been shown to have surface

receptors for IgE (Capron et al., 1981; Joseph et al., 1983; Joseph et al., 1986). Alveolar macrophages are a rich source of arachidonic acid metabolites, producing PGD_2, $PGF_{2\alpha}$, and TxA_2. An increased number of eosinophils in the blood, sputum, and airways of patients with asthma is common. Booy-Noord et al. (1972) noted that eosinophils increased in concurrence with an increase in bronchial responsiveness in peripheral blood after late-phase allergen-induced reactions. Eosinophils may be attracted to the lung by several chemotactic factors including PAF, PGD_2, LTB_4, histamine and serotonin (Digby and Nadel, 1988) and are activated by IL-3 and IL-5 (Silberstein and David, 1987). Their location in the airways makes them available for phagocytosis of inhaled particles; the nature of their secretory products makes them a likely candidate for involvement in BHR, both in increasing responsiveness and in limiting the extent of the inflammation and pathophysiological consequences (Postma et al., 1989).

Platelets are known to secrete chemotactic products for neutrophils, enhance their adhesion to vascular walls, augment release of enzymes, and stimulate the production of inflammatory mediators (Weksler, 1988). Day et al. (1975) suggest there is a relationship between the late-phase reaction of asthma and platelet activation. The release of PAF and the activation of the platelets may result in bronchoconstriction and BHR through an inflammatory reaction (Manzoni et al., 1985).

Lymphocytes have been shown in several animal models to modulate IgE production. Antigen-activated lymphocytes may release lymphokines and stimulate the production of neutrophils and macrophages by the bone marrow, chemotaxis of neutrophils to the site of inflammation, and prime eosinophils and macrophages for heightened cytotoxic activity (Postma et al., 1989). Lymphocytes have also been shown to produce a histamine releasing

factor (HRF) for mast cells and basophils (Sedgwick et al., 1981).

We still know very little about the factors that modulate the severity of bronchial responsiveness. Exposure to allergens and occupational agents, a history of smoking, viral respiratory infections, air pollution, and pre-existing airflow obstruction are thought to increase bronchial responsiveness in asthma and COPD (Postma et al., 1989).

Hypersensitivity to environmental antigens is often an important clinical feature of asthma (Weiss et al., 1989). Antigen challenge and longitudinal clinical studies have shown that allergy and allergen exposure may lead to increased non-specific bronchial responsiveness in asthmatics (Cockcroft et al., 1977). The ability of an allergen to produce increased airway responsiveness is dependent on the degree of allergy, the dose of antigen, and the degree of non-specific airway responsiveness (Cockcroft et al., 1979). In the laboratory, a subject's response to histamine or methacholine increases after allergen challenge or occupational agent exposure. In sensitized patients, natural exposure to airborne allergens or occupational asthma-inducers may also lead to an increase in airway responsiveness (Vedal and Chan-Yeung, 1989). Conversely, removing the patient from environmental exposure to domestic or occupational allergens often results in decreased airway responsiveness. The magnitude and duration of the increased airway responsiveness has been shown to correlated with the late-phase reaction of asthma (Durham, 1987).

Bronchial inflammation resulting from antigen exposure is likely to be at least partly responsible for the association between allergy and heightened airway responsiveness to non-antigenic stimuli. This inflammatory response may result in damage to the respiratory epithelium, submucosal edema, and alterations of the neural mechanism involved in the regulation of bronchial smooth muscle. Even in children who have been asymptomatic

throughout their lives and have no history of atopic disease, BHR appears to be closely linked to total serum IgE levels (Sears et al., 1991). Despite the association between heightened non-specific airway responsiveness and allergy, there have been no population studies that have related the degree of BHR to serum IgE levels (Burrows, 1989). Although allergen-induced airway hyperresponsiveness is the most studied of the airway hyperresponsiveness syndromes, it is by no means the only type and may not be the most common either epidemiologically or clinically (Postma et al., 1989).

Cigarette smoking has been shown to cause an acute increase in airway resistance to non-smokers exposed in the laboratory (Nadel and Comroe, 1961). Several studies have also shown increased BHR in smokers compared to non-smokers (Buczko et al., 1984; Gerrard et al., 1980; Taylor et al., 1984). Taylor et al. (1985) found that the decline in FEV_1 over a 7 year period was faster in smokers who had a $PC_{20} < 16$ mg/mL when compared to smokers who had lower bronchial responsiveness. In their study, 30% of the smokers and 5% of non-smokers had a PC20 < 16 mg/mL. It has also been suggested that exposure to cigarette smoke may predispose smokers and non-smokers to allergens (Taylor et al., 1985). Smokers also have a higher total serum IgE concentration and lower total serum IgG and IgM concentrations than non-smokers (Gerrard et al., 1980). Cigarette smoking appears to predispose workers to sensitization to some compounds that are responsible for occupational asthma (Vedal and Chan-Yeung, 1989). Smoking also appears to play an important role in the development of COPD in asthmatic patients with marked BHR and atopy (Sparrow and Weiss, 1989).

Population-based studies have provided conflicting evidence regarding the influence of passive smoking on non-specific bronchial responsiveness and asthma among children.

O'Connor et al. (1987) found an association between BHR and maternal smoking in 21 asthmatic children and young adults. They were unable to demonstrate a similar association in non-asthmatic subjects, despite the occurrence of significantly lower levels of FEV_1 and $FEF_{25-75\%}$ in association with maternal smoking. An association between parental smoking and symptoms of cough, phlegm, and wheeze were found in school children in two studies (Dodge, 1982; Weiss et al., 1980). Gortmaker et al. (1982) estimated that 18-34% of childhood asthma in a sample of children from Michigan and Massachusetts could be attributed to maternal smoking. In contrast to these results, Schenker et al. (1983) found no association between parental smoking and wheezing or asthma.

Several studies have suggested an association between viral respiratory infections in children, notably croup (Gurwitz et al., 1980; Zach et al., 1981) and bronchiolitis (Gurwitz et al., 1981; Pullan and Hey, 1982) and the subsequent development of increased levels of bronchial responsiveness. Viral infections are known to increase the permeability of the respiratory epithelium and cause loss of columnar epithelium and β-receptor down regulation (Busse, 1977). Respiratory illnesses are likely to exert their effects early in life when the lung is more vulnerable, and may be more important in boys, especially those who are atopic (Weiss et al., 1989). Weiss et al (1985) assessed the relationship between respiratory illness and airway responsiveness and atopy in a cohort of 194 children between the ages of 12-16 years. The results of their study suggest that respiratory illness in early life is associated with airway hyperresponsiveness as measured later in childhood. These results are not universal, however, and some studies have failed to find significant effects of viral infections using either histamine (Jenkins and Breslin, 1984) and cold air (Weiss et al., 1984).

In a cross-sectional study of the effects of air pollution on the chronic respiratory health of children, Dockery et al. (1989) showed positive associations between the prevalence of chronic cough, bronchitis, and chest illness and all measures of particulate pollution and positive, but less strong, associations with the concentrations of two gases, SO_2 and NO_2. No association was found between asthma, persistent wheeze, hay fever, or nonrespiratory illness, or between pulmonary function measures and the level of pollution. Air pollution measurements included total suspended particulates, particulate matter less than 15 μm and 2.5 μm aerodynamic diameter, fine fraction aerosol sulfate, SO_2, NO_2, and O_3.

Non-specific bronchial hyperresponsiveness is partially determined by the pre-challenge level of pulmonary function in both adults with intrinsic and extrinsic asthma (Ulrik, 1993). It has been suggested that the relationship between the baseline level of pulmonary function and the degree of non-specific bronchial responsiveness is extremely complex (Weiss et al., 1989), however, it is probably the single best indicator of bronchial responsiveness (Rijcken et al., 1988; Sparrow et al., 1987). This may reflect baseline airway caliber, aerosol deposition, or other aspects of test performance, or alternatively, may reflect a causal relationship between airway responsiveness and lower levels of pulmonary function. Increased levels of airway responsiveness might lead to lower levels of pulmonary function via chronic inflammation or a change in mechanical factors linking increased levels of airway responsiveness with diminished lung elastic recoil (Rijcken et al., 1988; Sparrow et al., 1987).

Several studies suggest that airway responsiveness is increased in the very young and the elderly (Hopp et al., 1985; Rijcken et al., 1987; Weiss et al., 1984) and this may reflect

the lower levels of lung function that are common at the extremes of age. Children who have symptoms early in life will have more severe asthma and more BHR (Seinra Monge and Balvanera Ortiz, 1991; Sparrow et al., 1987).

In the workplace, inhalation of agents that have known or suspected allergic or irritant properties may result in the development of a variant of asthma known as occupational asthma. Over 200 compounds have been reported to give rise to occupational asthma (Chan-Yeung and Malo, 1994). Almost all patients with symptomatic occupational asthma have increased bronchial responsiveness (Lam and Chan-Yeung, 1979). It has been shown that removal of patients from the offending agents results in recovery in approximately 40% of the patients, and this recovery is associated with gradual disappearance of BHR (Paggiaro et al., 1984). Re-exposure of the patients to the same working environment leads to recurrence of asthmatic symptoms and to an increase in bronchial responsiveness (Hargreave et al., 1984). Because exposure to these irritants in the workplace is common, a clear understanding of their role in occupational lung disease is important. If irritant exposures in the workplace can induce BHR, it is possible that the exposure may be implicated in the development of adult-onset asthma or COPD (Kennedy, 1992).

The agents that are responsible for occupational asthma can be divided into two categories: high molecular weight compounds and low molecular weight compounds (MW < 1,000 daltons) (Vedal and Chan-Yeung, 1989). In occupational asthma caused by exposure to high molecular weight compounds, specific IgE antibodies are found in the sera of affected patients. Skin tests with the extract of the appropriate allergen induce an immediate wheal and flare reaction. Clinically, the patients are usually atopic with a history

of allergic rhinitis and/or eczema and usually complain of asthma symptoms within a few minutes of exposure. In contrast, in occupational asthma due to low molecular weight compounds, specific IgE antibodies are either not found or found only in small proportion of the patients when the chemical is conjugated to a body protein (Vedal and Chan-Yeung, 1989).

Inhalation of respiratory irritants may also result in the development of occupational asthma. Because of its non-immunological etiology this form of asthma is known as irritant-induced asthma or Reactive Airways Dysfunction Syndrome (RADS). RADS is not uncommon in patients who have been referred for assessment of occupational asthma. It is estimated that between 2-6% of patients who are seen for assessment of occupational asthma will be clinically diagnosed with RADS (Brooks et al., 1985; Tarlo and Broder, 1989).

By definition, RADS occurs following a single, excessively high environmental or occupational exposure to irritants in the form of gases, vapours, fumes, or smoke (Brooks et al., 1985). Clinically, RADS is similar to asthma in that it is associated with symptoms of cough, dyspnea, and wheezing, and is almost universally associated with BHR. It differs from typical asthma in that it has a rapid onset, specific relationship to a single environmental exposure, and has no apparent pre-existing period for sensitization to occur, with the apparent lack of an allergic or immunologic etiology. Typically symptoms occur within 24 hours of the exposure and persist for a minimum of 3 months. Pulmonary mechanics, diffusing capacity, and chest x-rays may be normal, but methacholine challenge testing is usually positive (Brooks et al., 1985).

Most of the studies that have identified RADS have been case studies of patients involved in exposure to a wide variety of chemicals. Inhalation of glacial acetic acid (Kern,

1991), hydrochloric acid (Boulet, 1988; Promisloff et al., 1990), paint fumes, uranium hexafluoride, floor sealant, hydrazine, metal coat remover, propylene glycol, alpha-chlorophane (Brooks et al., 1985; Brooks, 1985), epoxy resins (Lerman and Kipen, 1988), SO_2 (Charan et al., 1979; Rabinovitch et al, 1989), chlorine gas (Chester et al., 1977; Moore and Sherman, 1991; Schwartz et al., 1990), toluene diisocyanate (Boulet, 1988), ammonia (Bernstein and Bernstein, 1989), reactive dyes (Park et al., 1990), latex (Tarlo et al., 1990), aluminum (Soyseth et al., 1992), dusts and molds (Gilbert and Auchincloss, 1989), cleaning fluids (Murphy et al., 1976), and to the products of combustion and pyrolysis in fires (Sherman et al., 1989) have been implicated in the development of RADS.

Mechanisms to explain the development of RADS have focused on the toxic effects of the irritant exposure on the airways. The increase in bronchial responsiveness in RADS is probably due to an inhalation injury (Brooks et al., 1985; Flury et al, 1983). Bronchial biopsies of RADS patients have shown damage to the respiratory epithelium with chronic non-specific airway inflammation. Mild inflammatory infiltrates in bronchial and bronchiolar walls have consisted mainly of lymphocytes and plasma cells. In addition, desquamation of the respiratory epithelium has occurred without significant increases in eosinophilic infiltrate or exudate, mucus gland hyperplasia, basement membrane thickening, or smooth muscle hypertrophy (Brooks et al., 1985). It has been suggested that these changes may cause altered neural and vagal reflexes, modify beta-adrenergic sympathetic tone, and increase the release of inflammatory mediators.

While the definition of RADS is restrictive and requires the presence of a high level exposure, it is conceivable that chronic, low level exposure could cause a similar process to occur (Brooks et al., 1985; Kennedy, 1992). Kennedy (1992) reported that there was

convincing experimental evidence to show that increases in BHR can occur following relatively low level irritant exposure in the workplace and that asthma may occur following high level irritant exposure. Exposure of healthy subjects to 0.6 ppm ozone for 2 hours has been associated with an increase in BHR in all subjects, irrespective of their atopic status (Holtzman et al., 1979). Three studies have implicated poor air quality in the development of respiratory symptoms, sensitization to aero-allergens, and BHR in swimmers who were exposed to low-levels of chemicals used in disinfecting pool water (Mustchin and Pickering, 1979; Penny, 1983; Zwick et al., 1990). The results of these last three studies suggest that problems in maintaining proper swimming pool chemistry using disinfectants such as chlorine may result in poor air quality and the development of BHR. There is also some anecdotal evidence to suggest that BHR may occur in swimmers who train in properly maintained facilities (Zwick et al., 1990).

Thus, chronic, low level exposure to chemical irritants can lead to increased BHR and the development of irritant-induced asthma. The purpose of this study was to: (1) determine the prevalence of BHR in a group of competitive swimmers using a methacholine challenge test; and (2) determine whether there are differences in the prevalence of BHR among competitive swimmers with asthma or swimming-related symptoms and those who have neither asthma nor swimming-related symptoms, and to compare their results with a group of non-swimming athletes who have neither asthma nor swimming-related symptoms.

METHODS

Subjects

The competitive swimmers were placed into either a Case Group or a Control Group depending on their responses to the questionnaire. A subject was considered eligible for the Case Group if he/she had a medical history that included physician-diagnosed asthma and/or symptoms suggestive of asthma (coughing, wheezing, chest tightness and difficulty breathing) while swimming in a pool. A total of 28 lower mainland swimmers met these criteria. Of those, 18 had a medical history which included asthma. Eighteen swimmers (64.3% of eligible participants) agreed to participate in the study and formed the Case Group. A total of 58 lower mainland swimmers stated that they never had asthma or symptoms suggestive of asthma while swimming in a pool. These swimmers were considered eligible for the Control Group and 17 (29.3% of eligible participants) agreed to participate.

In addition to the swimmers, we recruited 16 competitive athletes who did not use swimming as part of their training to act as a non-swimming control group. Among this groups of athletes there were 6 soccer players, 5 middle distance runners, 2 cyclists, 1 rower, 1 skater, and 1 field hockey player. Many of these athletes have participated in intercollegiate and national championships. None of the athletes had a medical history that included physician-diagnosed asthma and/or symptoms suggestive of asthma while exercising. The subjects were informed about the purpose of the test and the procedures to be followed. All of the subjects read and signed a consent form prior to participating in the study.

Preparation of the Methacholine Solution

Acetyl-β-methyl chloride (methacholine) solutions were prepared by the Pharmacy at University Hospital, U.B.C. Site. The following concentrations of methacholine were produced from stock methacholine powder (Valtec Labs, Montreal, PQ): 16.0 mg/mL, 8.0 mg/mL, 4.0 mg/mL, 2.0 mg/mL, 1.0 mg/mL, 0.5 mg/mL and 0.25 mg/mL. To prepare the required concentrations of methacholine, the hospital pharmacy diluted 1,920 mg of methacholine powder with 28.08 mL of bacteriostatic normal saline solution to produce 30 mL of 64.0 mg/mL methacholine solution. This solution was then diluted serially to produce 30 mL of each of the required concentrations of methacholine. Each of the methacholine solutions was placed in a 30 mL bacteriostatic vial, labelled, and sealed in an amber bag. The vials were stored in a refrigerator at 4°C in order to reduce the risk of chemical instability and contamination. The methacholine was removed from the refrigerator at least 30 minutes before testing and allowed to equilibrate to room temperature before use.

Calibration of the Nebulisers

Prior to beginning the study, 2 Wright nebulisers (Aerosol Medical Ltd, Colchester, Essex, UK) were calibrated using the procedures outlined by Juniper, Cockcroft and Hargreave (1991). Three mL of saline solution were placed into the vial of the nebuliser, the vial was attached to the nebuliser and weighed on an FX-40 analytical balance (ANO Company Ltd, Tokyo, Japan) that was accurate to 0.001 gm. The flow rate was adjusted to 7.0 L/min and the nebuliser was attached to the flow meter for exactly two minutes. The flow meter was used to control the flow of medical air (Medigas Ltd, Vancouver, BC) to the

nebuliser. The nebuliser was disconnected from the flow meter and the nebuliser and vial were weighed. The nebuliser output was determined from the difference in weight of the nebuliser and vial.

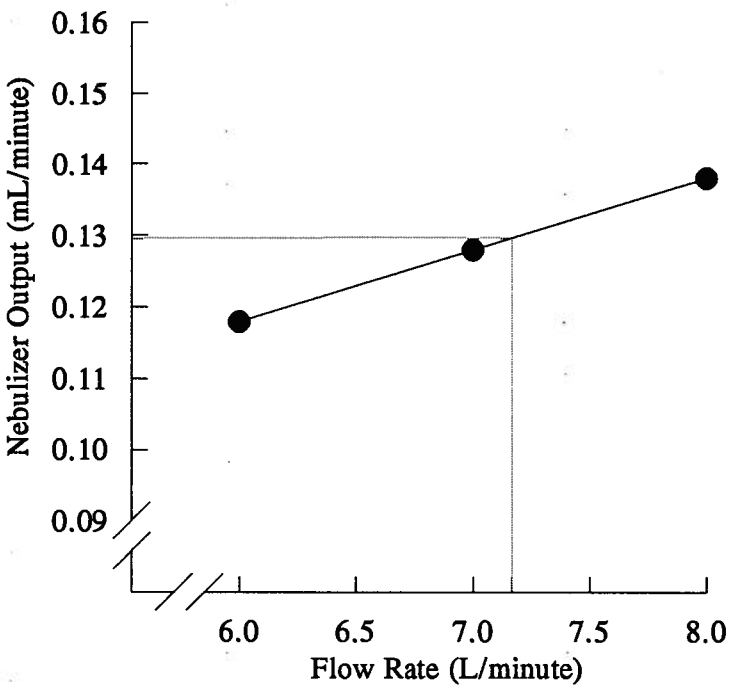
These procedures were repeated five times at each of the following flow rates: 7 L/min, 8 L/min and 9 L/min. The mean value of the five measurements for each flow rate was plotted against the flow rate in order to determine the flow rate that generated an output of 0.13 mL/min (Figure 1). Each set of measurements was reproducible to within $\pm$ 0.006 gm. A flow rate of 7 L/min was found to generate an output of 0.13 mL/min and this flow rate was used for all subsequent experiments.

Calibration of the Spirometer

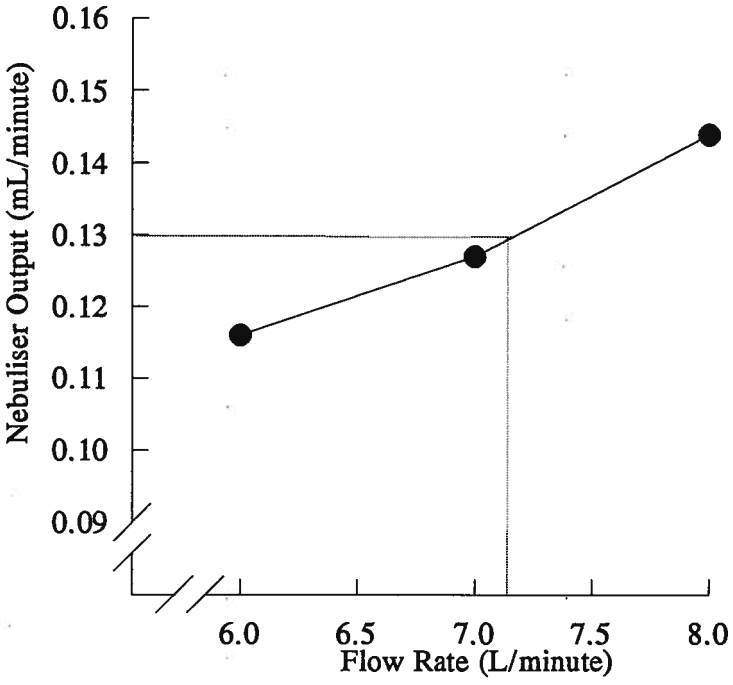
A 1070 Pneumotach (Medical Graphics Corporation, St. Paul, MN) was used to measure lung function. The pneumotach was calibrated prior to testing the first subject. The barometric pressure, room temperature and valve dead space were entered into the computer program operating the pneumotach and the pneumotach was calibrated for both expiratory and inspiratory manoeuvers. A 3 litre syringe was connected to 1⅜" tubing that was attached to the pneumotach. The pneumotach was zeroed to ensure there was no bias flow through the system. The calibration syringe was used to inject five samples of air into the pneumotach at varying flow rates. A calculated volume error of less than 2% was considered acceptable. The pneumotach was again zeroed and the calibration syringe was used to withdraw five samples of air from the pneumotach at varying flow rates. Once again, a calculated volume error of less than 2% was considered acceptable. These procedures were repeated every 3 hours.

Figure 1: Calibration of the Wright Nebulisers prior to methacholine challenge testing. The flow rate of medical air necessary to generate a nebuliser output of 0.13 mL/minute was determined for two nebulisers. Each of the nebulisers required a flow rate of 7 L/minute to generate this output. Figure (a) represents the calibration results for the first nebuliser and Figure (b) represents the calibration results for the second nebuliser.

(a)



(b)



Test Procedures

Prior to methacholine challenge testing, the subjects were asked to refrain from taking medications that are known to inhibit the response of the airways to methacholine. These drugs include inhaled β-agonists (8 hours), oral β-agonists (12 hours), inhaled anticholinergics (12 hours), theophylline (24 hours), slow-release theophylline and corticosteroids (48 hours) and antihistamines (4 days). The subjects were also asked to refrain from exercising or ingesting caffeine on the day of testing.

Lung function was assessed using spirometry. Spirometry was performed using criteria outlined by the American Thoracic Society's Standardization of Spirometry-1987 Update (American Thoracic Society, 1987). The subjects initially performed a Slow Vital Capacity (SVC) manoeuver. They were asked to breath normally for 4-5 breaths. At the end of the last normal expiration, the subjects were asked to take a deep breath and fill their lungs as completely as possible. When their lungs were completely full, the subjects were asked to expire the air until they felt their lungs were completely empty. No time limit was imposed on the manoeuver. They were then asked to take one more deep inspiration and fill their lungs as completely as possible. A minimum of 3 SVC manoeuvers were performed and the reported SVC was derived from the test that produced the largest SVC.

The subjects then performed a Forced Vital Capacity (FVC) manoeuver. They were asked to breath normally for 4-5 breaths. At the end of the last normal expiration, the subjects were asked to take a deep breath and fill their lungs as completely as possible. When their lungs were completely full, the subjects were asked to expire the air as hard and as fast as possible until they felt their lungs were completely empty. They were then asked to take one more deep breath and fill their lungs as completely as possible. A flow-volume

curve was generated and displayed on the computer screen, with flow (L/sec) on the ordinate and volume (L) on the abscissa. A minimum of 3 "acceptable" tests were performed. A test was considered acceptable if it met the following criteria: (1) a maximal, smooth effort was observed; (2) the subject did not cough, perform a valsalva manoeuver, prematurely stop his/her expiration or have an air leak; (3) the extrapolated volume was less than 5% of the FVC or less than 100 mL, whichever was greater; and (4) at least two out of the three tests were within $\pm$ 5% or $\pm$ 100 mL. The FVC, FEV_1, FEV_1/FVC, Mid Maximum Expiratory Flow Rate (FEF_{25-75}) and the Maximum Expiratory Flow Rate ($\dot{V}_{max}$) were recorded and displayed on the computer screen. The reported FVC was derived from the test that produced the largest FVC. The FEV_1 was derived from the test that produced the largest FEV_1. The ratio of the FEV_1/FVC was recorded as a percentage. The FEF_{25-75} and $\dot{V}_{max}$ were taken from the test that produced the largest sum of FVC and FEV_1. These values were entered into a database for statistical analysis.

Once the spirometry had been completed, a face mask (Puritan Bennett Corp, Los Angeles, CA) was attached to the output port of the nebuliser. Using a 3 mL syringe and needle, 3 mL of saline solution were placed into the nebuliser vial. The vial was attached to the nebuliser and the nebuliser was handed to the subject. The subject was instructed to hold the nebuliser and not the vial in order to prevent warming of the solution in the vial. As the flow meter was turned on, the face mask was placed loosely over the subject's nose and mouth. The subjects were instructed to relax and breathe quietly while they inhaled the saline solution. After exactly 2 minutes the flow meter was turned off and the mask and nebuliser were removed from the subject's face. The subject's FEV_1 was measured 30 and 90 seconds after the end of the inhalation. During the expiratory portion of the spirometry

manoeuver, the subjects were asked not to expire to residual volume in order to prevent fatigue or premature closure of the small airways. If the FEV_1 at 90 seconds was the same or lower than that at 30 seconds, the FEV_1 was repeated at 3 minutes and, if needed, at 2 minute intervals until the FEV_1 started to increase. The FEV_1 was only measured once at each time interval to prevent tiring the subject, however, if the subject's performance was not technically satisfactory, the FEV_1 measurement was repeated after 10 seconds. The lowest post-saline FEV_1 was used as a baseline measurement for all subsequent calculations.

The subjects were told that subsequent aerosols may produce a mild cough, chest tightness, wheezing or shortness of breath. They were instructed to remove the face mask and to stop inhaling the aerosol if any of these symptoms made them uncomfortable. The initial concentration of methacholine given to subjects who had asthma, or symptoms suggestive of asthma while swimming, was 0.25 mg/mL. All other subjects started at a concentration of 1.0 mg/mL. The procedures that were outlined for administrating the saline solution were repeated. The concentration of methacholine was doubled and given at 5 minute intervals until the FEV_1 fell by 20% from baseline (PC_{20}), the $FEV_1 \leq 1.5$ L or the highest concentration of methacholine (16.0 mg/mL) had been given. All subjects were then given 200 μg of Salbutamol (Glaxo Canada Inc, Toronto, ON) and their spirometry was repeated to ensure the subject's pulmonary function had returned to normal.

After each test, distilled water was placed in the nebuliser vial and the nebuliser was operated for at least 2 minutes in order to flush the methacholine from the nebuliser. The nebuliser was then washed and rinsed thoroughly and allowed to dry before further use or storage. The data was entered into a database for statistical analysis.

Statistical Analysis

A PC_{20} was calculated for all of the subjects who had a fall in FEV_1 of at least 20% following methacholine challenge testing. The PC_{20} was calculated using the following formula (Juniper et al., 1991):

$$PC_{20} = \text{antilog} \left\{ \log C1 + \frac{(\log C2 - \log C1) \times (20 - R1)}{(R2 - R1)} \right\}$$

where: C1 = second last concentration of methacholine (<20% fall in FEV_1)
C2 = last concentration of methacholine (>20% fall in FEV_1)
R1 = % fall in FEV_1 after C1
R2 = % fall in FEV_1 after C2

A $PC_{20} \leq 16$ mg/mL was considered to represent increased bronchial responsiveness. The prevalence of increased bronchial responsiveness was then determined for each group of athletes. A dose-response slope was calculated for all of the subjects (O'Connor et al., 1987). The dose-response slope was expressed as the FEV_1/MET_{Dose} ratio, where FEV_1 was the maximum decrease in FEV_1 from the post-saline value and MET_{Dose} was defined as the final cumulative dose of methacholine that was given to the subject. The tables for calculating MET_{Dose} are presented in APPENDIX B.

The mean, standard deviation, and standard error of the mean were calculated for all of the descriptive variables . Analysis of variance (ANOVA) was used to determine whether there were statistical differences in the mean values of the dependent variables for the three groups of athletes who participated in the study. If statistical differences were found, a Student-Newman-Keuls multiple range test was used to determine which groups differed.

Sensitivity and specificity were determined from 2 by 2 contingency tables in which "physician-diagnosed asthma" versus "no asthma" was tabulated against "positive test" and "negative test". Sensitivity was defined as the percentage of athletes with asthma and/or symptoms suggestive of asthma who had positive methacholine challenge tests ($PC_{20} \leq 16$ mg/mL). Specificity was defined as the percentage of athletes with neither asthma nor symptoms suggestive of asthma who had negative methacholine challenge tests ($PC_{20} > 16$ mg/mL).

An alpha level of 0.05 ($p < 0.05$) was considered to be statistically significant. All statistical analyses were completed using the SAS® Statistical Software Package (SAS Institute, Inc., Cary, NC).

RESULTS

A total of 51 subjects (25 male and 26 female) completed baseline spirometry and methacholine challenge testing. The physical characteristics of the subjects are presented in Table 14. There were no statistically significant differences in the age, height, or weight between the three groups of athletes. A comparison of the environmental conditions in the laboratory is presented in Table 15. The mean air temperature and relative humidity of the laboratory were significantly higher during testing of the Non-Swimming Control Group than during testing of either of the swimming groups ($p < 0.0069$ and $p < 0.0004$, respectively).

The pulmonary function data are presented in Table 16. The SVC, FVC, and FEV_1 were significantly lower in the Non-Swimming Control Group when compared to either of the swimming groups ($p < 0.0176$, $p < 0.0277$, and $p < 0.0207$, respectively). These differences could not be accounted for by differences in the subjects' height or age, and statistically significant differences between groups existed for SVC, FVC, FEV_1, and $\dot{V}_{max}$ when the percentage of predicted values were calculated. Only one of the 51 subjects (2.0%) had abnormal baseline spirometry. In this case the subject's FEV1/FVC ratio was only 66% which is suggestive of a mild obstructive pattern.

The overall prevalence of increased bronchial responsiveness ($PC_{20} \leq 16$ mg/mL) among the 51 athletes was 45.1%. This included eleven swimmers from the Case Group (61.1%), ten swimmers from the Control Group (58.8%), and two athletes from the Non-Swimming Control Group (12.5%). When we increased the specificity of the test to include only those athletes with a $PC_{20} \leq 8$ mg/mL, six swimmers from the Case Group (33.3%) and six swimmers from the Control Group (35.3%) had increased bronchial responsiveness. None of the non-swimming athletes had a $PC_{20} \leq 8$ mg/mL. The distribution of PC_{20} among

the three groups of athletes is outlined in Table 17. A summary of the dose-response curves for the three groups of athletes who participated in the methacholine challenge testing is presented in Figures 2-5.

The dose-response slope was calculated to be -6.55 $\pm$ 10.53 for the Case Group, -6.23 $\pm$ 8.63 for the Control Group, and -1.22 $\pm$ 0.72 for the Non-Swimming Control Group. The dose-response data were found to be positively skewed and was normalized by using the natural logarithm of each dose-response slope value. The log of the dose-response slope was 1.08 $\pm$ 1.36 for the Case Group, 1.01 $\pm$ 1.43 for the Control Group, and 0.01 $\pm$ 0.79 for the Non-Swimming Control Group. The log of the dose-response slope was significantly lower in the Non-Swimming Control Group when compared to either of the swimming groups ($p < 0.0257$).

The sensitivity and specificity of a $PC_{20} \leq 16$ mg/mL for identifying subjects with asthma or symptoms suggestive of asthma while swimming were 66.7% and 71.4%, respectively. The sensitivity and specificity of a $PC_{20} \leq 8$ mg/mL for identifying subjects with asthma or symptoms suggestive of asthma while swimming were 27.8% and 81.8%, respectively.

Table 14: A comparison of the physical characteristics of the 3 groups of competitive athletes. The $\bar{x} \pm$ SD are reported.

	Case Group	Control Group	Non-Swimming Control Group	Level of Significance
Age (years)	17.56 ± 2.99	19.18 ± 3.61	20.50 ± 4.76	NS
Height (cm)	174.43 ± 8.04	175.62 ± 9.25	173.94 ± 7.36	NS
Weight (kg)	67.88 ± 11.48	69.29 ± 9.49	69.02 ± 9.02	NS

NS = No statistically significant differences were found between groups.

Table 15: A comparison of the environmental conditions in the laboratory during methacholine challenge testing of the 3 groups of competitive athletes. The $\bar{x} \pm$ SD are reported.

	Case Group	Control Group	Non-Swimming Control Group	Level of Significance
Barometric Pressure (torr)	757.72 ± 4.66	754.94 ± 8.26	755.56 ± 2.68	NS
Air Temperature (°C)	21.50 ± 1.10	21.12 ± 0.78	22.25 ± 1.06	$p<0.0069$ *
Relative Humidity (%)	59.28 ± 5.14	58.06 ± 3.96	65.19 ± 5.99	$p<0.0004$ *

* The mean air temperature and relative humidity were higher during testing of the Non-Swimming Control Group.
NS = No statistically significant differences were found between groups.

Table 16: A comparison of the pulmonary function variables for the 3 groups of competitive athletes. The $\bar{x} \pm$ SD are reported. The percentage of predicted values (in parenthesis) were calculated using equations by Knudson et al. (1983) and Knudson et al. (1976).

	Case Group	Control Group	Non-Swimming Control Group	Level of Significance
SVC (L)	5.52 ± 1.00 (126%)	5.99 ± 1.30 (131%)	4.89 ± 0.82 (107%)	$p<0.0176$*
FVC (L)	5.46 ± 0.94 (125%)	5.89 ± 1.26 (128%)	4.89 ± 0.81 (107%)	$p<0.0277$*
FEV_1 (L)	4.47 ± 0.75 (117%)	4.86 ± 0.88 (122%)	4.10 ± 0.58 (103%)	$p<0.0207$*
FEV_1/FVC (%)	82.17 ± 5.48	83.29 ± 7.16	84.25 ± 6.07	NS
$FEF_{25\%-75\%}$ (L/sec)	4.31 ± 0.94 (98%)	4.79 ± 1.02 (105%)	4.55 ± 1.29 (98%)	NS
$\dot{V}_{max}$ (L/sec)	9.23 ± 1.83 (116%)	10.73 ± 2.70 (129%)	8.95 ± 1.70 (107%)	NS

* The mean SVC, FVC, and FEV_1 values of the Control Group were higher than the mean values of the Non-Swimming Control Group.
NS = No statistically significant differences were found between groups.

Table 17: The results of methacholine challenge testing. The distribution of PC_{20} is summarized for the three groups of athletes.

	Case Group	Control Group	Non-Swimming Control Group
$PC_{20} \leq 2$ mg/mL	2	1	
$2 < PC_{20} \leq 4$ mg/mL		3	
$4 < PC_{20} \leq 8$ mg/mL	4	2	
$8 < PC_{20} \leq 16$ mg/mL	5	4	2
$PC_{20} > 16$ mg/mL	7	7	14

Figure 2: Dose-response curves for all three groups of athletes during methacholine challenge testing. The percentage change in FEV_1 is plotted against the concentration of methacholine on a logarithmic scale.

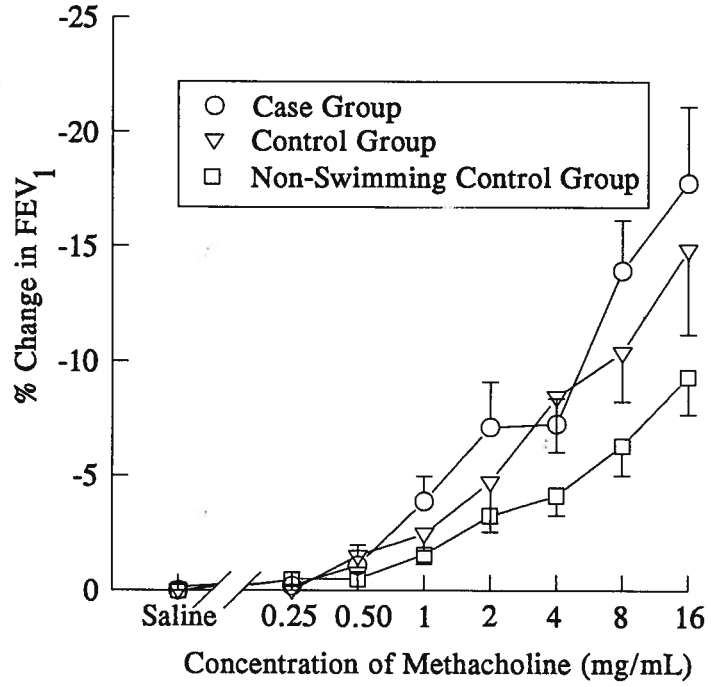


Figure 3: Dose-response curve for the Case Group (n=18) during methacholine challenge testing. The percentage change in FEV_1 is plotted against the concentration of methacholine on a logarithmic scale.

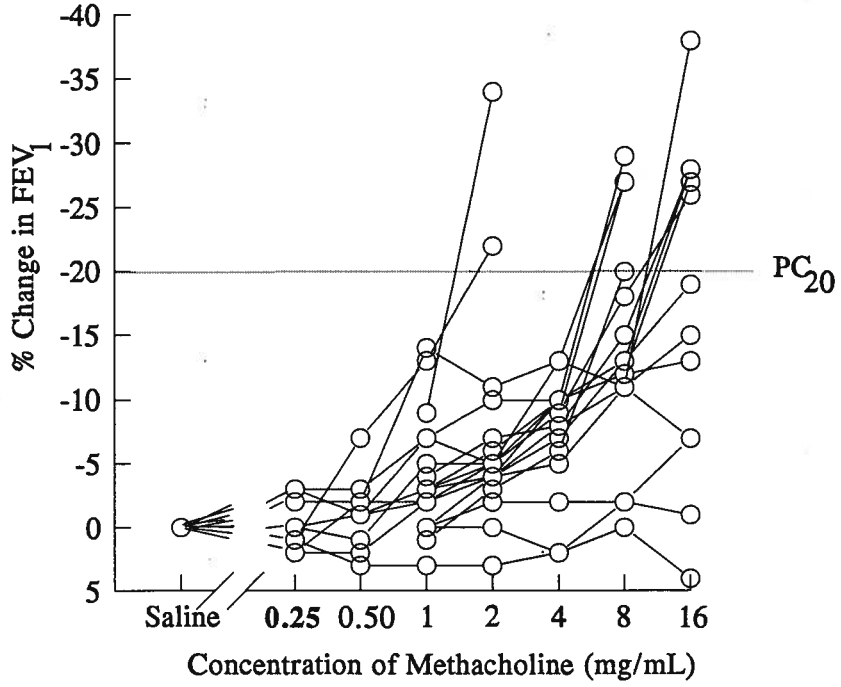


Figure 4: Dose-response curve for the Control Group (n=17) during methacholine challenge testing. The percentage change in FEV_1 is plotted against the concentration of methacholine on a logarithmic scale.

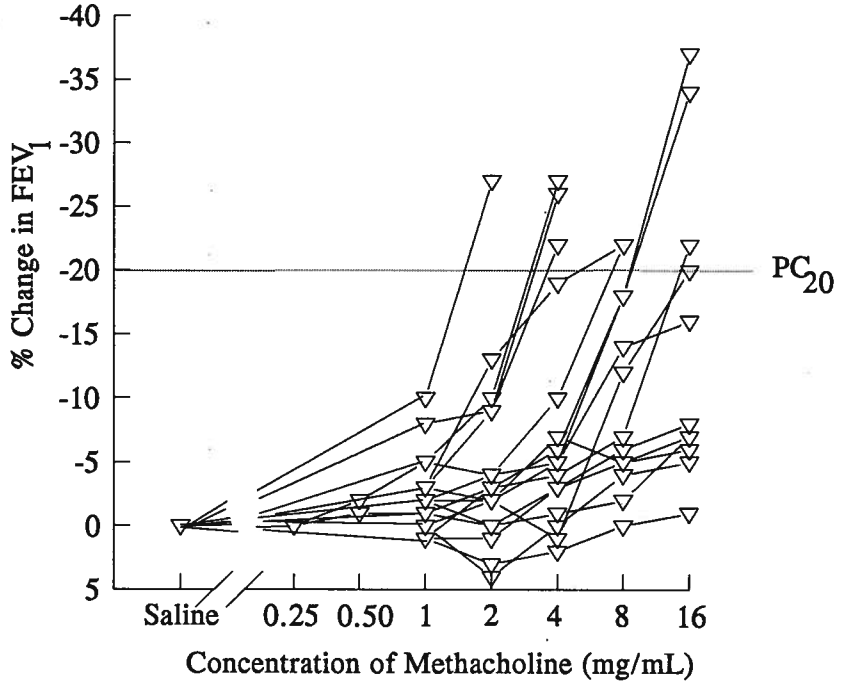
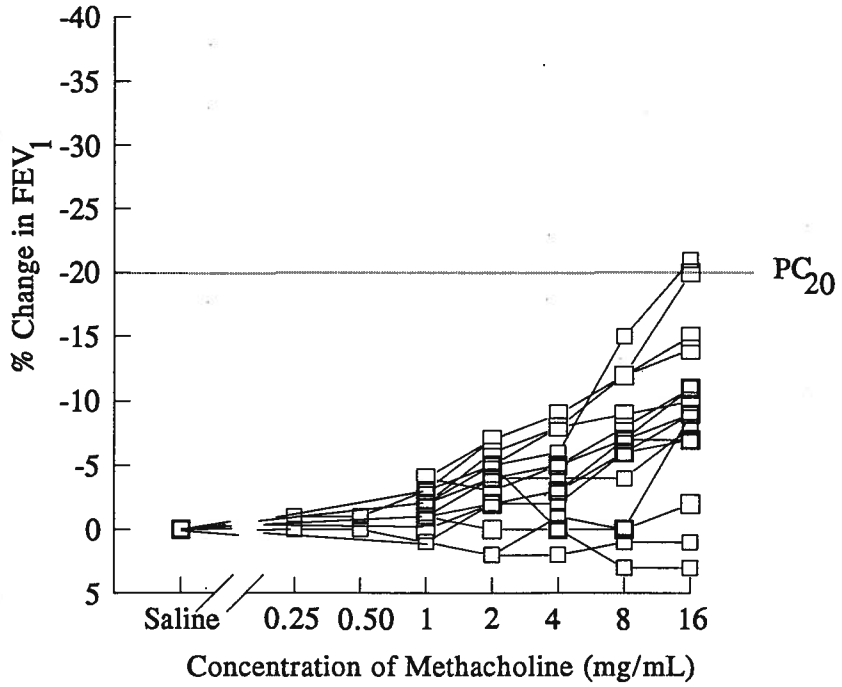


Figure 5: Dose-response curve for the Non-Swimming Control Group (n=16) during methacholine challenge testing. The percentage change in FEV_1 is plotted against the concentration of methacholine on a logarithmic scale.



DISCUSSION

This study shows that the prevalence of BHR ($PC_{20} \leq 16$ mg/mL) among competitive swimmers in the lower mainland of British Columbia is approximately 60.0%. This includes 61.1% of swimmers in the Case Group and 58.8% of swimmers in the Control Group. When the sensitivity of the methacholine challenge test is increased to include only those swimmers with a $PC_{20} \leq 8$ mg/mL, 33.3% of the swimmers in the Case Group and 35.3% of the swimmers in the Control Group demonstrated BHR. There does not appear to be any difference in the prevalence of BHR among swimmers who have asthma or complain of swimming-related symptoms when compared to those that have neither asthma nor swimming-related symptoms. However, the prevalence of BHR among non-swimming athletes appears to be significantly lower than that of swimmers: only 12.5% of the non-swimmers had a $PC_{20} \leq 16$ mg/mL and none had a $PC_{20} \leq 8$ mg/mL.

Several studies have attempted to establish the prevalence of BHR in the normal population. Cockcroft et al. (1992) conducted a survey of 500 college students and measured their PC_{20} using histamine. BHR ($PC_{20} \leq 8$ mg/mL) was observed in only 11.6% of the students. Woolcock et al. (1987) estimated the prevalence of BHR in 876 subjects from Western Australia to be approximately 11.4%. Their study identified strong associations between BHR and respiratory symptoms, atopy, smoking, and abnormal lung function, however, there was no association found between BHR and age, sex, or recent respiratory tract infections. Finally, Burney et al. (1987) estimated the prevalence of BHR to be 14% in 511 subjects from southern England. BHR was strongly associated with skin sensitivity to common allergens and a positive history of smoking. Both skin sensitivity and a history of smoking were dependent on age. Skin sensitivity was an important determinant of BHR in the young subjects and smoking was an

important determinant of BHR in the older subjects.

BHR has been found to be unimodally distributed in population samples and is negatively skewed, that is, skewed toward hyperresponsiveness (Cockcroft et al., 1983; Cockcroft et al., 1992; O'Connor et al., 1987; Weiss et al., 1984). Our results show that while BHR is unimodally distributed among the competitive swimmers, the data are positively skewed or skewed toward non-responsiveness. In addition, while a $PC_{20} \leq 8$ mg/mL is often used clinically to represent increased bronchial responsiveness, our results and those of several other studies have indicated the benefits of using a $PC20 \leq 16$ mg/mL in population studies (Cockcroft et al., 1992; Kennedy et al., 1990; Malo et al., 1991).

In their study of the sensitivity and specificity of PC_{20} in 500 students, Cockcroft et al. (1992) demonstrated that with "current symptomatic asthma" as the diagnosis and $PC_{20} \leq 8$ mg/mL as the positive test, the sensitivity was 100%, the specificity was 93%, the positive predictive value was 29%, and the negative predictive value was 100%. If the cut-off point for the positive test was reduced to a $PC_{20} < 1$ mg/mL, the sensitivity and negative predictive value were decreased to 41% and 98%, respectively, and the specificity and positive predictive value were both increased to 100%. In our study, the sensitivity and specificity of a $PC_{20} \leq 8$ mg/mL for identifying subjects with asthma or symptoms suggestive of asthma while swimming were 27.8% and 81.8%, respectively. In addition, a comparison of our pulmonary function and methacholine challenge results with those of Cockcroft et al. (1992) would suggest that among those swimmers with asthma or symptoms suggestive of asthma, very few are current asthmatics.

Our results suggest that the sensitivity and specificity of using a questionnaire to diagnose asthma in competitive swimmers is not very good. Part of the reason is that the prevalence of

BHR in swimmers who have neither asthma nor symptoms suggestive of asthma during exercise, whether you consider a positive test at a PC20 $\leq$ 16 mg/mL or PC20 $\leq$ 8 mg/mL, is higher than in the normal population and similar between our Case and Control Groups. Our results are similar to those of Malo et al. (1991) who assessed the validity of using a questionnaire to diagnose occupational asthma. Their results suggested that an open medical questionnaire is not a satisfactory means of diagnosing occupational asthma.

One of the disadvantages of using the PC_{20} as an index of responsiveness is that a number of subjects will fail to experience a significant drop in their FEV_1 and their data will be left out of any statistical analyses. O'Connor et al. (1987) have suggested that in a population study the loss of this information may be consequential to the results of the study. The authors recommended that the dose-response data be summarized by using the ratio of the percent decrease in FEV_1 over the cumulative dose of methacholine that was given (dose-response slope). In population studies, calculation of the dose-response slope allows for the inclusion of all of the individual dose-response data.

O'Connor et al. (1987) have shown that there can be more than a 3,000-fold difference between the least and most responsive subjects using this method. In our study there was approximately a 363-fold difference between the least and most responsive subjects. When the data were normalized by using the natural logarithm of each of the mean values, the dose-response slope was found to be significantly lower in the non-swimmers than in either of the swimming groups. This indicates that bronchial responsiveness was significantly lower in the non-swimmers.

The remarkable differences in the prevalence of BHR between the swimmers and non-swimmers is one of the interesting findings of this study. To our knowledge, there are only two

other studies that have evaluated BHR among highly trained athletes. Zwick et al. (1990) studied 14 competitive swimmers and 14 matched control subjects and found that 78.6% of the swimmers and 35.7% of the control subjects had increased bronchial responsiveness after being given 140 μg, 1540 μg, and 8540 μg of nebulised methacholine. The increase in non-specific bronchial responsiveness in the swimmers was associated with conjunctival or respiratory symptoms (78.6%), sensitization to aeroallergens (78.6%), and altered cellular immunity (50.0%). The control group had significantly lower prevalences of symptoms (21.4%), sensitization to aeroallergens (35.7%), and altered cellular immunity (14.3%). The authors concluded that frequent exposure to chlorine, chlorine gas, or their constituents may facilitate sensitization to different allergens and increase non-specific bronchial responsiveness.

Weiler et al. (1986) tested college athletes and students at the University of Iowa and found BHR in 50% of the football players, 25% of the basketball players, and 41% of the students. In their study, BHR occurred if the FEV_1 fell by 20% or more after administration of 150 breath units of nebulised methacholine (1 breath unit = 1 mg/mL). Only 12% of the football players and 7% of the students had a history of asthma. The athletes and students without nasal symptoms (allergic rhinitis or hay fever) were less likely to have BHR than those with symptoms and, contrary to other studies that have been published, athletes and students with current or recent upper respiratory tract infections were no more likely to have BHR than those who did not. The authors suggested that the high prevalence of BHR among the football players may have occurred as a result of living and exercising in a polluted or cold environment, deconditioning, or because of allergies.

The extremely high prevalence of BHR among the competitive swimmers may result from chronic, low level exposure to chemical irritants in pool water. While this theory is speculative,

there are a number of studies which have shown that competitive swimmers may develop mild bronchial irritation from chronic, low level exposure to chemical irritants in pool water. Mustchin and Pickering (1979) described the sudden onset of reversible airways disease in 3 swimmers during a training session in a recently opened indoor pool. Many of the 24 swimmers who were training in the pool at the time of the incident developed a cough, sore throat, and chest tightness, and nearly half of the swimmers had to leave the water as a result. The development of these symptoms were apparently associated with a strong chemical odor in the pool. The authors suggested that low concentrations of chlorine gas may have resulted in a mild degree of bronchial irritation.

Penny (1983) described a case report of a 57 year old man who also complained of coughing for 12-24 hours after swimming in a recently opened pool. He also noticed a strong chemical odor in the pool. The patient's symptoms were associated with a reduction in FEV_1 following an exercise challenge swim in the pool. This facility used a heat reclamation system that recirculated a high proportion of the air in the pool. Penny suggested that this irritant exposure also resulted in a mild degree of bronchial irritation and increased bronchial responsiveness.

Our results suggest that the swimming-related exposure results in increased non-specific bronchial responsiveness without causing any measurable change in baseline lung function among the competitive swimmers. What we do not know is why some swimmers have swimming-related symptoms suggestive of asthma and others do not. A possible explanation might be that those swimmers who have swimming-related symptoms may have higher training volumes or cumulative exposures, or may have been exposed to higher concentrations of pool chemicals than those swimmers without swimming-related symptoms. However, our data suggests that there

were no differences in the training volumes or cumulative exposures among the two groups of swimmers. Whether or not swimmers with swimming-related symptoms were exposed to higher concentrations of chemicals used to treat the pool water remains speculative. The clinical manifestations of this swimming-related exposure, whether it is related to the chemical treatment of the pool water, exercise, or both, may simply be to increase BHR and, in some individuals, to cause swimming-related symptoms suggestive of asthma.

Kennedy (1992) has suggested that chronic, low level exposure to environmental irritants may cause a significant increase in non-specific bronchial responsiveness. She goes on to suggest that persons who are exposed accidentally or episodically to irritants at higher concentrations may also develop symptoms suggestive of asthma, variable airflow obstruction, and even greater BHR. Other studies have shown that chemical irritation of the respiratory tract may damage the respiratory epithelium and cause chronic, non-specific airway inflammation (Brooks et al., 1985; Gautrin et al., 1994).

Most theories that relate epithelial damage and airway responsiveness are based on the assumption that epithelial damage and loss result in increased exposure of afferent receptors, increased sensitivity of the receptors, and enhanced accessibility of bronchoconstrictor agents to bronchial smooth muscle and/or sensory nerve endings under the mucosa (Brooks et al., 1985; Postma et al., 1989). Tracheo-bronchial irritant receptors and pulmonary C-fibers are likely involved in the physiological response to these chemical irritants. In particular, when C-fibers are exposed to inflammatory mediators they may trigger an axon reflex which results in the release of several neuropeptides that enhance smooth muscle contraction and inflammation (Barnes, 1986; Lundberg et al., 1988). We postulate that this mechanism may be responsible for the increased non-specific bronchial responsiveness found in the competitive swimmers

involved in our study.

The possibility also exists that chronic, low level exposure to chemically-treated pool water may result in the development of occupational asthma. Bernstein et al. (1993) defined occupational asthma as a disease that is "characterized by variable airflow limitation and/or bronchial hyperresponsiveness due to causes and conditions that are attributable to a particular occupational environment and not to stimuli encountered outside of the workplace". Zwick et al. (1990) have demonstrated that competitive swimmers have increased sensitization to aero-allergens and it is possible that the chemicals used to treat the pool water are not only irritants, but sensitizing agents as well. In a recently published study by Gautrin et al. (1994), the authors assessed the reversibility of airway obstruction, determined the prevalence of BHR, and described the pathological changes that occurred in the airways of patients with immunologically-induced occupational asthma and a severe form of irritant-induced occupational asthma, RADS.

The results of this study show that patients with occupational asthma have greater reversibility of airway obstruction following the administration of the β_2-adrenergic agent, albuterol, however, they also have more pronounced BHR. The average improvement in FEV_1 following the administration of albuterol was 19.4% and 9.6% in patients with occupational asthma and RADS, respectively. The average PC_{20} in the patients with occupational asthma was 0.4 mg/mL, while the average PC_{20} in the patients with RADS was 2.0 mg/mL. The pathological data retrieved from BAL fluid and biopsy specimens from the subjects suggests that patients with RADS have an increased number of inflammatory cells (including lymphocytes), focal desquamation of the epithelial layer in association with squamous cell metaplasia and the loss of cilia, the presence of inflammatory cells (lymphocytes, polymorphonuclear neutrophils and eosinophils, mastocytes and monocytes/macrophages), extensive reticulocollagenic fibrosis

of the bronchial wall, and severe thickening of the basement membrane (Gautrin et al., 1994).

The authors concluded that occupational asthma and RADS can be distinguished by differences in airway reversibility, BHR, and some of their pathological features. They also suggested that patients with RADS who have normal airway caliber, mild BHR, and minimal functional changes in airway function, may also have extensive pathological changes to their airways. While the competitive swimmers in our study appear to have normal airway caliber and mild BHR, it is hoped that chronic, low level exposure to chemically-treated pool water does not result in the severe pathological changes that occur to the airways of individuals with occupational asthma or RADS.

CONCLUSIONS

In conclusion, this study shows that the prevalence of BHR ($PC_{20} \leq 16$ mg/mL) among lower mainland competitive swimmers is 60.0%. When the sensitivity of the methacholine challenge test was decreased to include only those swimmers with a $PC_{20} \leq 8$ mg/mL, the prevalence of BHR is 34.3%. These values are significantly higher than the 12.5% and 0% prevalences that were observed for 16 non-swimming athletes in our study and the 11-14% prevalence reported in several population-based studies. There was no difference in the prevalence of BHR among competitive swimmers who have a clinical history of asthma or symptoms suggestive of asthma while exercising (61.1%) and those who have neither asthma nor symptoms (58.8%). When the sensitivity of the methacholine challenge test was decreased to include only those swimmers with a PC20 ≤ 8 mg/mL, 33.3% of the swimmers in the Case Group and 35.3% of the swimmers in the Control Group demonstrated BHR.

The use of the dose-response slope was effective in assessing differences in BHR among the three groups of athletes. In our study there was approximately a 363-fold difference between the least and most responsive subjects using this method. The dose-response slope was significantly lower in the non-swimmers, indicating a lower prevalence of BHR in that group of athletes. The use of a clinical history to identify subjects with asthma was extremely poor using either a PC20 ≤ 8 mg/mL or a $PC_{20} \leq 16$ mg/mL. As an example, in our study the sensitivity and specificity of a $PC_{20} \leq 8$ mg/mL for identifying subjects with asthma or symptoms suggestive of asthma were 27.8% and 81.8%, respectively. In addition, a comparison of our pulmonary function and methacholine challenge test results with those of Cockcroft et al. (1992) suggests that among swimmers who reported asthma or symptoms suggestive of asthma, very few are current asthmatics.

The clinical manifestations of this swimming-related exposure, whether it is related to the chemical treatment of the pool water, exercise, or both, may simply be to increase BHR and, in some individuals, cause swimming-related symptoms suggestive of asthma. What remains unknown is why some swimmers develop swimming-related symptoms suggestive of asthma and others do not. A possible explanation might be that swimmers with swimming-related symptoms may have been exposed to higher concentrations of pool chemicals than those swimmers without swimming-related symptoms, however, this theory remains speculative.

The most likely mechanism for the increased non-specific bronchial responsiveness in these competitive swimmers is that chronic, low level exposure to the chemicals used to disinfect the pool water may cause damage to the epithelial layer of the swimmer's airways. This damage may result in increased exposure of afferent receptors, increased sensitivity of the receptors, and enhanced accessibility of bronchoconstrictor agents to bronchial smooth muscle and/or sensory nerve endings under the mucosa. The tracheo-bronchial irritant receptors and pulmonary C-fibers are likely involved in this physiological response and inflammatory mediators may trigger an axon reflex which results in the release of several neuropeptides that enhance smooth muscle contraction and inflammation.

While there is some clinical evidence from other studies to suggest that competitive swimmers may have increased sensitization to a number of common aero-allergens, it is hoped that chronic, low level exposure to chemically-treated pool water does not result in the severe pathological changes that occur to the airways of individuals with immunological- or irritant-induced occupational asthma.

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CHAPTER 3

The Prevalence of Exercise-Induced Asthma in a Select Group of Competitive Swimmers and Non-Swimmers

ABSTRACT

Exercise has been shown to be a potent, non-antigenic, non-pharmacologic stimulus for assessing bronchial responsiveness. Exercise-induced asthma (EIA) is the manifestation of increased bronchial responsiveness and is characterized by reversible airflow obstruction following several minutes of exercise. Exercise differs from other initiators of asthma in that it does not produce any long-term sequelae and, in about 50% of subjects with EIA, there is a significant refractory period during which repeated exercise will attenuate further bronchoconstriction. The underlying pathophysiology of EIA is that during exercise heat and water are lost from the respiratory epithelium in warming the inspired air from ambient to body conditions. The net effect is to cool and dehydrate the airways which, in turn, leads to the development of the post-exercise symptoms and bronchoconstriction which are typical of EIA.

A number of researchers have suggested that an increase in bronchial responsiveness may also occur in athletes without EIA who have been exposed to swimming pool disinfectants such as chlorine or chloramines, or photochemical air pollutants such as ozone, nitrogen dioxide, and sulphur dioxide. Concurrent with this hypothesis, we have previously shown that 60% of the competitive swimmers that were tested had increased non-specific bronchial responsiveness to methacholine. What remained to be determined was whether this was a response to chronic, low level exposure to chemical irritants in the water and air of the swimming pool, an exercise response, or both.

Therefore, the purpose of this study was to: (1) establish the prevalence of EIA in a group of competitive swimmers using a standard exercise challenge test in the laboratory; (2) establish the prevalence of EIA in the same group of swimmers using an exercise protocol in the swimming pool; (3) determine whether there are differences in the prevalence of asthma among competitive swimmers with asthma or exercise-related symptoms and those who have neither asthma nor exercise-related symptoms, and to compare their results with a group of non swimming athletes who have neither asthma nor exercise-related symptoms; and (4) determine whether a prolonged exercise challenge test in the swimming pool results in the development of respiratory symptoms and significant changes in pulmonary mechanics among the two groups of competitive swimmers.

Our results show that the prevalence of EIA among lower mainland competitive swimmers is 9.8%. This value is within the 3-11% prevalence reported for other competitive athletes, and is higher than the 6.3% that was observed for the non-swimming athletes in our study. The prevalence of EIA among the swimmers was also higher in the laboratory (9.8%) when compared to the swimming pool (3.6%). Our results are in agreement with those of other researchers who have shown the lower asthmogenicity of swimming when compared to land-based activities. The mechanisms for this protective effect are not clear and, in our study, do not appear to be related to differences in the subjects' $\dot{V}E$ or the temperature and relative humidity of the inspired air. There were also no differences in the prevalence of EIA among competitive swimmers who have asthma or exercise related symptoms (11.1%) and those who have neither asthma nor exercise-related symptoms (11.8%).

While continuous submaximal swimming for 45 minutes results in the swimmers complaining of many of the symptoms reported on the questionnaire, we were unable to demonstrate significant pre- to post-exercise changes in FEV_1. However, the swimmers in the

Case Group adopted a restrictive breathing pattern similar to that of athletes who are exposed to ozone during exercise. It is possible that this might be an early indicator of respiratory distress. Finally, there is a remarkable discrepancy between the prevalence of BHR and EIA among the competitive swimmers. These results provide us with substantial evidence that there is something about the swimming-related exposure that increases non-specific bronchial responsiveness, but does not incite EIA.

INTRODUCTION

Exercise is a potent, naturally-occurring, non-antigenic, non-pharmacologic stimulus for assessing bronchial responsiveness in subjects with asthma, allergic rhinitis, hay fever, and in athletes with symptoms suggestive of asthma during or after exercise. Exercise-induced asthma (EIA) is the manifestation of increased bronchial responsiveness that occurs in response to physical activity and is characterized by reversible airflow obstruction following several minutes of exercise.

The prevalence of EIA in asthmatics, atopic individuals and athletes has been well documented. Theoretically, any subject with current symptoms of asthma should develop EIA if challenged under the appropriate exercise conditions, however, only 60-90% of asthmatics and 35-40% of subjects with allergic rhinitis or hay fever develop EIA (Anderson, 1985; Bundgaard, 1981; Chan-Yeung et al., 1971; Itkin and Nacman, 1966; James et al., 1976; Kawabori et al., 1976; McNeill et al., 1966; Rupp et al., 1992). The prevalence of EIA among athletes ranges between 3-11% (Fitch, 1984; Helbling and Muller, 1991; Huftel et al., 1991; Rice et al., 1985; Voy, 1986) and is approximately 7% in healthy controls (Bierman et al., 1975). The wide range of values reported in the literature for asthmatics is probably due to variability in the type, intensity and duration of exercise that were used to assess EIA and to discrepancies in the definitions of asthma and a positive exercise test.

The clinical presentation of EIA may vary among individuals. Its presentation may be similar to an acute attack of asthma, with the subject developing symptoms of wheezing, chest tightness, dyspnea, sputum production and coughing. Others may develop breathlessness that is inappropriate to the exercise task, demonstrate a transient post-exercise cough, or perform poorly (McKenzie, 1991). The pattern of response of the airways to exercise is well known.

There is mild bronchodilation of the airways during exercise that is followed by bronchoconstriction and an increase in airway resistance in the immediate post-exercise period (Morton et al., 1981; Stirling et al., 1983). The increase in airway resistance reaches maximal values in 3-5 minutes in children and 5-7 minutes in adults (Gilbert et al., 1988) and returns to normal values in 30-90 minutes (McFadden, 1991; McKenzie, 1991).

The use of an exercise challenge test offers the advantage that normal subjects do not respond to the challenge with any significant change in their lung function (Deal et al., 1980; McFadden, 1991). A positive exercise challenge test is defined as either a 15-20% decrease in the subject's baseline FEV_1 or a 35-40% decrease in the specific conductance of the airways following 6-8 minutes of exercise at an intensity of 85-90% of the subject's maximal heart rate (Eggleston et al., 1979; McFadden, 1991; McKenzie, 1991; Mahler, 1993).

There is good correlation between the prevalence of increased bronchial responsiveness as determined by exercise, histamine challenge or methacholine challenge (O'Byrne et al., 1982; Weiss et al., 1983). However, as McFadden (1991) points out, there is not one-to-one correspondence and individuals may be more sensitive to exercise than to pharmacological stimuli, and vice versa. His article suggests that a negative exercise challenge test does not necessarily exclude the existence of increased bronchial responsiveness.

Exercise differs from other initiators of asthma in that it does not seem to produce any long-term sequelae and it has a refractory period. Asthmatic subjects who are exposed to allergens or occupational sensitizing agents develop acute bronchospasm that is associated with inflammation of the airways (Crimi et al., 1992; De Monchy et al., 1985; Rossi et al., 1991; Zawadski et al., 1988). One of the controversial issues surrounding EIA is whether a late-phase, inflammatory response to exercise occurs. While exercise has been shown to be

associated with mast cell degranulation and the influx of eosinophils and other inflammatory mediators into the airway lumen, the delayed bronchoconstriction observed 3-6 hours after exercise is now thought to be unrelated to exercise and is more likely related to underlying airway inflammation and to the withdrawal of medication in asthmatic subjects (Crimi et al., 1992; Zawadski et al., 1988). Rubinstein et al. (1987) also suggested that the biphasic asthmatic response to exercise is uncommon and is related to the withdrawal of medication or methodological problems in the experimental design of the study.

Approximately 50% of all subjects with EIA demonstrate significant refractoriness to repeated exercise challenge (McNeill et al., 1966; Schoeffel et al., 1980; Anderson, 1984). During this refractory period, the response of the airways to exercise can be attenuated for as long as 4 hours (Edmunds et al., 1978; McNeill et al., 1966; Schoeffel et al., 1980). It was originally thought that the degree of refractoriness may be related to the severity of exercise and the degree of bronchoconstriction and could be explained on the basis of respiratory heat loss (RHL) (Edmunds et al., 1978). This hypothesis has been rejected because we now know that a good warm-up prior to exercise, and breathing warm, humid air during exercise, may abolish EIA even though refractoriness to further exercise is maintained (Ben-Dov, 1982). Also, Anderson and Schoeffel (1982) have shown that about 50% of asthmatic subjects who were exposed to two exercise challenge tests 40-52 minutes apart had significant protection from EIA following the second challenge even though the RHL was the same.

The refractoriness to exercise can be blocked by indomethacin and acetylsalicylic acid, both of which are cyclo-oxygenase inhibitors. This suggests that prostaglandins may play a role in mediating the bronchodilation that occurs during exercise and the subsequent refractoriness that occurs after exercise (Hahn et al., 1984, 1985; Margolskee et al., 1988; O'Byrne and Jones,

1986; Reiff et al., 1989). Manning et al. (1993) studied 14 asthmatic subjects who were challenged with exercise or inhaled LTD_4. Several of the subjects then took part in a series of double-blind, randomized, cross-over studies with flurbiprofen, a prostaglandin synthetase inhibitor, to determine whether cross-over refractoriness occurred between exercise and LTD_4, whether flurbiprofen attenuated this effect, and whether flurbiprofen attenuated LTD_4 tachyphylaxis. The results of this study showed that there was a reduction in the intensity of bronchoconstriction to the second challenge both with exercise (refractoriness) and with LTD_4 (tachyphylaxis). The authors suggested that LTD_4 released in asthmatic airways as a result of exercise stimulates prostaglandin release which is, in part, responsible for exercise refractoriness.

Belcher et al. (1988) have proposed that the refractory period in EIA is also not caused by the depletion of mediators such as histamine or neutrophil chemotactic factor of anaphylaxis (NCFA). An alternative hypothesis suggests that increased sympathoadrenal activity may be responsible for the refractoriness following exercise. This hypothesis has yet to be proven because the measurement of circulating catecholamines (epinephrine and norepinephrine) has shown only modest increases during exercise and are supposedly blunted in asthmatic subjects (Barnes et al., 1981; Belcher et al., 1988). Is the depletion of mediators from mast cells and other inflammatory cells or increased catecholamine release during exercise responsible for the refractory period following exercise? As we have not yet been able to identify the cause of either EIA or its refractoriness to further exercise, there may be a number of inter-related factors that are responsible (Reiff et al., 1989).

One of the methods that is thought to induce refractoriness and attenuate the airways' response to exercise is to warm-up prior to participating in vigorous physical activity. Repeated

short sprints result in significantly less bronchoconstriction in asthmatic subjects (Schnall and Landau, 1980). Fifteen minutes of continuous treadmill running at an exercise intensity of 60% of maximal oxygen consumption ($\dot{V}O_2max$) (McLuckie, 1986) and for 30 minutes at a submaximal intensity (Reiff et al., 1989) have both been shown to be effective in inducing refractoriness and decreasing the level of bronchoconstriction in subsequent exercise sessions. A study by Morton et al. (1979) used three minutes of treadmill running at an exercise intensity of 60% $\dot{V}O_2max$ to determine the effect of warm-up. Their study failed to show any benefit of warm-up, but suggested that the intensity and duration of the warm-up be increased before rejecting the hypothesis of the benefits of warm-up on EIA.

The type of physical activity also plays an important role in determining the degree of bronchoconstriction that occurs following exercise. Early studies used a variety of methods to induce EIA. These included ascending and descending stairs (Davies, 1968; Fisher et al., 1970; McNeill et al., 1966), running along hospital corridors (Pierson and Bierman, 1975), treadmill walking (Sly, 1970), bicycle ergometry (Pierson et al., 1969) and swimming (Bar-Yishay et al., 1982; Fitch, 1975). It was soon realized that different modes of exercise did not produce comparable effects (Anderson et al., 1971). Outdoor running is considered to be the most asthmogenic activity, followed by treadmill running, cycling, swimming and walking (Anderson et al., 1971; Fitch and Morton, 1971). Respiratory heat loss and exposure to cold and dry air, dust, and photo-chemical air pollution (Bar-Or et al., 1977; McKenzie et al., 1987; Strauss et al., 1977) may help to explain why some activities cause more or less bronchoconstriction than others.

It has now been shown that intermittent exercise causes less bronchoconstriction than continuous exercise, although the differences can be minimized by equalizing the minute

ventilation ($\dot{V}E$) and presumably equalizing the RHL (McKenzie, 1991; Noviski et al., 1987). Fitch and Godfrey (1976) and Godfrey (1984) have clearly demonstrated a lower prevalence of EIA among athletes involved in intermittent activities. Part of the reason for this is that intermittent activities allow the athlete to work at a high intensity for a short period of time. Exercise intensities of between 65-75% of the subject's $\dot{V}O_2max$ have been shown to result in the greatest post-exercise bronchoconstriction, while exercise intensities above 85% of the subject's $\dot{V}O_2max$ result in little or no change in the degree of bronchoconstriction (Silverman and Anderson, 1972).

In the past, a number of mechanisms have been proposed to explain the post-exercise bronchoconstriction that is typical of EIA. The underlying pathophysiology of EIA is that during exercise heat and water are lost from the respiratory tract in warming the inspired air from ambient conditions (ATPS) to body conditions (BTPS). The net effect of this process is to cool and dehydrate the airways which, in turn, leads to the development of post-exercise respiratory symptoms and bronchoconstriction. The question that remains to be answered is how this cooling and dehydration of the airways triggers EIA. A number of hypotheses have been proposed, but the scientific evidence is not currently supportive of one theory.

Airway cooling was thought to have a direct bronchoconstrictor effect on bronchial smooth muscle and was responsible for the conversion of β-adrenergic receptors into α-adrenergic receptors (Bleeker et al., 1983; Sly, 1983; Venugopalan et al., 1988) and an increased sensitivity to cholinergic stimulation (Sly, 1983). This hypothesis is supported by scattered reports of the efficacy of alpha adrenergic receptor antagonists in preventing EIA. McFadden (1991) has suggested that while airway cooling may initiate EIA, other mechanisms are responsible for sustaining it. His hypothesis is supported by the fact that airway warming

is quite rapid following exercise, with resting airway temperatures being reached in 15-30 seconds. Also, despite these thermal changes, increases in airway resistance develop over this time and last for 30 minutes or more (Gilbert et al., 1988).

The release of chemical mediators from mast cells has been proposed as a mechanism for the development of EIA. Belcher et al. (1988) and Lee et al. (1984) have shown that elevated levels of histamine and NCFA are associated with EIA. The leukotriennes C4, D4, and E4 are released from the mast cells during exercise and are thought to play a major role in pathogenesis of EIA. This hypothesis has been supported by the inhibitory effects of the leukotrienne D4 receptor antagonist, ICI 204219, on post-exercise bronchoconstriction (Finnerty et al., 1992). Pliss et al. (1990) showed increases in bronchoalveolar lavage (BAL) concentrations of leukotrienes, eosinophils, and epithelial cells and a trend towards significant increases in neutrophils and prostaglandin D2. Neuman et al. (1984) suggested that elevated kallikrein levels may trigger EIA. In asthmatics, pre-treatment with H1 receptor antagonists and cyclo-oxygenase inhibitors have both been shown to minimize the effects of histamine and prostaglandins on EIA (Finnerty and Holgate, 1990).

In-spite of this supportive evidence, BAL studies of atopic subjects with EIA have shown no significant differences in pre- to post-exercise histamine or tryptase levels (Broide et al., 1990; Jarjour and Calhoun, 1992). Finnerty et al. (1991) have shown that a thromboxane antagonist, GR32191, has no effect on EIA. This suggests that prostaglandins that act via the thromboxane receptor do not have an important role in EIA. EIA does not produce an increase in either immediate or delayed non-specific bronchial responsiveness to methacholine in atopic asthmatics. Hence, if mediators are released during exercise they must function differently than when released by antigen (Lin et al., 1991; Zawadski et al., 1988). These results suggest that

the manifestation of EIA is not dependent on the release of chemical mediators from mast cells.

Hvidsten et al. (1986) have questioned the role of gastrointestinal regulatory peptides in the pathogenesis of EIA. In a comparison of subjects with EIA and controls, plasma levels of Vasoactive Intestinal Polypeptide (VIP) and Cholecystokinin (CCK) were significantly higher after 6 minutes of exercise. The plasma levels of somatostatin, secretin, pancreatic polypeptide, and motilin showed no significant differences between the groups. More research is needed to determine what role, if any, the gastrointestinal regulatory peptides play in the pathogenesis of EIA.

It has been proposed that stimulation of pulmonary C-fibres by a number of chemical and physical factors results in the release of neuropeptides such as tachykinins and calcitonin gene-related peptide from synaptic vesicles (Solway and Leff, 1991). In the airways, these sensory neuropeptides act on the bronchial smooth muscle, the mucosal vasculature and submucosal glands to promote airflow obstruction, hyperemia, increased permeability and increased mucous secretion. In addition, tachykinins may potentiate cholinergic transmission and promote the recruitment, adherence, and activation of granulocytes (Solway and Leff, 1991).

It has been suggested that asthmatic subjects may have a blunted catecholamine response to exercise (Barnes et al., 1981). Berkin et al. (1988) and Gilbert et al. (1988) have clearly demonstrated that asthmatics do not have a defect in catecholamine release during exercise. In their studies, epinephrine and norepinephrine levels rose with repetitive exercise and resulted in concurrent bronchodilation. It has been proposed that, in addition to their effects on smooth muscle relaxation, the alpha-adrenergic actions of the catecholamines are also responsible for reducing airway wall hyperemia and edema (Gilbert et al., 1988).

As mentioned earlier, our current understanding of EIA suggests that the post-exercise

bronchoconstriction is initiated by thermal events. The severity of airway narrowing following exercise has been shown to be a function of the $\dot{V}_E$ and the temperature and water content of the inspired air (Deal et al., 1979). For a given set of inspired air conditions, high minute ventilations result in more obstruction than do low levels, and cooling and drying the air at any level of ventilation cause more obstruction than when breathing warm and humid air (Deal et al., 1979; McFadden, 1991; Strauss et al., 1978). EIA can virtually be abolished if subjects breathe air that has been warmed to BTPS (Deal et al., 1979).

It has been suggested by McFadden et al. (1986) and McFadden (1991) that EIA is a vascular event. This hypothesis suggests that asthmatics have a hyperplastic capillary bed in their airway walls and during exercise airway cooling is followed by rapid rewarming in the immediate-post exercise period. The rapid change in airway temperature leads to reactive hyperemia and edema of the bronchial vascular bed which, in turn, leads to physical obstruction of the airways. Gilbert and McFadden (1992) have shown that alterations in blood supply directly affect bronchial heat flux and influence obstruction following isocapnic hyperventilation of cold air. By reducing the mucosal blood supply of the airways with the administration of norepinephrine there was limited rewarming of the airways which attenuated the obstructive response. Farley et al. (1988) also suggest that the rate of cooling of the upper airway is the predominant stimulus in hyperventilation induced asthma in asthmatic and non-asthmatic subjects exposed to isocapnic cold air hyperventilation.

Anderson et al. (1989) suggest that the events that trigger EIA are not due to airway cooling and rapid rewarming, but are due to airway drying and an increase in the osmolarity of the fluid lining the airway surface. These changes result in the degranulation of mast cells and release of chemical mediators such as histamine and NCFA. McFadden (1991) has been very

critical of these conclusions and has cited a number of reasons that support his criticism. Airway and esophageal temperatures fall whenever there is evaporative water loss, airway obstruction does not occur in the absence of cooling and rewarming, and airway drying is not a feature of hyperpnea (Deal et al., 1979; Gilbert et al., 1987; 1988). Schmidt and Bundgaard (1986) studied asthmatic subjects who were administered inhaled aerosols of different osmolarities. There were no differences in the response to the different aerosols and it was concluded that the osmolarity of the inhaled aerosol was of little or no importance in EIA.

It has been suggested by Bar-Or and Inbar (1992), Frampton et al. (1991), McKenzie (1991), and Penny (1983) that an increase in bronchial responsiveness may also occur in athletes without EIA who have been exposed to swimming pool disinfectants such as chlorine or chloramines, or photochemical air pollutants such as ozone, nitrogen dioxide, and sulphur dioxide. In concurrence with this hypothesis, we have shown that 60% of the competitive swimmers that we tested had increased non-specific bronchial responsiveness to methacholine. What remains to be determined is whether this is a response to chronic, low level exposure to chemical irritants in the water and air of the swimming pool, an exercise response, or both. If the prevalence of EIA is found to be relatively low compared with the high prevalence of increased non-specific bronchial responsiveness that we have shown, this may indicate that in these competitive swimmers there are separate mechanisms involved in the pathogenesis of EIA and the increased non-specific bronchial responsiveness that we see. This would also indicate that the increased non-specific bronchial responsiveness is likely due to chronic, low level exposure to chemical irritants in the swimming pool.

The purpose of this study was to: (1) establish the prevalence of EIA in a group of competitive swimmers using a standard exercise challenge test in the laboratory; (2) establish

the prevalence of EIA in the same group of swimmers using an exercise protocol in the swimming pool; (3) determine whether there are differences in the prevalence of asthma among competitive swimmers with asthma or exercise-related symptoms and those who have neither asthma or exercise-related symptoms, and to compare their results with a group of non-swimming athletes who have neither asthma or exercise-related symptoms; and (4) determine whether a prolonged exercise challenge test in the swimming pool results in the development respiratory symptoms and significant changes in pulmonary mechanics among the two groups of competitive swimmers.

METHODS

Laboratory Testing for EIA

Subjects

The 35 swimmers and 16 non-swimming control subjects who completed the methacholine challenge test agreed to participate in the laboratory test for EIA. The subjects were asked to refrain from exercising or ingesting caffeine on the day of testing. They were informed about the purpose of the test and the procedures to be followed. All of the subjects read and signed a consent form prior to participating in this study.

Calibration of the Spirometer

A 1070 Pneumotach was used to measure lung function. The pneumotach was calibrated prior to testing the first subject using procedures that were described in the previous chapter. The pneumotach was re-calibrated every 3 hours.

Calibration of the Metabolic Measurement Cart

A Beckman Metabolic Measurement Cart (MMC) (Beckman Instruments Inc, Schiller Park, IL) was used to collect the metabolic and respiratory variables during the exercise test. The MMC was calibrated prior to each exercise test. On the day before testing, the power to the OM-11 Oxygen (O_2) Analyzer and the LB-2 Carbon Dioxide (CO_2) Analyzer was turned on to allow for proper warm-up of the analyzers. The power to the OM-11 and LB-2 Pickup Heads was turned on at least 1 hour prior to testing. The MMC barometric pressure and temperature readouts were adjusted to match the conditions in the laboratory.

The OM-11 and LB-2 analyzers were calibrated using a calibration gas containing 15.95% O_2, 4.06% CO_2 and 79.99% N_2. The calibration gas was turned on, adjusted to produce a flow rate of 800 mL/min and connected to a sample line coming from the bottom of the drying tube on the MMC. The OM-11 and LB-2 gain settings were adjusted to read 15.95% and 4.06%, respectively. The calibration gas was then turned off and room air values of 20.93% and 0.03% for O_2 and CO_2 were obtained. Since CO_2 is known to interfere with the operation of the OM-11 analyzer, we had to wait several minutes before a room air value of 20.93% was obtained.

In order to ensure that there was no bias flow through the volume turbine, the sample flow was adjusted so that there was no upscale or downscale drifting during a 30 second collection period. A two litre syringe was attached to the mouthpiece of a non-rebreathing valve (Hans-Rudolph Inc. Kansas City, MO). 1⅜ inch tubing was connected between the expiratory port of the mouthpiece and the mixing chamber of the MMC. The syringe was used to inject 10 litres of air into the system at a flow rate and frequency approximating resting conditions. An additional 10 litres of air was then injected into the system at a higher flow rate and frequency approximating exercise conditions. These procedures were repeated until a span calibration of 10.00 $\pm$ 0.10 L was obtained for both conditions.

The MMC was programmed to collect data every 30 seconds during the exercise tests. Expired air samples were averaged and the following variables were calculated by a Monroe 1810 calculator integrated into the MMC: minute ventilation ($\dot{V}E$), respiratory frequency (f), tidal volume (VT), oxygen consumption ($\dot{V}O_2$) in mL/min and mL/min/kg, carbon dioxide production ($\dot{V}CO_2$), the respiratory exchange ratio (R), and total time (ΣT). These values were entered into a database for statistical analysis.

Test Procedures

Prior to beginning each test, a heart rate approximating 85% of the subject's predicted maximum was calculated using the following formula:

$$\text{Target Heart Rate} = [210 - (0.65 \times \text{Age})] \times 0.85$$

The subjects performed baseline spirometry manoeuvers according to procedures that have previously been described. Their best FEV_1 was recorded. Thirty-one of the 35 subjects performed the exercise test on a motor-driven treadmill (Quinton Instruments, Seattle, WA). The remaining 4 subjects performed the exercise test on an electronically-braked bicycle ergometer (Mijnhardt KEM 3, Bunnik, Holland) because of lower leg injuries or a strong preference for cycling over running. All 16 of the non-swimming control subjects performed the exercise test on the electronically-braked bike.

Diaphoretic electrodes (3M Ltd., St. Paul's, MN) were placed on the subjects' chest in a modified Lead II configuration. The heart rate was monitored by direct-lead electrocardiography (ECG) using a Lifepac 6 cardioscope/recorder module (Physio-Control, Scarborough, ON). The subject was connected to the mouthpiece of the non-rebreathing valve. 1⅜ inch tubing was connected between the expiratory port of the mouthpiece and the mixing chamber of the MMC. During the first 2 minutes of the exercise test the speed of the treadmill, or the resistance on the bicycle ergometer, was adjusted in order to allow the subject to reach his or her target heart rate. The elevation of the treadmill remained at a 0% grade. At the end of the first two minutes of exercise data collection was started and data was collected every 30 seconds for six minutes. The speed of the treadmill, or the resistance on the bicycle ergometer, was continually adjusted in order to maintain the subject's target heart rate. At the end of the exercise test the subject was disconnected from the non-rebreathing valve and ECG equipment.

Spirometry was performed immediately and 5, 10 and 15 minutes after exercise. During the expiratory portion of the spirometry manoeuver, the subjects were asked not to expire to residual volume in order to prevent fatigue or premature closure of the small airways.

Heart rate, $\dot{V}E$, f, VT, $\dot{V}O_2$, R, ΣT, the baseline FEV_1 and the post-exercise FEV_1s were recorded for each subject and entered into a database for statistical analysis.

Swimming Pool Testing for EIA

Subjects

Swimmers who completed the methacholine challenge test and the laboratory test for EIA were considered eligible for the tethered swimming protocol to assess EIA. A total of 28 of the 35 eligible subjects agreed to participate in this study. Seven subjects did not participate because of illness, injury, or non-compliance. Thirteen subjects formed the Case Group and 15 subjects formed the Control Group. Six out of the 13 subjects in the Case Group had physician-diagnosed asthma, while the remaining 7 had symptoms suggestive of asthma while swimming. The subjects were asked to refrain from exercising or ingesting caffeine on the day of testing. They were informed about the purpose of the test and the procedures to be followed. All of the subjects read and signed a consent form prior to participating in the remaining exercise studies.

Calibration of the Spirometer

A 2130 Dry-Rolling Seal Spirometer (SensorMedics Corporation, Yorba-Linda, CA) interfaced to an IBM-compatible 386DX computer was used to measure lung function. The barometric pressure and room temperature were entered into the computer program operating the spirometer. The spirometer bell was positioned at the mid-point of its operating range. A

3 litre syringe was connected to 2 inch tubing which was connected to the spirometer. To calibrate the spirometer six 3 litre samples of air were alternately injected and withdrawn from the spirometer at varying flow rates. These procedures were then repeated to verify the calibration of the spirometer. The last four 3 litre samples were averaged and a correction factor introduced for all subsequent calculations. The spirometer was re-calibrated every 3 hours.

Calibration of the Metabolic Measurement Cart

A Beckman MMC was used to collect the metabolic and respiratory variables during the tethered swimming protocol. The MMC was calibrated prior to each exercise test using procedures that have previously been described.

Test Procedures

In order to equate the exercise intensity from the 8 minute laboratory test to the 8 minute tethered swimming protocol, the average $\dot{V}E$ from the laboratory test was recorded for each subject and an attempt was made to match this $\dot{V}E$ during the tethered swimming protocol. The subjects performed baseline spirometry manoeuvers according to procedures that have previously been described. Their best FEV_1 was recorded.

Diaphoretic electrodes were placed on the subjects' chest in a modified Lead II configuration. Water-proof plastic adhesive tape (Johnson and Johnson, Montreal, PQ) was then placed over each of the electrodes in order to prevent loss of the ECG signal. The heart rate was monitored by direct-lead electrocardiography using a EK-10 ECG Module (Burdick Corporation, Milton, WI). A belt was placed around the waist of the subject. The belt was

attached to a tethering apparatus located on the side of the pool deck. The tethering apparatus consisted of a pulley system that was attached to a bucket containing weighted sand bags. The resistance of the tethering apparatus was controlled by either adding or removing sand bags. The subject was asked to get into the water and was then connected to a non-rebreathing valve. The subject breathed air through 1⅜ inch tubing that was located 6 inches off the surface of the water and connected to the inspiratory port of the mouthpiece. 1⅜ inch tubing was also connected between the expiratory port of the mouthpiece and the mixing chamber of the MMC.

The subjects were instructed to swim in a stationary position over a marker that was placed on the bottom of the pool. They were also instructed to use front crawl during the tethered swimming protocol because it is the stroke they use during most of their training. During the first 2 minutes of the exercise test the resistance of the tethering apparatus was adjusted in order to reach the subject's target $\dot{V}E$. At the end of the first two minutes of exercise, data collection was started and data was collected every 30 seconds for six minutes. The resistance of the tethering apparatus was continually adjusted in order to maintain the subject's target $\dot{V}E$. At the end of the exercise test the subject was disconnected from the non-rebreathing valve, tethering apparatus and ECG equipment. Spirometry was performed immediately and 5, 10 and 15 minutes after exercise. During the expiratory portion of the spirometry manoeuver, the subjects were asked not to expire to residual volume in order to prevent fatigue and premature closure of the small airways.

Heart rate, $\dot{V}E$, f, VT, $\dot{V}O_2$, R, ΣT, the baseline FEV_1 and the post-exercise FEV_1s were recorded for each subject and entered into a database for statistical analysis.

The Prolonged Exercise Challenge Test in the Swimming Pool

Subjects

The 28 subjects who participated in the 8 minute tethered swimming protocol completed the 45 minute protocol. The subjects were informed about the purpose of the test and the procedures to be followed.

Calibration of the Spirometer

The spirometry tests were performed using the System 2130 dry-rolling seal spirometer. The dry-rolling seal spirometer was calibrated prior to testing the first subject using procedures that have previously been described. The spirometer was re-calibrated every 3 hours.

Calibration of the Metabolic Measurement Cart

A Beckman MMC was used to collect the metabolic and respiratory variables during the tethered swimming protocol. The MMC was calibrated prior to each exercise test using procedures that have previously been described.

Test Procedures

Prior to beginning each test, a heart rate approximating 70% of the subject's predicted maximum was calculated using the following formula:

$$\text{Target Heart Rate} = [210 - (0.65 \times \text{Age})] \times 0.70$$

The subjects performed baseline spirometry manoeuvers according to procedures that have previously been described. Their best FEV_1 was recorded.

The tethered swimming protocol was performed using procedures that have previously been described, except that data was collected for 30 seconds every 5 minutes during the 45 minute test. Spirometry was performed immediately and 5, 10 and 15 minutes after exercise. During the expiratory portion of the spirometry manoeuvers, the subjects were asked not to expire to residual volume in order to prevent fatigue and premature closure of the small airways.

Heart rate, $\dot{V}_E$, f, V_T, $\dot{V}O_2$, R, Σ_T, the baseline FEV_1 and the post-exercise FEV_1s, and any symptoms reported by the swimmers during or after the test were recorded for each subject and entered into a database for statistical analysis.

Statistical Analysis

The mean, standard deviation, and the standard error of the mean were calculated for all of the descriptive variables. Analysis of variance (ANOVA) was used to determine whether there were statistical differences in the mean values of the dependent variables for the three groups of athletes who participated in the exercise challenge test in the laboratory. If statistical differences were found, a Student-Newman-Keuls multiple range test was used to determine which groups differed. Independent t-tests were used to determine whether there were statistical differences in the mean values of the dependent variables for the two groups of swimmers who participated in the exercise challenge tests in the swimming pool.

The prevalence of EIA was calculated for each of the three groups of athletes. The exercise test was considered to be positive if the pre- to post-exercise FEV_1 fell by 15% or more. Sensitivity and specificity were determined from 2 by 2 contingency tables in which "physician-diagnosed asthma" versus "no asthma" was tabulated against "positive test" and "negative test". Sensitivity was defined as the percentage of athletes with asthma and/or

symptoms suggestive of asthma while exercising who had positive exercise tests ($\Delta FEV_1 \geq 15\%$). Specificity was defined as the percentage of athletes with neither asthma nor symptoms suggestive of asthma while exercising who had negative exercise tests.

An alpha level of 0.05 ($p < 0.05$) was considered to be statistically significant. All statistical analyses were completed using the SAS® Statistical Software Package (SAS Institute, Inc., Cary, NC).

RESULTS

Laboratory Testing for EIA

All of the subjects who completed the methacholine challenge test completed the exercise challenge test in the laboratory. Briefly, this study included fifty-one (25 male and 26 female) subjects who were divided into three groups. The Case Group was composed of 18 competitive swimmers who had either physician-diagnosed asthma or symptoms suggestive of asthma while swimming. The Control Group was composed of 17 swimmers who had neither physician-diagnosed asthma nor symptoms suggestive of asthma while swimming. The Non-Swimming Control Group was composed of 16 non-swimming athletes who had neither physician-diagnosed asthma nor symptoms suggestive of asthma while exercising. The physical characteristics and lung function measurements of these subjects were reported in the previous chapter (Tables 14 and 16). The environmental conditions during testing in the laboratory were also reported in the previous chapter (Table 15).

A comparison of the exercise data between the three groups of athletes is presented in Table 18. The mean predicted heart rate for the Case Group was statistically significantly higher than that of the Non-Swimming Control Group ($p < 0.0449$), but the difference was only 2 bpm. The mean heart rate calculated over the last 6 minutes of exercise was significantly higher in the Case Group when compared with either of the control groups ($p < 0.0029$ and $p < 0.0001$, respectively). Similarly, the mean heart rate of the Control Group was significantly higher than that of the Non-Swimming Control Group ($p < 0.0029$) (Figure 6). There was no difference in the mean values for $\dot{V}E$, VT, f, and $\dot{V}O_2$ calculated over the last 6 minutes of exercise between the three groups of athletes (Figures 7-10). The mean R value calculated over the last 6 minutes of exercise for the Non-Swimming Control Group was significantly higher than either of the two

swimming groups ($p < 0.0001$ and $p < 0.0001$, respectively) (Figure 11).

The overall prevalence of EIA among the 51 athletes was 9.8%. This included two swimmers from the Case Group (11.1%), two swimmers from the Control Group (11.8%), and one athlete from the Non-Swimming Control Group (6.3%). Neither of the swimmers in the Case Group who had positive exercise tests had physician-diagnosed asthma, but one of the subjects had increased bronchial responsiveness with a PC_{20} of 1.36 mg/mL. Both of the swimmers in the Control Group who had positive exercise tests had increased bronchial responsiveness with PC_{20}s of 3.01 and 3.13 mg/mL, respectively. The one subject in the Non-Swimming Control Group who had a positive exercise test had normal bronchial responsiveness with a $PC_{20} > 16$ mg/mL, but his baseline spirometry showed a mild obstructive pattern in his large airways ($FEV_1/FVC < 70\%$). Figure 12 shows the mean percentage change in FEV_1 values following the 8 minute exercise challenge test in the laboratory. Figures 13-15 show the individual post-exercise FEV_1 plots for each of the groups of athletes. The sensitivity and specificity of the laboratory test for EIA for identifying subjects with asthma or symptoms suggestive of asthma while exercising were 11.1% and 90.9%, respectively.

Table 18: The mean values for the cardiorespiratory variables collected during the 8 minute exercise challenge test in the laboratory. The $\bar{x} \pm$ SD are reported.

	Case Group	Control Group	Non-Swimming Control Group	Level of Significance
Predicted Heart Rate (bpm)	168.22 ± 1.52	167.53 ± 2.00	166.44 ± 2.50	$p<0.0449$ *
Exercise Heart Rate (bpm)	173.89 ± 4.61	168.35 ± 5.47	158.40 ± 8.10	$p<0.0001$ †
$\dot{V}_E$ (L/min)	76.62 ± 16.15	74.29 ± 15.75	82.24 ± 18.14	NS
V_T (mL)	2,099.17 ± 632.22	2,305.88 ± 555.64	2,408.38 ± 734.95	NS
f (b/min)	37.84 ± 6.79	32.85 ± 5.67	34.79 ± 5.63	NS
$\dot{V}O_2$ (L/min)	2.79 ± 0.70	2.85 ± 0.59	2.77 ± 0.78	NS
$\dot{V}O_2$ (mL/min/kg)	40.89 ± 6.15	40.92 ± 5.25	39.68 ± 7.80	NS
R	0.94 ± 0.04	0.93 ± 0.07	1.04 ± 0.06	$p<0.0001$ ‡

* The mean predicted heart rate of the Case Group was significantly higher than that of the Non-Swimming Control Group.

† The mean heart rate of the Case Group was significantly higher than the mean heart rate of either of the control groups. Similarly, the mean heart rate of the Control Group was significantly higher than the mean heart rate of the Non-Swimming Control Group.

‡ The mean respiratory exchange ratio of the Non-Swimming Control Group was significantly higher than the mean respiratory exchange ratio of the Case Group and the Control Group.

NS = No statistically significant differences were found between groups.

Figure 6: The mean heart rates measured during the last 6 minutes of the laboratory test for EIA. Overall, the mean heart rate for the Case Group was significantly higher than that of either of the Control Groups ($p < 0.0029$ and $p < 0.0001$, respectively). Similarly, The mean heart rate for the Control Group was significantly higher than that of the Non-Swimming Control Group ($p < 0.0029$). The $\bar{x} \pm$ SEM are reported.

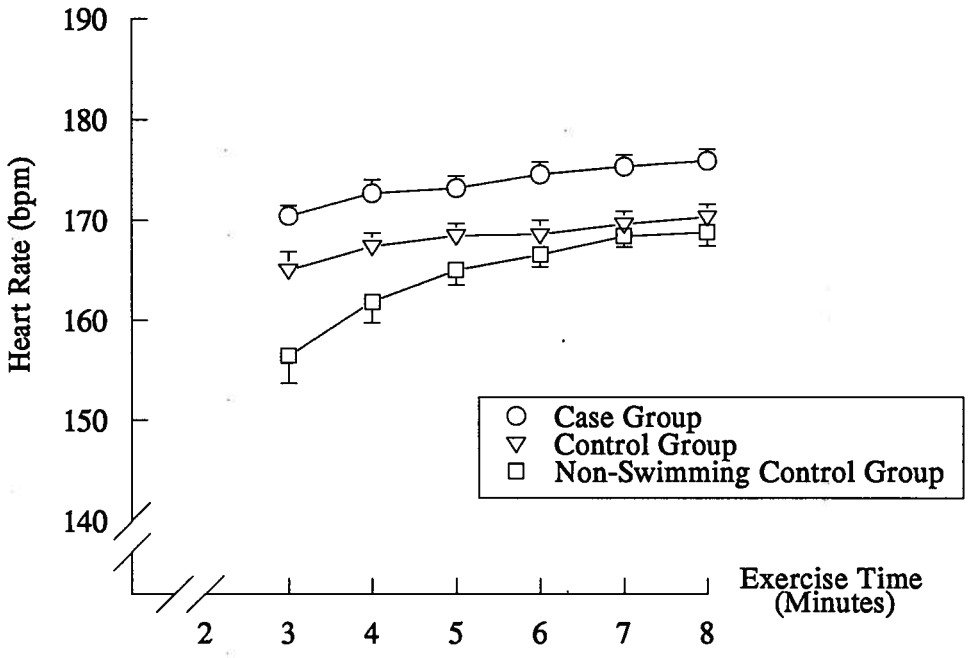


Figure 7: The mean $\dot{V}_E$ values measured during the last 6 minutes of the laboratory test for EIA. Overall, there was no difference in the mean $\dot{V}_E$ value between the three groups of athletes. The $\bar{x} \pm$ SEM are reported.

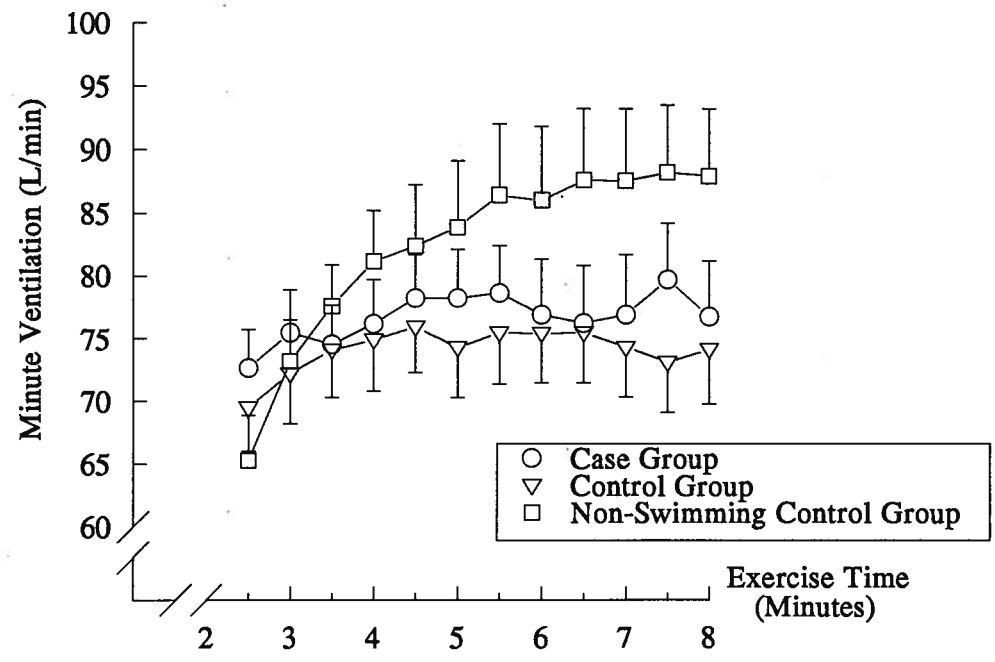


Figure 8: The mean tidal volume (VT) values measured during the last 6 minutes of the laboratory test for EIA. Overall, there was no difference in the mean VT value between the three groups of athletes. The $\bar{x} \pm$ SEM are reported.

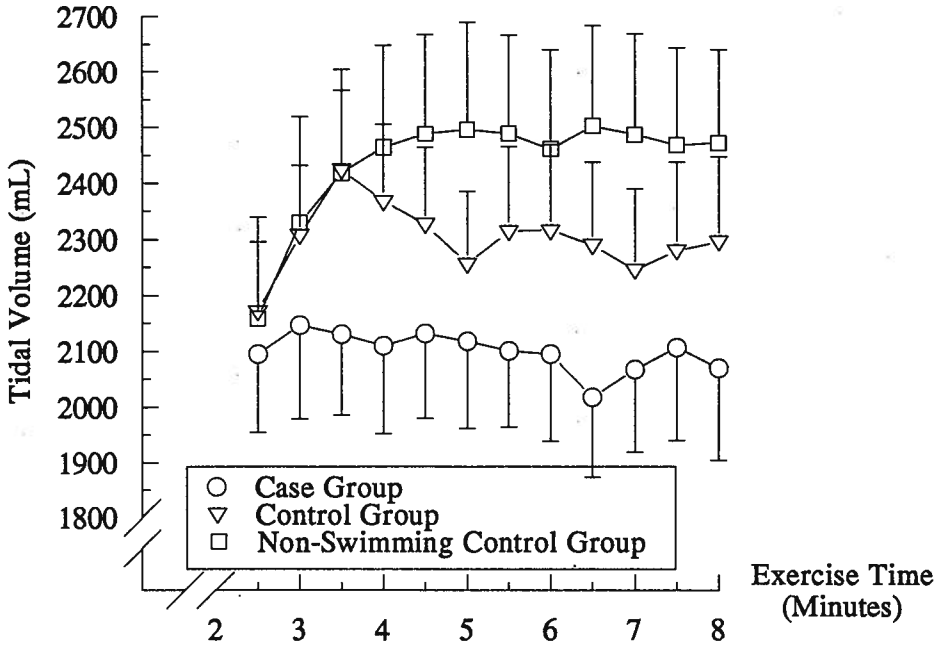


Figure 9: The mean respiratory frequency (f) values measured during the last 6 minutes of the laboratory test for EIA. Overall, the mean f for the Case Group was significantly higher than that of the Control Group ($p<0.0242$). The $\bar{x} \pm$ SEM are reported.

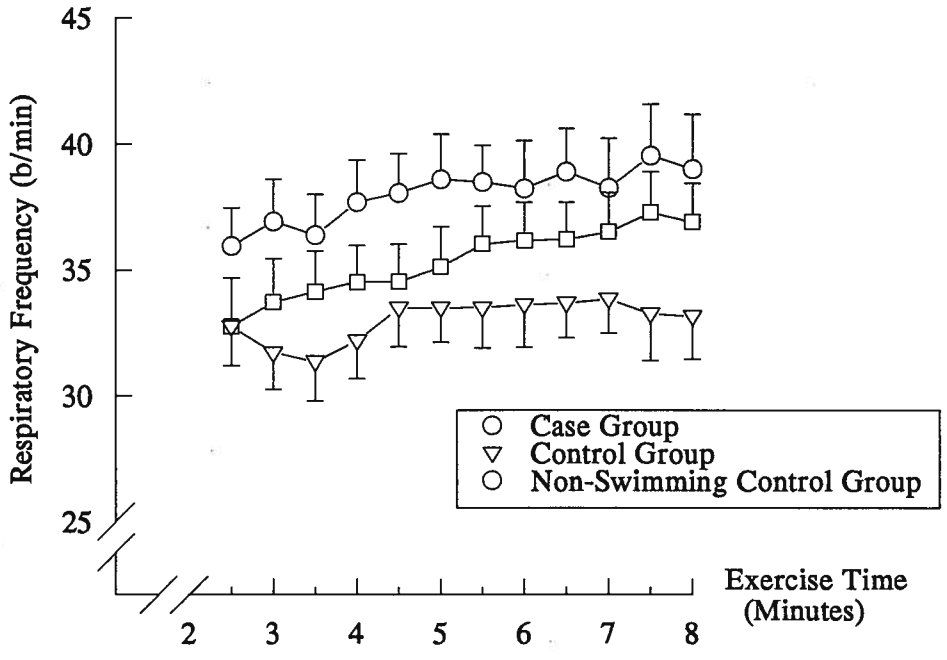


Figure 10: The mean oxygen consumption ($\dot{V}O_2$) values measured during the last 6 minutes of the laboratory test for EIA. Overall, there was no difference in the mean $\dot{V}O_2$ value between the three groups of athletes. The $\bar{x} \pm$ SEM are reported.

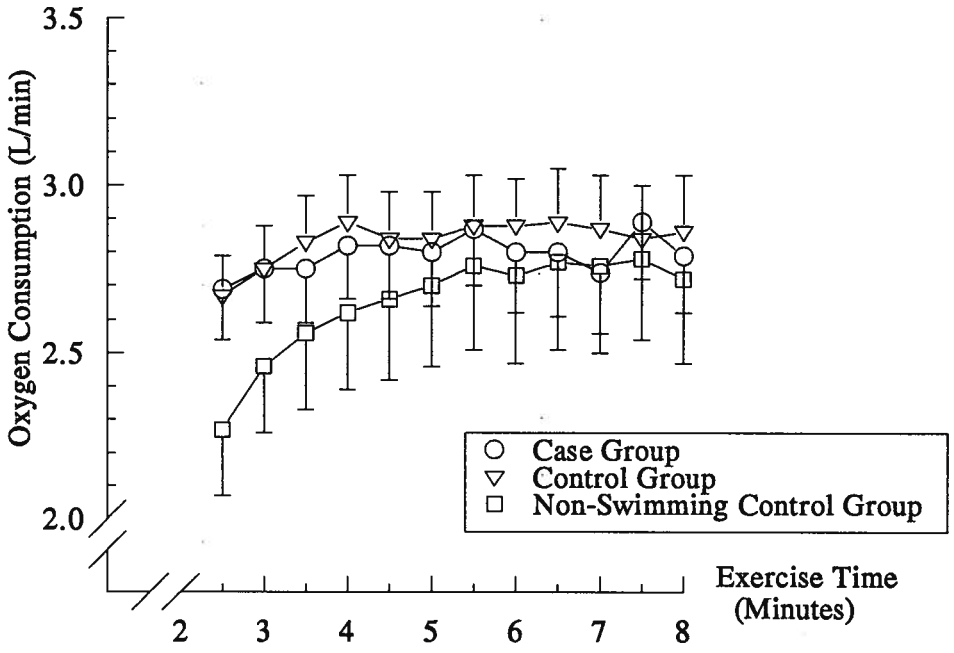


Figure 11: The mean respiratory exchange ratio (R) values measured during the last 6 minutes of the laboratory test for EIA. Overall, the mean R value of the Non-Swimming Control Group was significantly higher than that of either of the swimming groups ($p < 0.0001$). The $\bar{x} \pm$ SEM are reported.

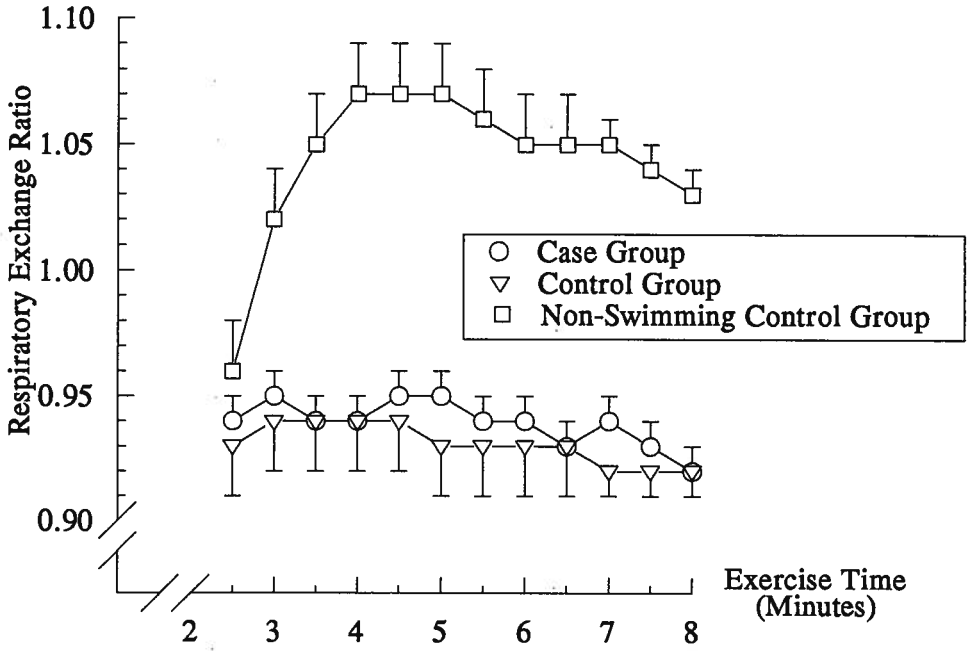


Figure 12: The mean FEV_1 values following the 8 minute exercise challenge test in the laboratory. The $\bar{x} \pm$ SEM are reported.

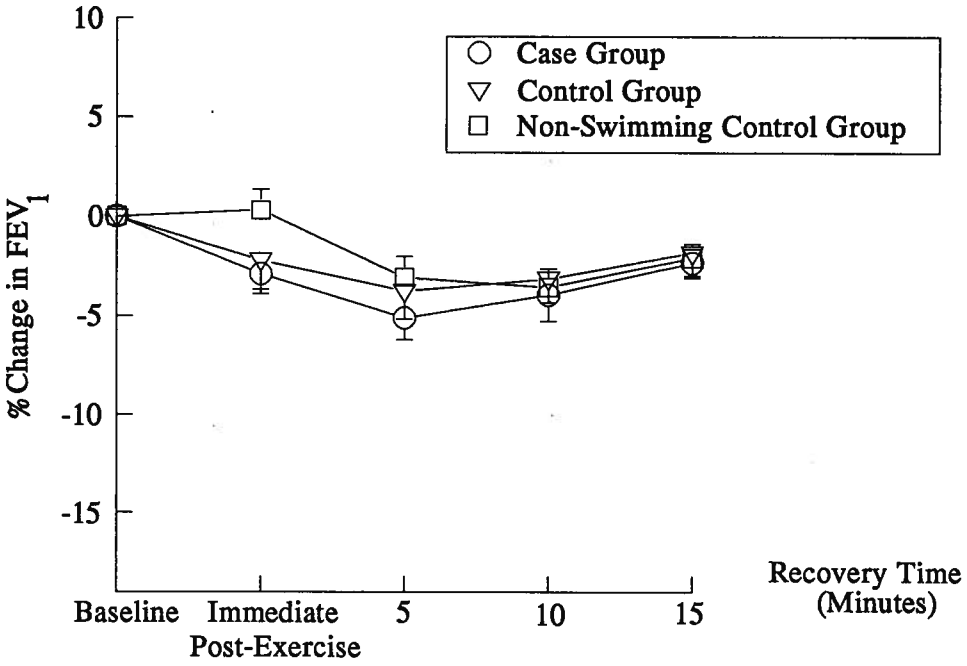


Figure 13: The individual FEV_1 plots for the Case Group following the 8 minute exercise challenge test in the laboratory.

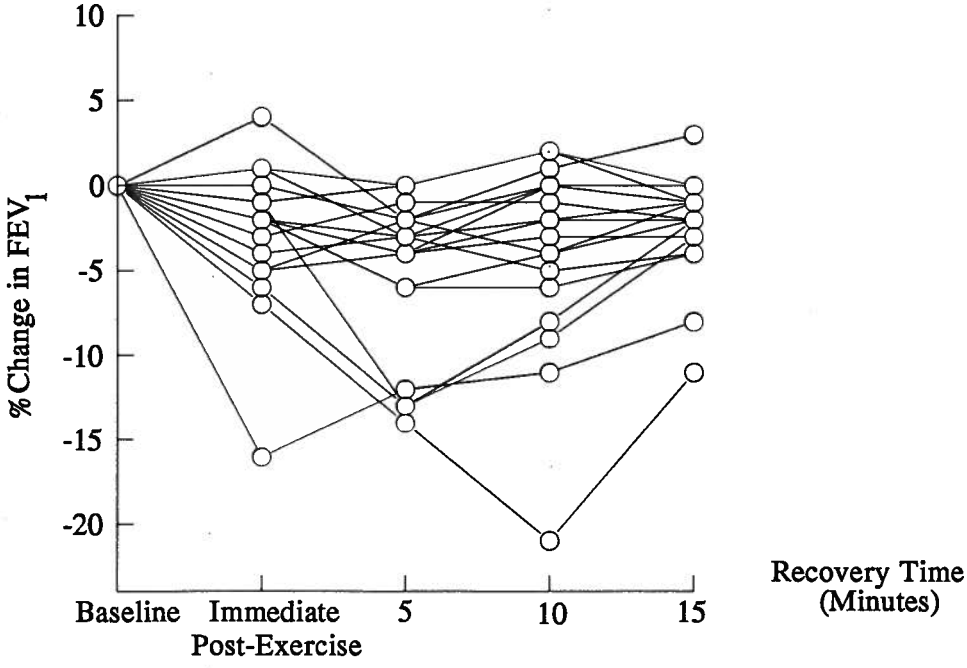


Figure 14: The individual FEV_1 plots for the Control Group following the 8 minute exercise challenge test in the laboratory.

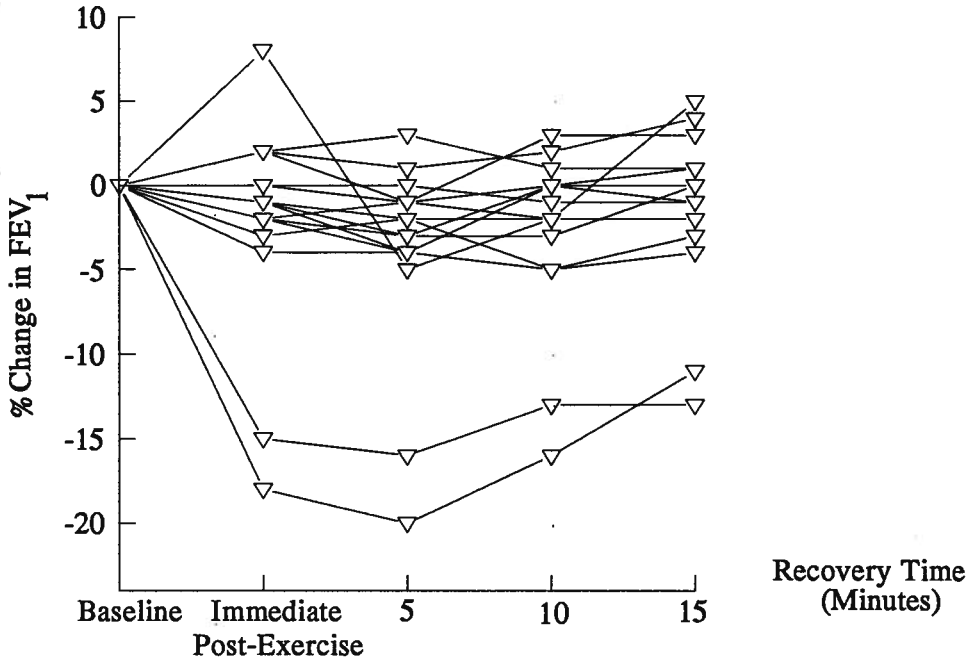
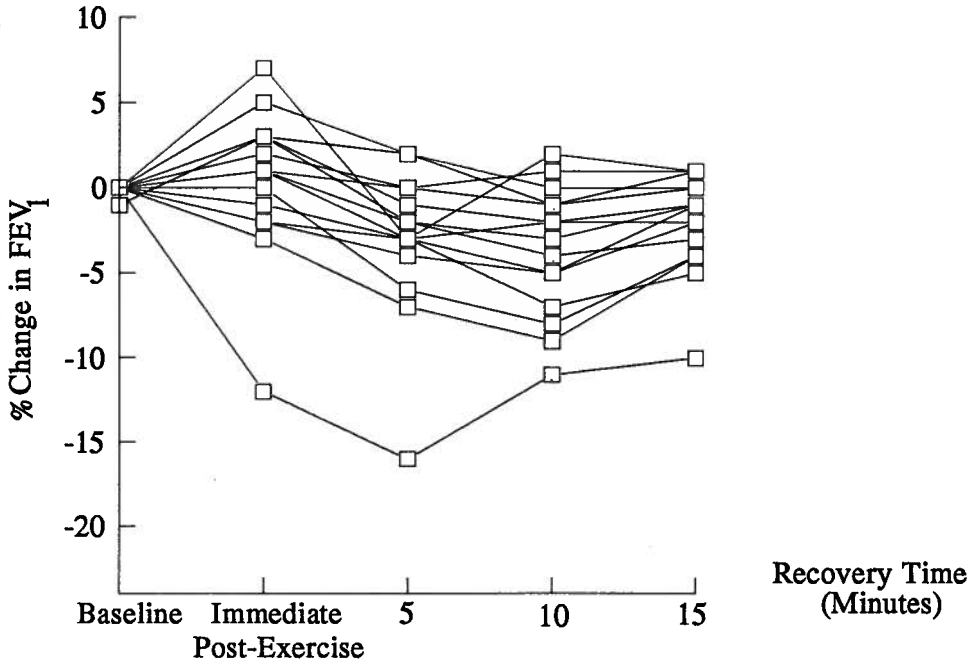


Figure 15: The individual FEV_1 plots for the Non-Swimming Control Group following the 8 minute exercise challenge test in the laboratory.



Swimming Pool Testing for EIA

This study included twenty-eight (15 male and 13 female) competitive swimmers who had participated in the previous study. The Case Group was composed of 13 competitive swimmers and the Control Group was composed of 15 swimmers. The criteria for placement into each of the groups remained the same. The physical characteristics of the subjects are presented in Table 19. There were no statistically significant differences in the mean values for age, height, and weight between the two groups of swimmers. During testing, the barometric pressure was 758.11 $\pm$ 5.95 torr, the air temperature was 24.04 $\pm$ 0.43 °C, the water temperature was 27.96 $\pm$ 0.19 °C, and the relative humidity was 59.75 $\pm$ 2.90 %. There were no statistically significant differences in these values between the two groups of swimmers.

A comparison of the exercise data between the two groups of swimmers is presented in Table 20. There was no difference in the mean values for heart rate, $\dot{V}E$, VT, f, and $\dot{V}O_2$ calculated over the last 6 minutes of exercise between the two groups of swimmers (Figures 16-20). The mean R value calculated over the last 6 minutes of exercise for the Case Group was significantly higher than that of the Control Group ($p < 0.0029$) (Figure 21). Figure 22 shows the mean percentage change in FEV_1 values following the 8 minute exercise challenge test in the swimming pool.

The overall prevalence of EIA among the 28 swimmers was 3.6%. This included one swimmer from the Case Group (7.7%) and no swimmers from the Control Group. The one swimmer from the Case Group who had a positive exercise test did not have physician-diagnosed asthma, but had symptoms suggestive of asthma while swimming and increased bronchial responsiveness with a PC_{20} of 9.51 mg/mL. Interestingly, this subject was not one of the subjects who had a positive exercise test in the laboratory. The sensitivity and specificity of the

swimming pool test for EIA for identifying swimmers with asthma or symptoms suggestive of asthma while exercising were 6.7% and 100%, respectively.

Table 19: The physical characteristics of the 2 groups of competitive swimmers who participated in the exercise challenge tests in the swimming pool. The $\bar{x} \pm SD$ are reported.

	Case Group	Control Group	Level of Significance
Age (years)	17.85 ± 3.39	19.80 ± 3.36	NS
Height (cm)	174.46 ± 8.42	175.53 ± 9.72	NS
Weight (kg)	68.18 ± 12.34	69.76 ± 9.64	NS

NS = No statistically significant differences were found between groups.

Table 20: The mean values for the cardiorespiratory variables collected during the 8 minute exercise challenge test in the swimming pool. The $\bar{x} \pm$ are reported.

	Case Group	Control Group	Level of Significance
Exercise Heart Rate (bpm)	160.00 ± 7.21	158.40 ± 8.10	NS
$\dot{V}_E$ (L/min)	78.14 ± 16.79	73.28 ± 17.32	NS
V_T (mL)	2,158.92 ± 706.82	2,132.60 ± 572.50	NS
f (b/min)	37.53 ± 6.14	35.48 ± 7.71	NS
$\dot{V}O_2$ (L/min)	2.98 ± 0.71	3.02 ± 0.64	NS
$\dot{V}O_2$ (mL/min/kg)	43.21 ± 5.44	43.09 ± 5.85	NS
R	0.96 ± 0.05	0.90 ± 0.04	$p<0.0029$ *

* The mean respiratory exchange ratio of the Case Group was significantly higher than that of the Control Group.
NS = No statistically significant differences were found between groups.

Figure 16: The mean heart rates measured during the last 6 minutes of the swimming pool test for EIA. Overall, there was no difference in the mean heart rate between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

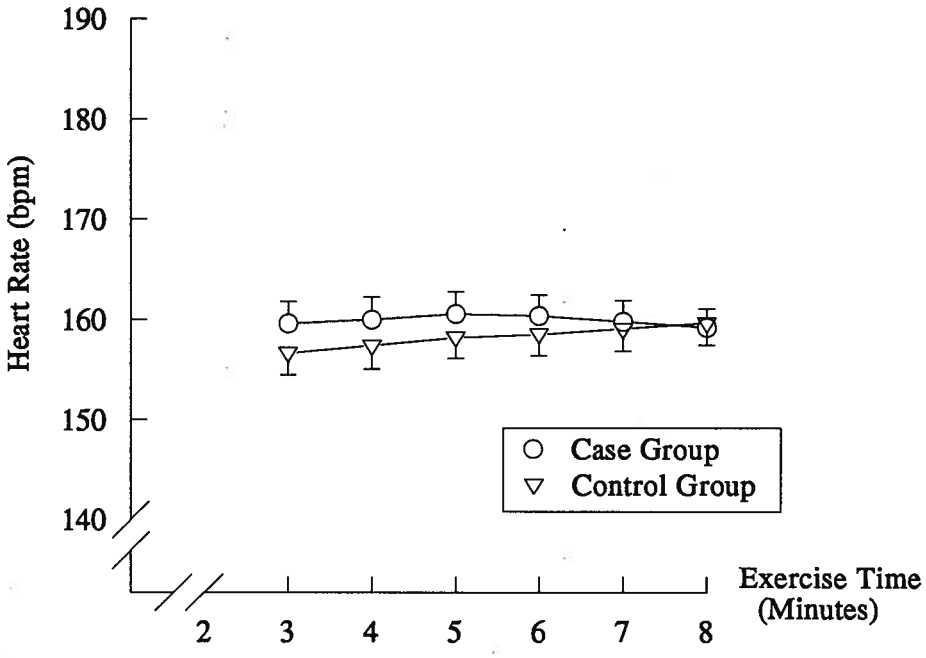


Figure 17: The mean $\dot{V}E$ values measured during the last 6 minutes of the swimming pool test for EIA. Overall, there was no difference in the mean $\dot{V}E$ value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

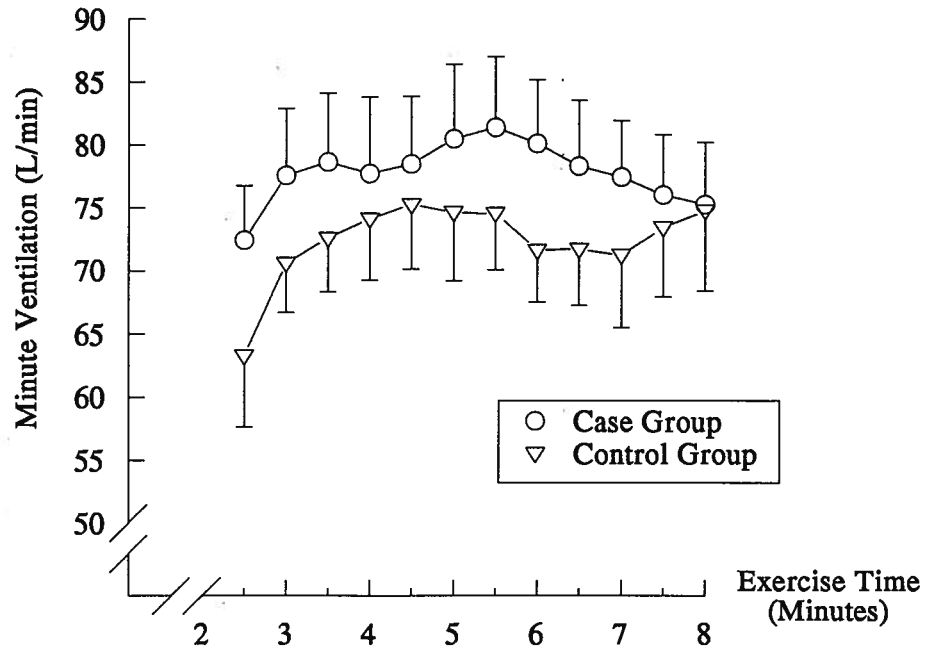


Figure 18: The mean tidal volume (VT) values measured during the last 6 minutes of the laboratory test for EIA. Overall, there was no difference in the mean VT value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

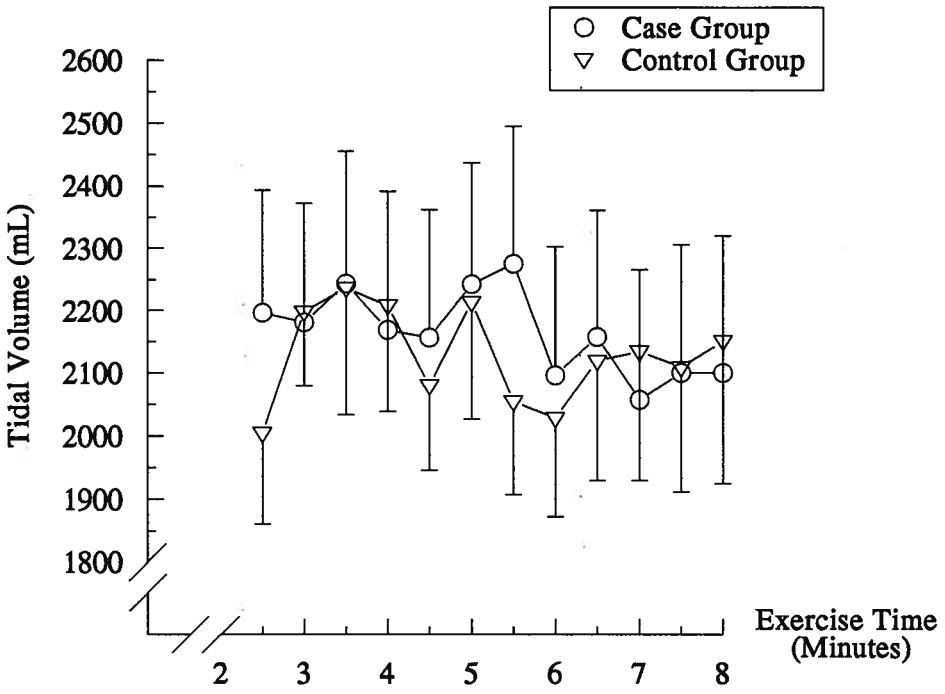


Figure 19: The mean respiratory frequency (f) values measured during the last 6 minutes of the swimming pool test for EIA. Overall, there was no difference in the mean f value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

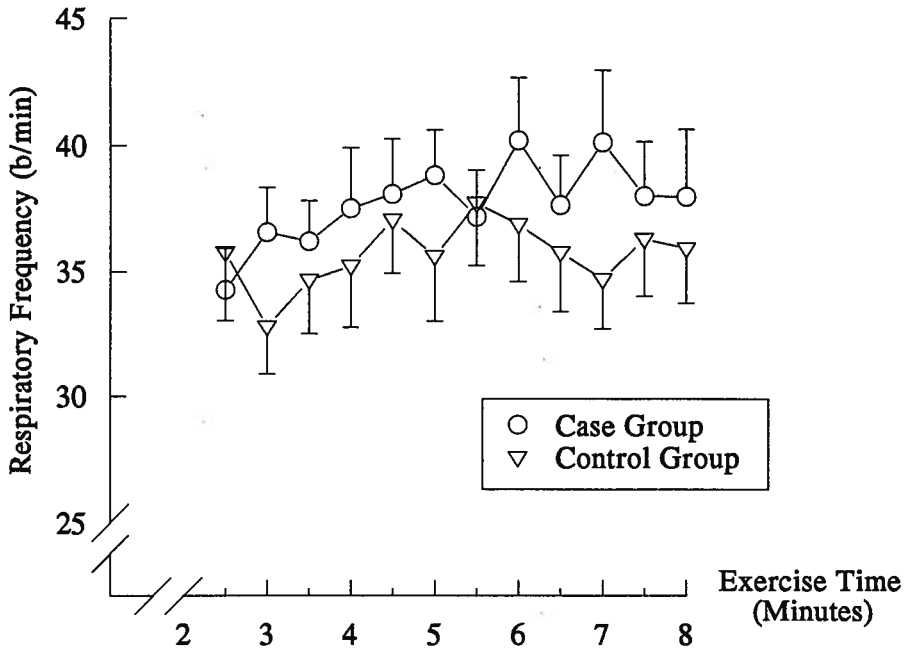


Figure 20: The mean oxygen consumption ($\dot{V}O_2$) values measured during the last 6 minutes of the swimming pool test for EIA. Overall, there was no difference in the mean $\dot{V}O_2$ value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

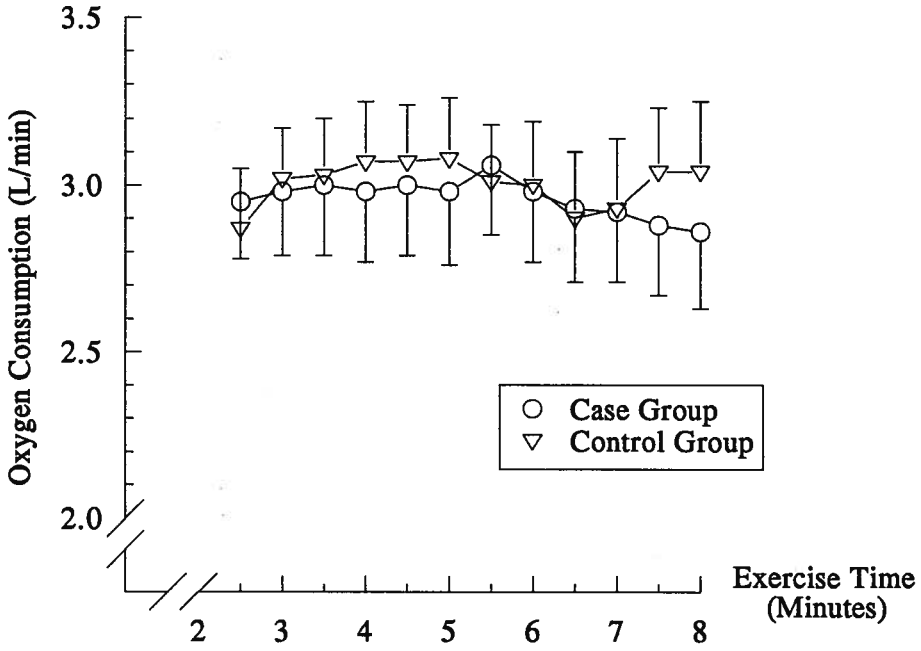


Figure 21: The mean respiratory exchange ratio (R) values measured during the last 6 minutes of the swimming pool test for EIA. Overall, the mean R value for the Case Group was significantly higher than that of the Control Group ($p < 0.0029$). The $\bar{x} \pm$ SEM are reported.

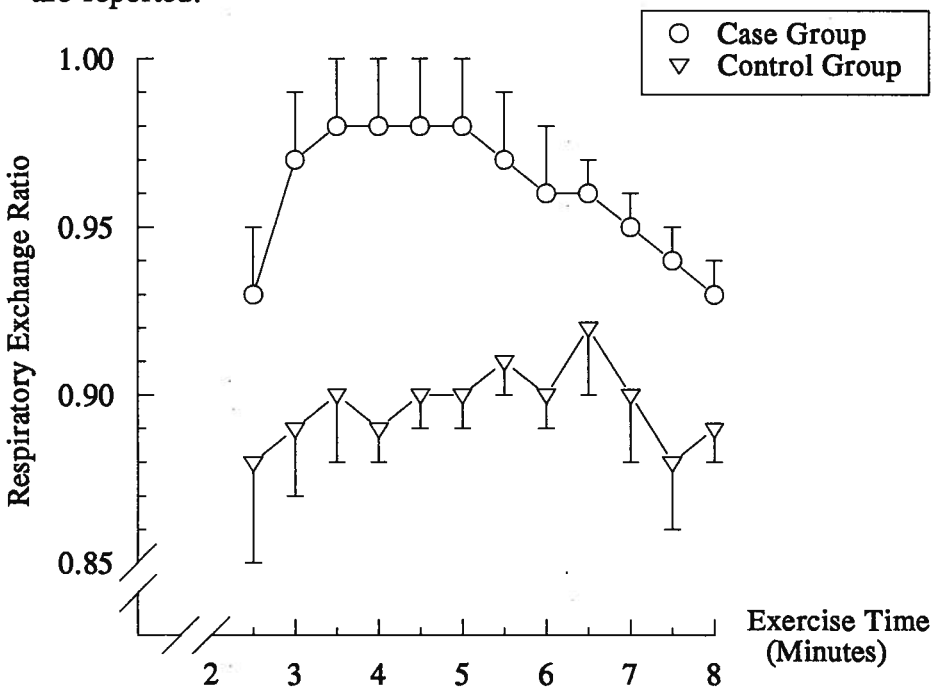
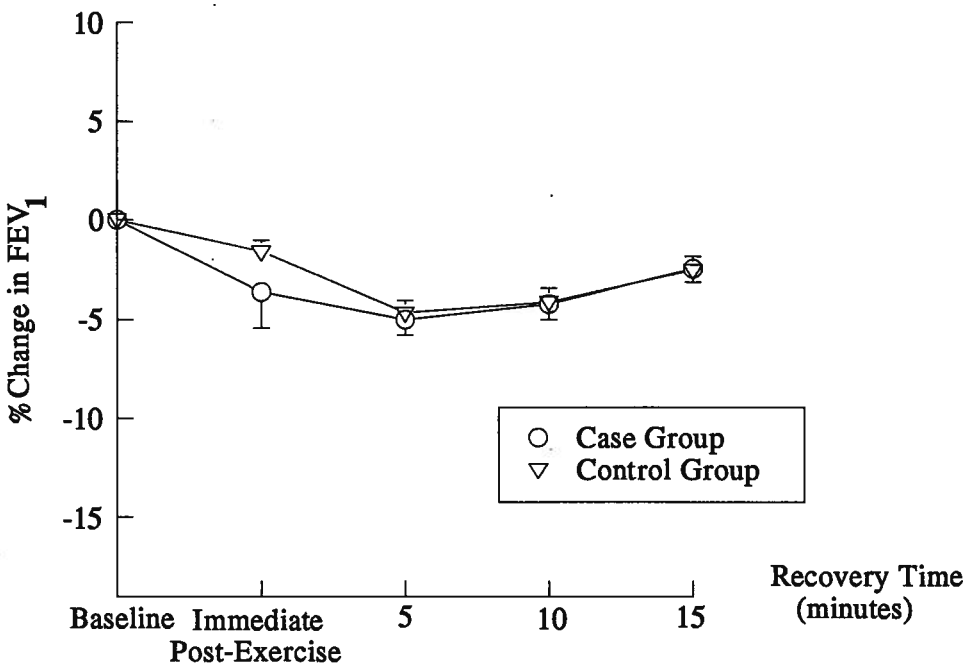


Figure 22: The mean FEV_1 values following the 8 minute exercise challenge test in the swimming pool. The $\bar{x} \pm$ SEM are reported.



A Comparison of the Results from the Laboratory and Swimming Pool Tests

A comparison of the environmental conditions during testing in the laboratory and swimming pool is presented in Table 21. The air temperature was significantly higher during testing in the swimming pool when compared to the laboratory ($p < .0001$). A comparison of the exercise data during testing in the laboratory and swimming pool is presented in Table 22. The mean heart rate calculated over the last 6 minutes of exercise was significantly higher during running or cycling when compared to swimming ($p < 0.0001$) (Figure 23). There was no difference in the mean values for $\dot{V}E$, VT, f, $\dot{V}O_2$, and R calculated over the last 6 minutes of exercise between the two groups of swimmers (Figures 24-28). Figure 29 compares the mean percentage change in FEV_1 values following each of the 8 minute exercise challenge tests.

Table 21: A comparison of the environmental conditions during 8 minute exercise challenge tests in the laboratory and swimming pool. The $\bar{x} \pm$ SD are reported.

	Running/Cycling	Swimming	Level of Significance
Barometric Pressure (torr)	756.29 ± 6.65	758.11 ± 5.95	NS
Air Temperature (°C)	21.42 ± 0.84	24.04 ± 0.43	$p<0.0001$ *
Relative Humidity (%)	58.71 ± 5.05	59.75 ± 2.90	NS

* The mean air temperature was significantly higher during exercise challenge in the swimming pool.
NS = No statistically significant differences were found between groups.

Table 22: A comparison of the mean values for the cardiorespiratory variables collected during the exercise challenge tests in the laboratory and in the swimming pool. The $\bar{x} \pm$ SD are reported.

	Running/Cycling	Swimming	Level of Significance
Exercise Heart Rate (bpm)	170.82 ± 6.02	159.14 ± 7.60	$p<0.0001$ *
$\dot{V}_E$ (L/min)	76.01 ± 15.64	75.54 ± 16.94	NS
V_T (mL)	2,254.39 ± 627.48	2,144.82 ± 626.23	NS
f (b/min)	34.92 ± 6.88	36.43± 5.97	NS
$\dot{V}O_2$ (L/min)	2.88 ± 0.65	3.00 ± 0.66	NS
$\dot{V}O_2$ (mL/min/kg)	41.57 ± 5.65	43.15 ± 5.56	NS
R	0.94 ± 0.064	0.93 ± 0.05	NS

* The mean heart rate during running or cycling was significantly higher than during swimming.
NS = No statistically significant differences were found between groups.

Figure 23: A comparison of the mean heart rates measured during the last 6 minutes of the laboratory and swimming pool tests for EIA. Overall, the mean heart rate was significantly higher during tethered swimming in comparison with running or cycling ($p < 0.0001$). The $\bar{x} \pm$ SEM are reported.

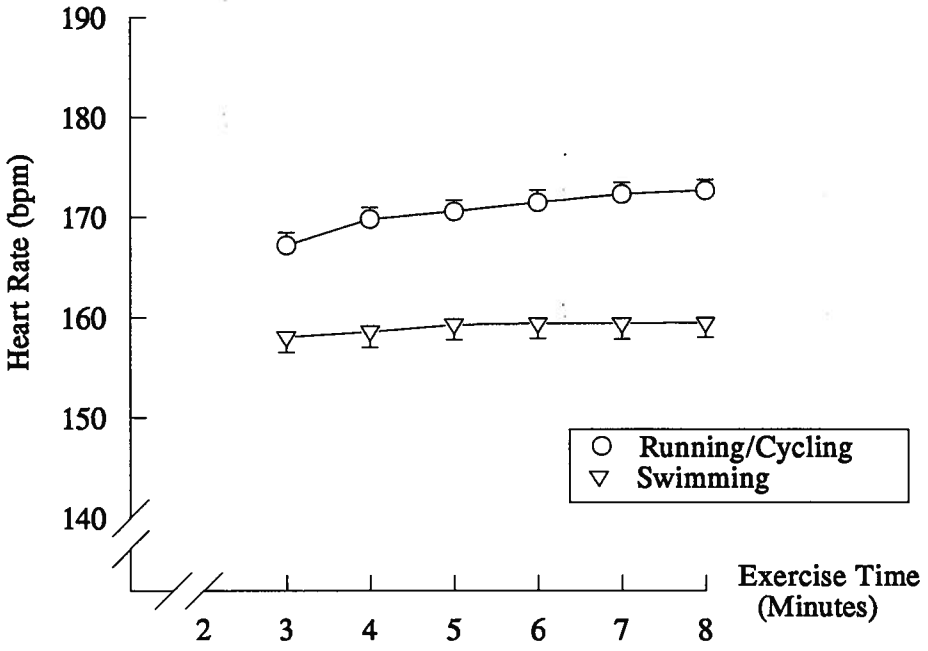


Figure 24: A comparison of the mean $\dot{V}E$ measured during the last 6 minutes of the laboratory and swimming pool tests for EIA. Overall, there was no difference in the mean $\dot{V}E$ value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

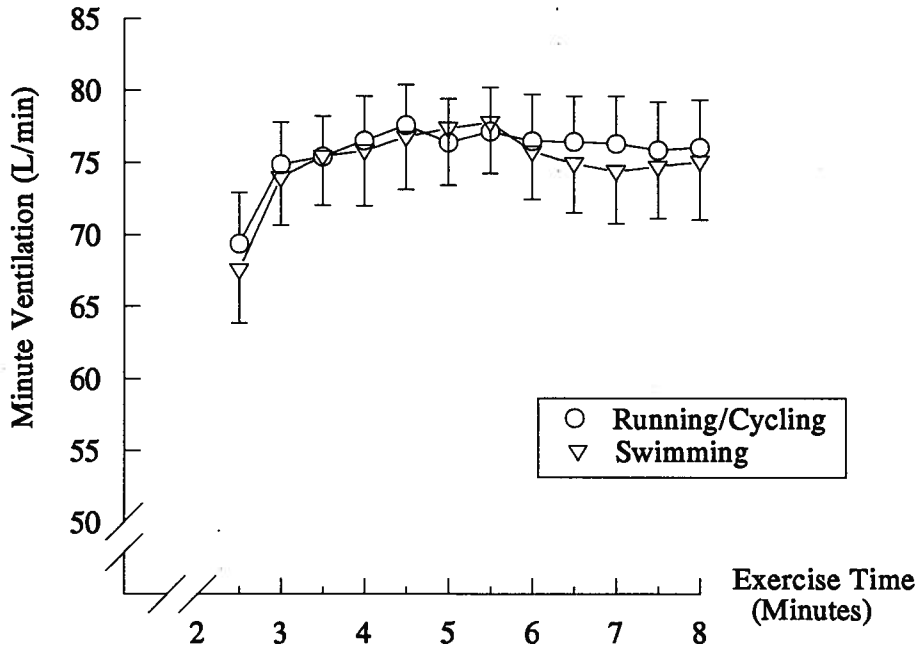


Figure 25: A comparison of the mean tidal volume (VT) values measured during the last 6 minutes of the laboratory and swimming pool tests for EIA. Overall, there was no difference in the mean VT value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

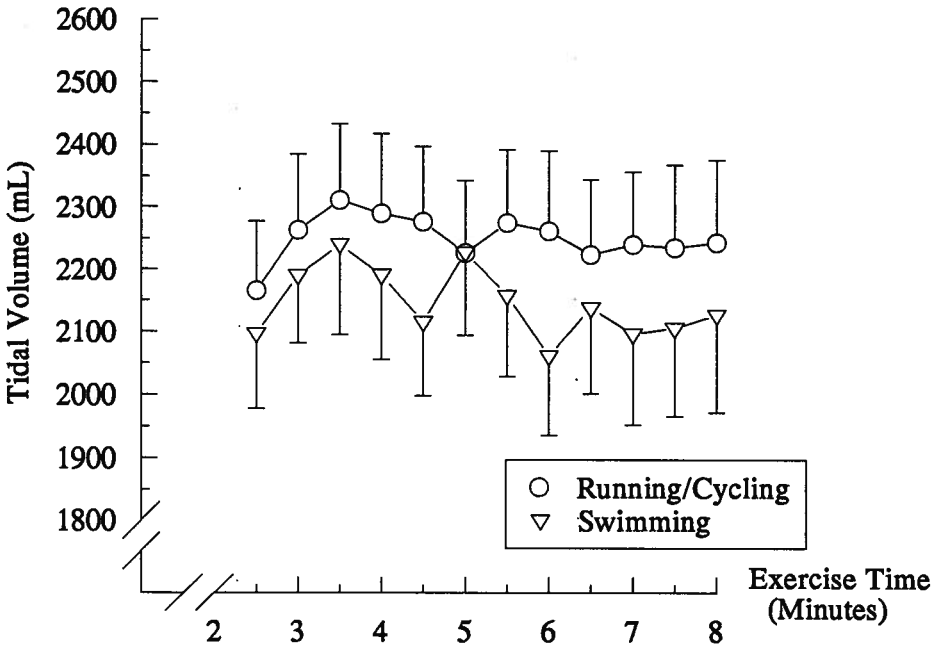


Figure 26: A comparison of the mean respiratory frequency (f) values measured during the last 6 minutes of the laboratory and swimming pool tests for EIA. Overall, there was no difference in the mean f value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

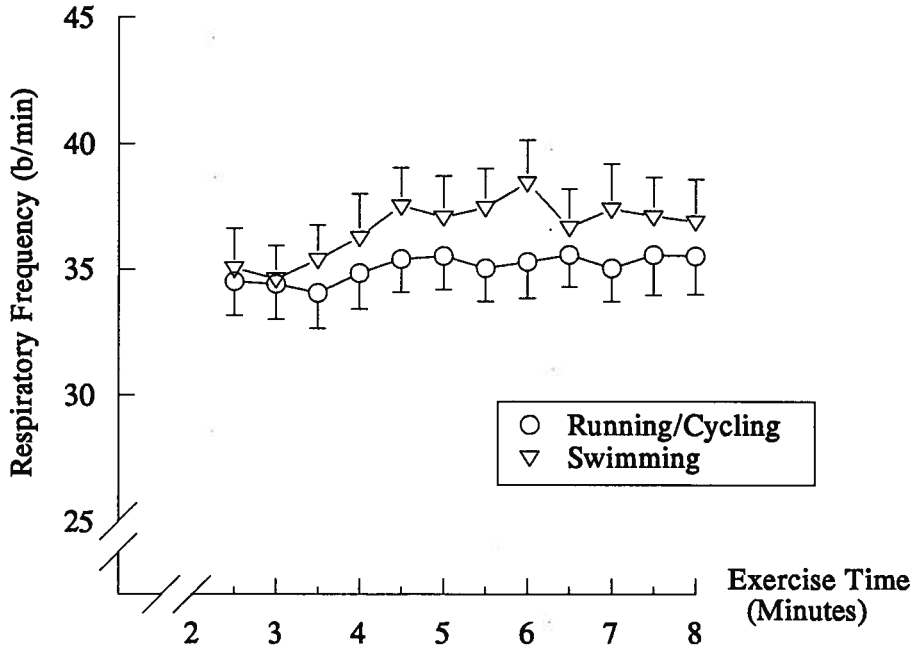


Figure 27: A comparison of the mean oxygen consumption ($\dot{V}O_2$) values measured during the last 6 minutes of the laboratory and swimming pool tests for EIA. Overall, there was no difference in the mean $\dot{V}O_2$ value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

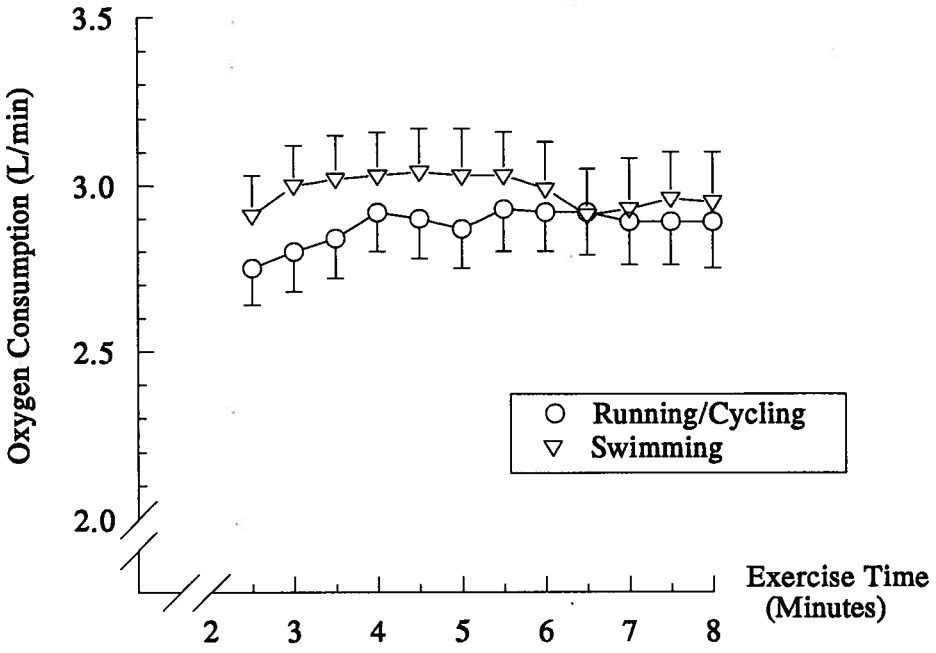


Figure 28: A comparison of the mean respiratory exchange ratio (R) values measured during the last 6 minutes of the laboratory and swimming pool tests for EIA. Overall, there was no difference in the mean R value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

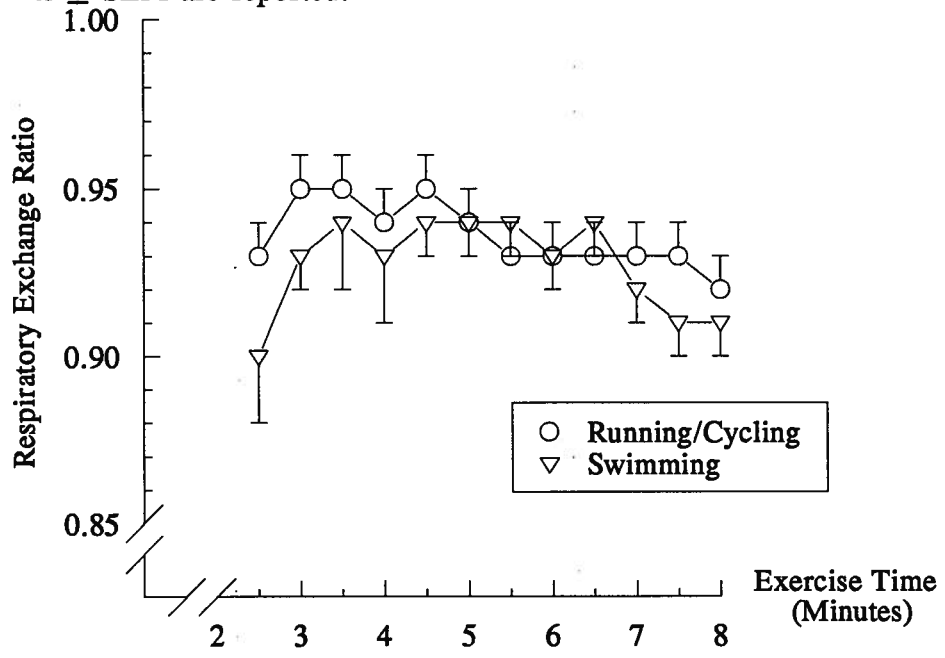
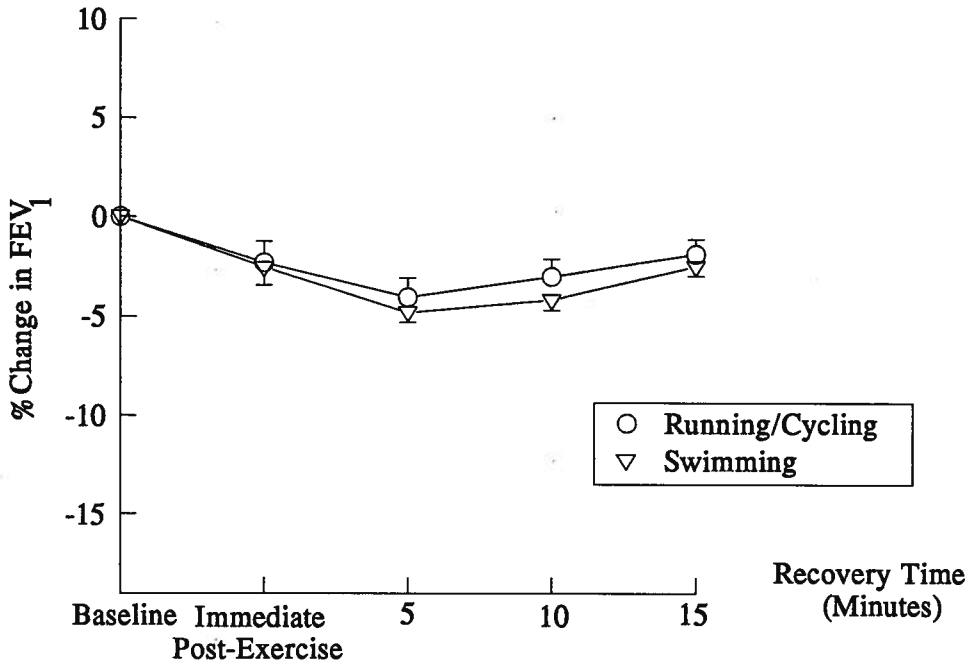


Figure 29: A comparison of the mean FEV_1 values following the 8 minute exercise challenge tests in the laboratory and swimming pool. The $\bar{x} \pm$ SEM are reported.



The Prolonged Exercise Challenge Test in the Swimming Pool

A comparison of the exercise data between the two groups of swimmers is presented in Table 23. The mean predicted heart rate for the Case Group was significantly higher than that of the Control Group ($p<0.0444$). There was no difference in the mean values for heart rate, $\dot{V}E$, VT, f, $\dot{V}O_2$, and R calculated over the 45 minutes of exercise between the two groups of swimmers (Figures 30-35). Figure 36 shows the mean percentage change in FEV_1 values following the test. The most common symptom reported by the swimmers following the prolonged exercise challenge test was a sore throat (53.6% of participants). Other symptoms reported by the swimmers included coughing (25.0%), chest tightness or headache (14.3%), dry mouth (10.7%), sneezing or chest congestion (7.1%), and sore eyes or nasal congestion (3.6%). A total of 8 swimmers (28.6%) reported no symptoms following the test.

Table 23: The mean values for the cardiorespiratory variables collected during the 45 minute exercise challenge test in the swimming pool. The $\bar{x} \pm$ SD are reported.

	Case Group	Control Group	Level of Significance
Predicted Heart Rate (bpm)	138.69 ± 1.44	137.53 ± 1.46	$p<0.0444$ *
Exercise Heart Rate (bpm)	139.46 ± 2.82	137.20 ± 5.00	NS
$\dot{V}E$ (L/min)	50.40 ± 8.37	51.31 ± 10.09	NS
VT (mL)	1,719.54 ± 505.66	1,877.40 ± 512.57	NS
f (b/min)	31.19 ± 8.72	28.40 ± 5.94	NS
$\dot{V}O_2$ (L/min)	2.26 ± 0.47	2.24 ± 0.43	NS
$\dot{V}O_2$ (mL/min/kg)	33.14 ± 4.64	32.04 ± 3.64	NS
R	0.88 ± 0.04	0.88 ± 0.05	NS

* The mean predicted heart rate for the Case Group was significantly higher than that of the Control Group.
NS = No statistically significant differences were found between groups.

Figure 30: The mean heart rates measured during the 45 minute exercise challenge test. Overall, there was no difference in the mean heart rate value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

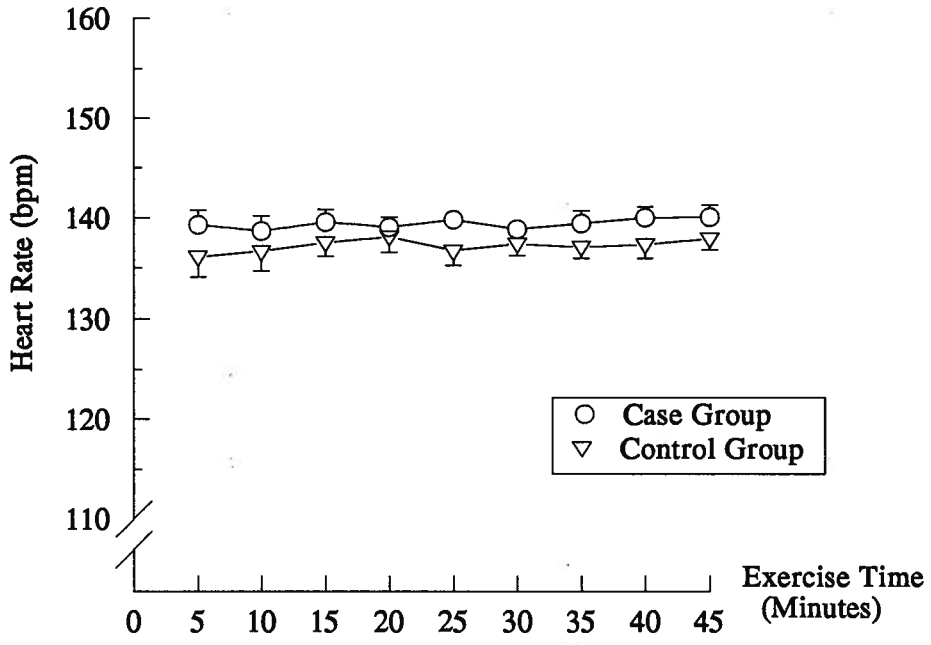


Figure 31: The mean $\dot{V}E$ values measured during the 45 minute exercise challenge test. Overall, there was no difference in the mean $\dot{V}E$ value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

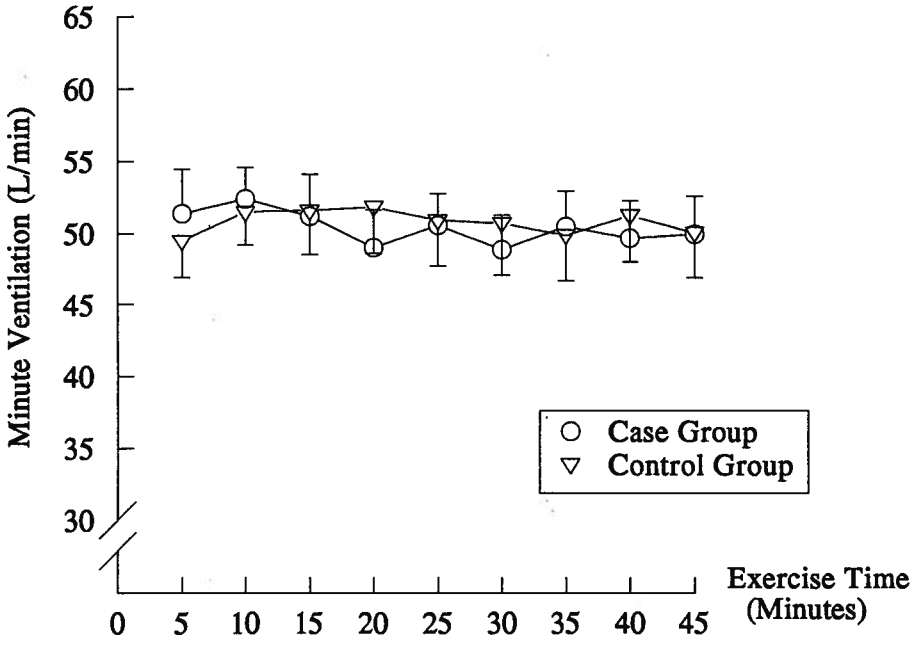


Figure 32: The mean tidal volume (VT) values measured during the 45 exercise challenge test. Overall, there was no difference in the mean VT value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

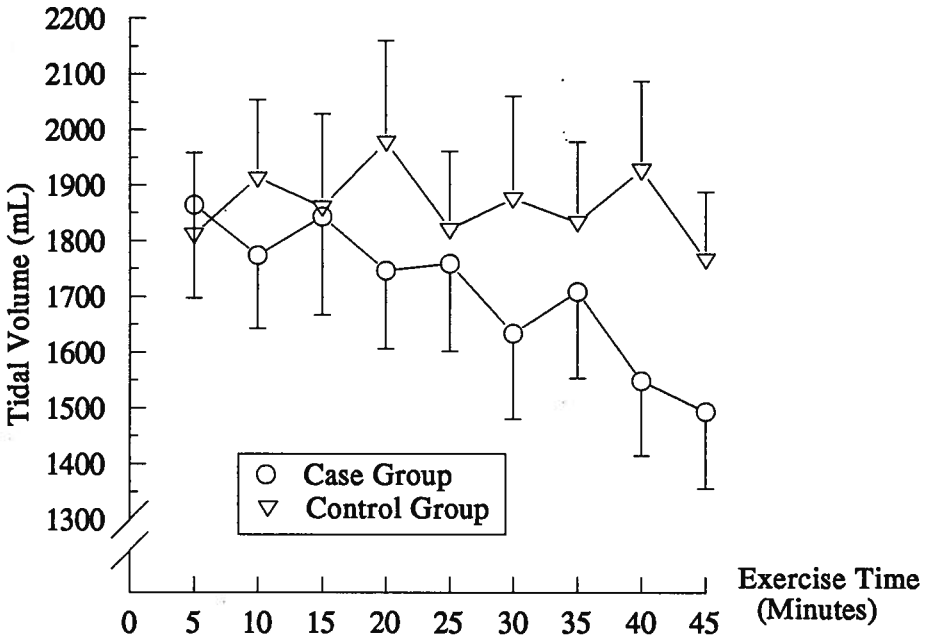


Figure 33: The mean respiratory frequency (f) values measured during the 45 minute exercise challenge test in the swimming pool. Overall, there was no difference in the mean f value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

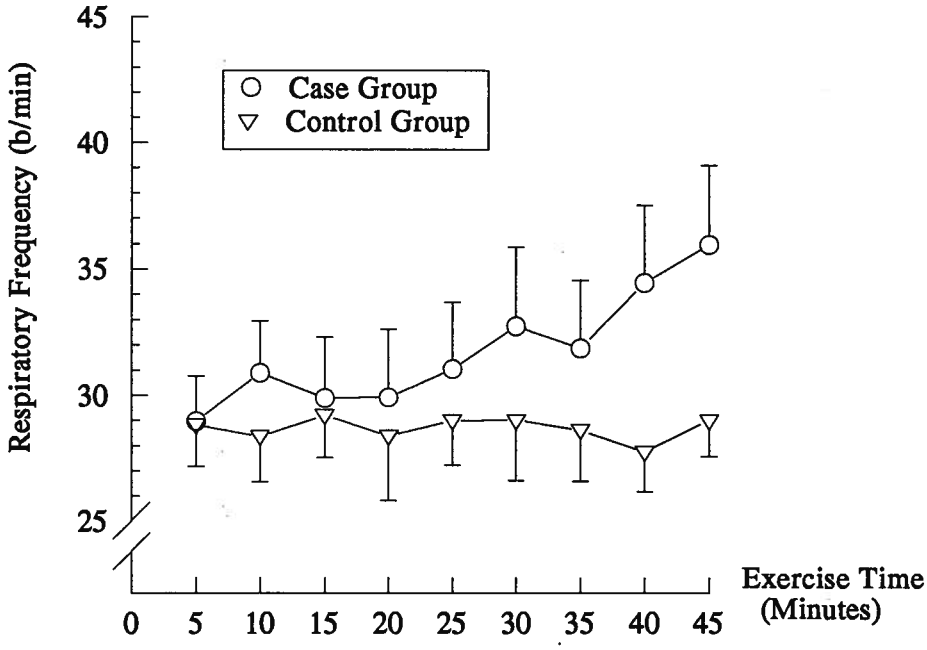


Figure 34: The mean oxygen consumption ($\dot{V}O_2$) values measured during the 45 minute exercise challenge test in the swimming pool. Overall, there was no difference in the mean $\dot{V}O_2$ value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

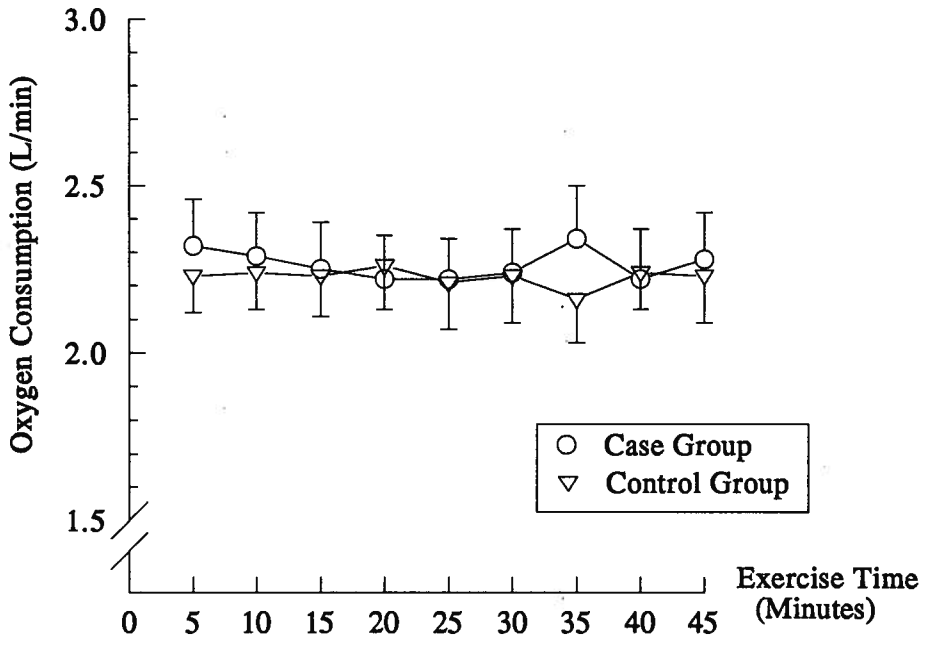


Figure 35: The mean respiratory exchange ratio (R) values measured during the 45 minute exercise challenge test in the swimming pool. Overall, there was no difference in the mean R value between the two groups of swimmers. The $\bar{x} \pm$ SEM are reported.

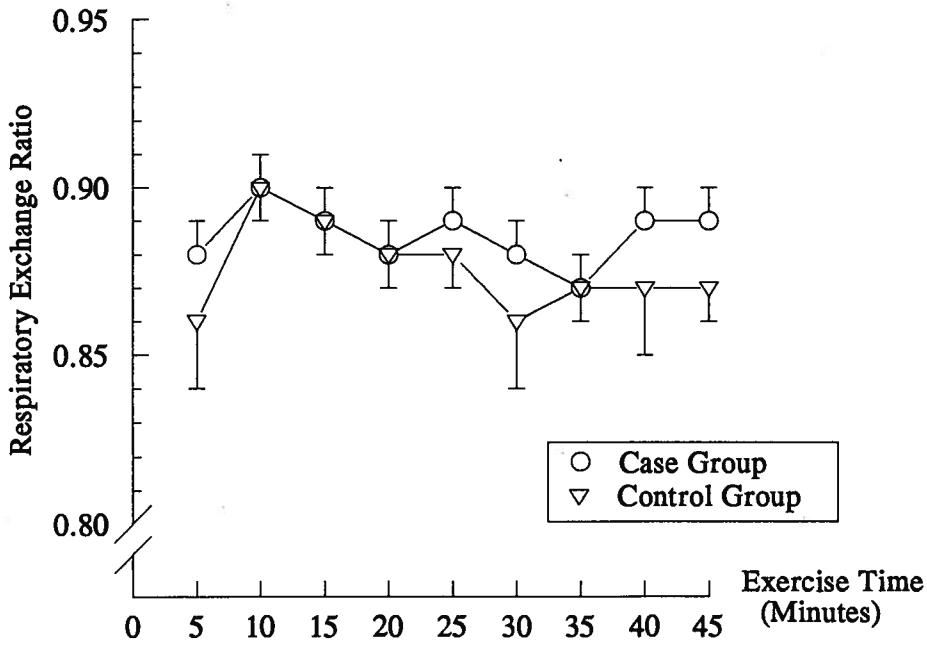
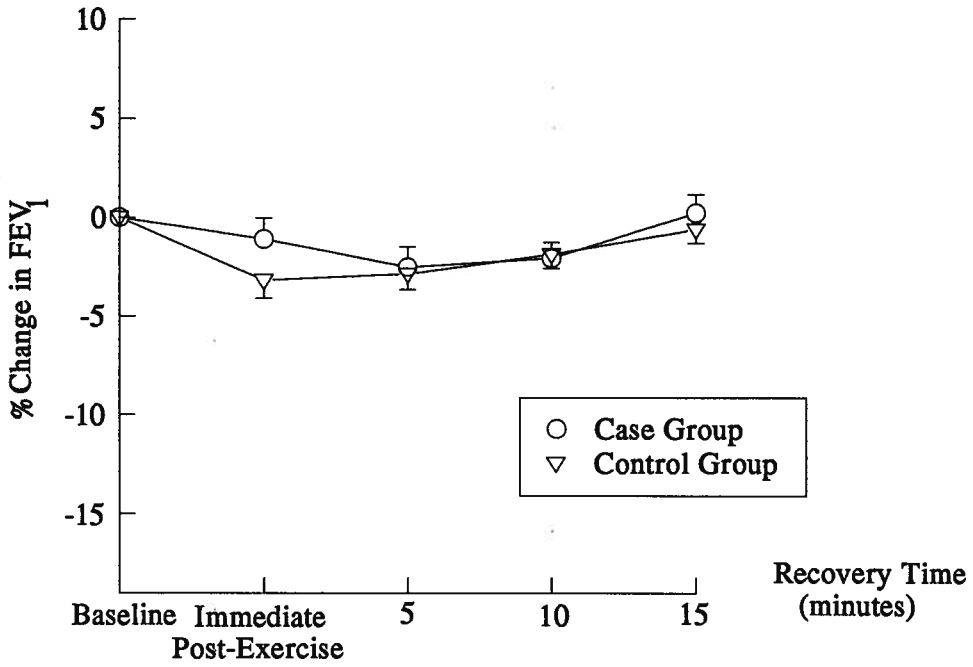


Figure 36: The mean FEV_1 values following the 45 minute exercise challenge test in the swimming pool. The $\bar{x} \pm$ SEM are reported.



DISCUSSION

This study shows that the prevalence of EIA in competitive swimmers is within the 3-11% range that has been reported for other competitive athletes (Fitch, 1984; Helbling and Muller, 1991; Huftel et al., 1991; Rice et al., 1985; Voy, 1986). Overall, the prevalence of EIA in the group of athletes that we tested was 9.8%. This includes 11.1% of the Case Group, 11.8% of the Control Group, and 6.3% of the Non-Swimming Control Group. There do not appear to be differences in the prevalence of EIA among swimmers with asthma or exercise-related respiratory symptoms when compared to swimmers who have neither asthma nor exercise-related symptoms. Also, the prevalence of EIA among swimmers appears to be similar to that of non-swimmers. Although we found a 3.5% higher prevalence rate in swimmers, this difference may partially be explained by differences in the mode of exercise used by the two groups of athletes. Most of the swimmers were tested while running on a treadmill, while all of the non-swimmers were tested on a bicycle ergometer. Anderson et al. (1971) and Fitch and Morton (1971) have shown that treadmill running is more asthmogenic than bicycle ergometry.

Our current understanding of EIA suggests that the post-exercise bronchoconstriction is initiated by thermal events. Deal et al. (1979) suggest that the magnitude of RHL appears to be directly related to the severity of EIA and Noviski et al. (1987) suggest that the intensity of exercise determines and, climatic conditions modify, the severity of EIA. The severity of airway narrowing has been shown to be a function of the $\dot{V}E$ and the temperature and water content of the inspired air. For a given set of inspired conditions, high minute ventilations result in more obstruction than do low levels, and drying and cooling the air at any level of ventilation cause more obstruction than when breathing warm and humid air. Low inspired air temperatures produce greater convective cooling and low humidity enhances evaporative cooling of the airway

mucosa.

In our study we did not measure either inspired or expired air conditions at the mouth and, therefore, we could not calculate RHL. Even though the temperature and relative humidity of the inspired air was higher in the non-swimming control group, it is likely that there were minimal differences in RHL among the three groups of athletes who were tested for EIA in the laboratory. Based on our results it could be suggested that the non-swimming control group would have a lower RHL, however, when we compare the differences between the $\dot{V}_E$, temperature and relative humidity of the inspired air between the three groups of athletes these differences are minimal, especially since we are only dealing with a 1°C difference in temperature and a 5% difference in relative humidity of the inspired air. Also, within the range of values that we measured, we are not dealing with extremes in either the temperature or relative humidity of the inspired air.

The prevalence of EIA among the swimmers appears to be dependent on whether the exercise protocol is performed in the laboratory or swimming pool. The prevalence of EIA was higher in the laboratory (9.8%) when compared to the swimming pool (3.6%). These results are similar to those of others in that they illustrate the lower asthmogenicity of swimming when compared to land-based exercise (Anderson, 1972; Bar-Yishay et al., 1982). The mechanisms for this protective effect of swimming are not clear, but a number of mechanisms have been proposed.

Inbar et al. (1980) conducted a study involving asthmatics in which they manipulated the humidity of the inspired air between 25-30% during tethered swimming and treadmill running and 80-90% during a second 8 minute tethered swimming protocol. Even though $\dot{V}_E$ and $\dot{V}O_2$ were equated during each of the exercise sessions, EIA occurred following running, but neither

of the swimming protocols induced EIA, irrespective of the water content of the inspired air. Bar-Yishai et al. (1982) did a similar experiment in which asthmatics were asked to run and swim under two conditions. The humidity of the inspired air alternated between 8% and 100% and $\dot{V}E$ and $\dot{V}O_2$ were equated during each of the exercise sessions. Irrespective of the humidity of the inspired air, running induced greater bronchoconstriction than swimming. However, the humidification of the inspired air reduced the post-exercise fall in FEV_1 by 57%. Bundgaard et al. (1987) compared the effects of indoor cycling and swimming on EIA by administering dry air with a relative humidity of 15% during both exercise sessions. Their results showed similar changes in post-exercise PEFR. Boulet and Turcotte (1991) showed that bronchoconstriction could be minimized by exercising in humid air and recovering in dry air and was maximized if the exercise was performed in dry air and recovery occurred in humid air. The results of these studies suggest that the high humidity of the inspired air in indoor swimming pools can only partially explain the lower asthmogenicity of swimming.

A second possible mechanism for the protective effect of swimming may result from the subjects being immersed in the water. Immersion in water is a simple and common maneuver that is used to study physiological changes in cardiovascular, respiratory, renal, endocrine, and thermoregulatory function. These changes include increases in intrathoracic blood volume, stroke volume, and cardiac output, diuresis, natriuresis, kaliuresis, increases in plasma atrial natriuretic peptide, inhibition of epinephrine, norepinephrine, renin, aldosterone, arginine vasopressin, and an increase in the ambient temperature zone for thermoregulation. Three factors are thought to be responsible for these changes: the high density of water supports the extra-thoracic blood vessels (analogous to a gravity-free state); the differential pressure distribution over the body (which gives rise to negative-pressure breathing); and the high

thermoconductivity of water (Lin and Hong, 1984). Water immersion has also been shown to improve gas diffusion and ventilation-perfusion matching in the lung (Arborelius et al., 1972; Löllgen et al., 1976). These immersion-related changes are thought to result from elevation of the diaphragm, a decrease in residual volume, and the influence of hydrostatic pressure on the blood vessels and thoracic wall (Löllgen et al., 1976). Kelly et al. (1986) suggested that the peripheral vasoconstriction and increase in central blood volume that occurs during immersion may result in a lower RHL and less bronchoconstriction.

Most of the research involving water immersion has been conducted with the subjects in a vertical orientation in the water. Exercise in the recumbent position has also been shown to improve gas diffusion and ventilation-perfusion matching in the lung (Craig et al., 1971; Prefaut et al., 1979). The effects of water immersion and posture on EIA were evaluated in two recent studies. Inbar et al. (1991) studied the effects of upright and prone body positions on EIA and isocapnic hyperventilation in 12 asthmatic children. All of the subjects had their FEV_1 tested before and after completing 8 minute exercise or isocapnic hyperventilation sessions in the upright and prone positions. The subjects' $\dot{V}E$ was kept constant for each of the sessions and the subjects were tested in an environmental chamber where the air temperature was 10° and the relative humidity was 31%. No difference was found in the FEV_1 between the prone and upright body positions following either exercise or isocapnic hyperventilation. The authors concluded that on land, body posture has no effect on the severity of bronchoconstriction in asthmatic children. However, the authors suggested that there may be some physiological benefits of the prone position in water.

Inbar et al. (1993) then studied the effects of prone immersion on isocapnic hyperventilation in 12 asthmatic children. The subjects performed 8 minutes of isocapnic

hyperventilation on land (upright) and in the water (prone) with the temperature and relative humidity of the inspired air kept at 20°C and 10%, respectively. The subjects' $\dot{V}E$ was similar during each session and the authors observed similar decreases in FEV_1 following each session. However, some of the subjects had less bronchoconstriction in the water and some had less bronchoconstriction on land.

In our study there was no difference in the relative humidity of the inspired air between the laboratory (59%) and the swimming pool (60%). Similar results have been reported by Bar-Yishay et al. (1982). As well, the mean value for $\dot{V}E$ between swimmers who completed both the laboratory and swimming pool tests for EIA were similar. Even though the temperature of the air was 3°C higher in the swimming pool, it is unlikely that this difference alone could account for significant differences in RHL between swimmers who completed both the laboratory and swimming pool tests for EIA. Even though we were able to show that swimming is associated with lower asthmogenicity than treadmill running or cycling in competitive swimmers, the pathophysiological mechanism of the lower asthmogenicity does not appear to be related to RHL. It appears that while the humidity of the inspired air can partially explain the lower asthmogenicity of swimming, the effect of body position is not important and, based on the few studies that have been done, the effect of immersion is equivocal and varies among individuals.

Our study was designed to match $\dot{V}E$, $\dot{V}O_2$, and heart rate during exercise testing. There were no statistically significant differences in the mean values for $\dot{V}E$ and $\dot{V}O_2$ between any of the 3 groups of athletes involved in the laboratory test for EIA, or for the 2 groups of swimmers involved in the swimming pool test for EIA. However, the mean heart rate for the Non-Swimming Control Group was significantly lower than the mean heart rate for either of the two swimming groups, and the mean heart rate for the Control Group was significantly lower than

that of the Case Group. It is difficult to assess the importance of these findings given that there were no differences in the mean values for $\dot{V}E$ and $\dot{V}O_2$ between the three groups of athletes. However, because we were using heart rate to control for the intensity of exercise, it does suggest that we were not able to control it very well during the laboratory test for EIA.

The differences in heart rate could be due to differences in the aerobic fitness level of the athletes, the specificity of training on land as opposed to water, or to individual differences among the sample of subjects that were studied. If we evaluate the relationship between $\dot{V}E$ and heart rate ($\dot{V}E$/HR) or $\dot{V}O_2$ and heart rate ($\dot{V}O_2$/HR), we obtain a hierarchy of values that suggest the Non-Swimming Control Group may be more aerobically fit than the Control Group, and both of these groups are more aerobically fit than the Case Group. However, the mean R values obtained during exercise testing would suggest otherwise. The mean R value of the Case and Control Groups (0.94 and 0.93, respectively) were significantly lower than that of the Non-Swimming Control Group (1.04). The higher R values also suggest that at a given level of $\dot{V}E$, the non-swimmers are producing more $\dot{V}CO_2$ than are the swimmers which would result in a lower $\dot{V}E/\dot{V}CO_2$ ratio.

Clausen (1976), Holmer and Atrand (1972), and Saltin et al. (1976) have shown that following training $\dot{V}E$, $\dot{V}O_2$, heart rate, and R are lower at any level of submaximal exercise, all of which indicates an improvement in the aerobic fitness of the subject. These changes also indicate the importance of the specificity of training and since swimmers do not use running or cycling as an integral part of their training they may be expected to have higher heart rates than individuals who use either training methods extensively. This assumption does not explain the differences in heart rates between the two swimming groups. Thus, in the laboratory, the differences in the mean values for heart rate between the three groups of athletes are not likely

due to differences in aerobic fitness, but may be due to the specificity of training among the non-swimmers and swimmers or to the sample population that represents each group of athletes.

There was no difference in the mean heart rate between the Case and Control Groups during exercise challenge testing in the swimming pool. However, at a similar $\dot{V}E$ and $\dot{V}O_2$, the mean heart rate in the swimming pool was 11 beats/minute lower than in the laboratory. Lower heart rates have been reported for many studies that have evaluated the physiological effects of the diving reflex or water immersion and comparative studies of exercise on land and in the water. Although the diving reflex is thought to be weak in man, it is known to be associated with apnea, peripheral vasoconstriction, and bradycardia. Berk et al. (1991) have shown that cold water facial immersion induces bradycardia. Immersion to the chest in thermoneutral water or cold water may decrease resting heart rate by 15%; whereas, immersion to the chest in hot water may increase heart rate by 32% (Bonde-Petersen et al., 1992).

Inbar et al. (1980) found heart rates to be significantly lower during swimming than during treadmill running. A number of studies comparing water running to free or treadmill running have shown heart rates to be significantly lower during water running (Ritchie and Hopkins, 1991; Svedenhag and Seger, 1992). Forgays and McClure (1988) found no difference in the heart rates of subjects immersed in water in either a vertical or horizontal position, suggesting that it is not the body position during immersion that accounts for the lower heart rates. Thus, the lower heart rates probably occur as a result of the diving reflex with facial immersion as well as the effects of whole body immersion.

Studies of occupational lung disease often use spirometry or peak flow measurements to assess lung function before and after work exposure. We attempted to assess the effects of prolonged swimming on lung function by measuring FEV_1 before and after a 45 minute exercise

challenge test. We were unable to detect any change in lung function following exercise, although the swimmers did complain of a number of respiratory and other health-related symptoms. The prevalence of chest congestion, sneezing, chest tightness, sore eyes, and headaches following the 45 minute swim was lower than the prevalence of post-exercise symptoms reported on the questionnaire. Sore throats and a dry mouth were reported more frequently following the 45 minute swim and this may be due to the fact that the swimmers had to breathe air through a mouthpiece and a long section of tubing for the duration of the test. The intensity of the 45 minute exercise test was 15-20% lower than that of the 8 minute exercise challenge test, which may partially explain the fact why none of the swimmers reported wheezing or dyspnea.

There was also an interesting trend in the $\dot{V}E$ and f data for the Case Group during the 45 minute test. There was a progressive fall in $\dot{V}E$ and a continual rise in f which suggests that these swimmers were adopting a restrictive breathing pattern. This breathing pattern is similar to that reported for exercising athletes who are exposed to low level concentrations of ozone (Adams and Schelegle, 1983; Follinsbee et al., 1988; McKenzie et al., 1987). Symptoms of substernal soreness, dyspnea, coughing, wheezing, congestion, sore throats, headaches, and nausea are common during exercise under these conditions. Perhaps prolonged exposure to the chemicals used to disinfect the pool water have a similar effect on breathing pattern and symptom responses, and what we are seeing is an early indicator of respiratory distress.

There is a remarkable discrepancy between the prevalence of BHR (60.0%) and EIA (9.8%) among these competitive swimmers. While the prevalence of BHR is significantly higher in swimmers than in non-swimmers, there is no difference in the prevalence of EIA among the two groups of athletes. We also know that the prevalence of BHR is similar between swimmers

with and without asthma and/or exercise-related symptoms, and even though swimmers have a high prevalence of exercise-related symptoms suggestive of asthma, these symptoms don't manifest themselves as EIA. These results provide us with substantial evidence that there is something about the swimming-related exposure that increases non-specific bronchial responsiveness, but does not incite EIA.

CONCLUSIONS

In conclusion, this study shows that the prevalence of EIA among lower mainland competitive swimmers is 9.8%. This value is within the 3-11% prevalence reported for other competitive athletes, and is similar to the 6.3% prevalence that was observed for 16 non-swimming athletes in our study. Our study also confirms the lower asthmogenicity of swimming when compared to land-based activities. The prevalence of EIA was higher in the laboratory (9.8%) when compared to the swimming pool (3.6%). The mechanisms for this protective effect are not clear, but in our study it does not appear to be related to RHL or to differences in the temperature or humidity of the inspired air. There were no differences in the prevalence of EIA among competitive swimmers who have asthma or exercise-related symptoms (11.1%) in comparison with those who have neither asthma nor exercise-related symptoms (11.8%).

Throughout this study we were able to match $\dot{V}E$ and $\dot{V}O_2$ for the three groups of athletes involved in the laboratory study for EIA and the two groups of swimmers involved in the swimming pool study for EIA. Despite this, there were significant differences in heart rate among the three groups of athletes involved in the laboratory study, and when comparing heart rates between the laboratory and pool studies. The mean heart rate of the Non-Swimming Control Group was significantly lower than that of either of the swimming groups. Similarly, the mean heart rate of the Control Group was significantly lower than the Case Group. These differences are likely due to the specificity of training among the non-swimmers and swimmers or to differences in the sample population which represents each group of athletes. The mean heart rate of the swimmers during the swimming pool test for EIA was 11 beats/minute lower than during the laboratory test for EIA. This finding is similar to many of the comparative studies that have evaluated the physiological effects of exercise on land and in the water. These

lower heart rates probably occur as a result of the diving reflex with facial immersion as well as the effects of whole body immersion.

Finally, while continuous submaximal swimming for 45 minutes results in the swimmers complaining of many of the symptoms reported on our questionnaire, there were no significant pre- to post-exercise changes in FEV_1. However, the swimmers in the Case Group adopted a restrictive breathing pattern similar to that of athletes who are exposed to ozone during exercise. It is possible that this might be an early indicator of respiratory distress.

Our results provide us with substantial evidence that there is something about the swimming-related exposure that increases non-specific bronchial responsiveness, but does not incite EIA. The remarkable discrepancy between the prevalence of BHR and EIA among the competitive swimmers is supported by a number of other findings. These include the higher prevalence of BHR in swimmers when compared to non-swimmers, a similar prevalence of BHR among swimmers with and without asthma and/or exercise-related symptoms, a similar prevalence of EIA among swimmers and non-swimmers and, despite a low prevalence of EIA, there is a high prevalence of exercise-related symptoms suggestive of asthma among the swimmers.

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GENERAL SUMMARY AND CONCLUSIONS

This study has provided us with the answers to a number of questions that originally evolved from anecdotal reports of respiratory and other health-related problems among competitive swimmers. In the first chapter, we determined the prevalence of respiratory and other health-related symptoms, illnesses, and allergies among competitive swimmers, and established whether the symptoms were associated with a swimming-related exposure as defined by the amount of time spent swimming, or the distance covered, during training sessions in the swimming pool. To accomplish these objectives, we modified the American Thoracic Society's Respiratory Disease Questionnaire for Adults and Children into a single questionnaire and administered it to 738 competitive swimmers from Canada, the United States, and a number of Pacific Rim countries.

The prevalence of respiratory and other health-related symptoms, illnesses, and allergies were extremely common among competitive swimmers. The overall prevalence of physician-diagnosed asthma among the 738 competitive swimmers was 13.4%. This is significantly higher than the 7.1% to 9.7% reported for other competitive athletes. There was a significant difference in the prevalence rates of asthma for the three groups of competitive swimmers that we identified. The range of values included 10.6% of Age Group Swimmers, 12.4% of National Qualifiers, and 20.6% of International Level Swimmers. The extremely high prevalence of asthma among the International Level Swimmers was associated with a high prevalence of swimming-related symptoms suggestive of asthma and the use of β2-agonists among 9.1% of the swimmers in this group.

There was a tendency for Age Group Swimmers to have their asthma diagnosed before they began competitive swimming, while the National Qualifiers and International Level Swimmers had their asthma diagnosed after they began competitive swimming. This suggests that a combination of exercise and the swimming-related exposure may have caused swimming-related respiratory symptoms that were severe enough for the swimmers to see their physician for medical advice.

Among the other respiratory illnesses that we identified, the prevalence of bronchitis (24.9%) and pneumonia (10.2%) were higher than that reported for the general population. The prevalence of hay fever (16.9%) was significantly lower than that reported for other high performance athletes, but is slightly higher than that reported for the general population. The most common allergies among the competitive swimmers were to dust (20.9%), pollen (19.2%), animal hair (17.1%), grasses (17.1%), and molds (8.5%). These prevalences appear to be similar to those reported for high performance athletes as well as the general population.

A high percentage (43.5%) of the swimmers had at least one chest illness that kept them from participating in their normal daily activities for 3 days or more during the past year. The prevalence of swimming-related symptoms included sneezing (45.0%), difficulty breathing (39.4%), coughing (36.4%), sore eyes (36.0%), headaches (35.9%), sore throat (27.1%), wheezing (26.3%), chest tightness (24.8%), and chest congestion (22.8%). This suggests that both upper and lower respiratory tract irritation occurs as a result of the swimming-related exposure. All of the symptoms, except for sore eyes, were strongly associated with the swimming-related exposure. These results imply that there is a dose-response relationship between the amount of training and the occurrence of symptoms.

We identified a number of gender- and age-related differences for several of the swimming-related symptoms. Female swimmers were more likely to cough, feel congested, have difficulty breathing, and experience headaches. Older swimmers were more likely to feel congested, sneeze, wheeze, have chest tightness, difficulty breathing, sore throats, and headaches. A majority of the swimmers with swimming-related symptoms reported that their symptoms were less severe, less noticeable, or absent if they spent several days away from the swimming pool.

In the second chapter, we established the prevalence of bronchial hyperresponsiveness (BHR) in a group of competitive swimmers from the lower mainland using a methacholine challenge test. In addition, we determined whether there were differences in the prevalence of BHR among competitive swimmers with asthma or swimming-related symptoms (Case Group) and those who had neither asthma nor symptoms (Control Group), and compared their results with a group of non-swimming athletes who had neither asthma nor symptoms (Non-Swimming Control Group).

This study showed that the prevalence of BHR ($PC_{20} \leq 16$ mg/mL) among lower mainland competitive swimmers was 60.0%. When the sensitivity of the methacholine challenge test was decreased to include only those swimmers with a $PC_{20} \leq 8$ mg/mL, the prevalence of BHR was 34.3%. These values are significantly higher than the 12.5% and 0% prevalences that were observed for 16 non-swimming athletes in our study and the 11-14% prevalence reported in several population-based studies. There was no difference in the prevalence of BHR among competitive swimmers who have a clinical history of asthma or symptoms suggestive of asthma while swimming (61.1%) and those who have neither asthma nor symptoms (58.8%). When the sensitivity of the methacholine challenge test was decreased to include only those swimmers with

a PC20 $\leq$ 8 mg/mL, 33.3% of the swimmers in the Case Group and 35.3% of the swimmers in the Control Group demonstrated BHR.

The use of the dose-response slope was effective in assessing differences in BHR among the three groups of athletes. In our study there was approximately a 363-fold difference between the least and most responsive subjects using this method. The dose-response slope was significantly lower in the non-swimmers, indicating a lower prevalence of BHR in that group of athletes. The extremely high prevalence of BHR among the competitive swimmers when compared to the non-swimmers leads us to believe that there is something about the swimming-related exposure that may be responsible for the BHR among the swimmers. These competitive swimmers have a high prevalence of asthma, respiratory symptoms suggestive of asthma, and non-specific BHR to methacholine. However, their lung function is normal and there is no difference in the prevalence of BHR among swimmers with or without asthma or swimming-related symptoms. At this time, we can only speculate that the chemicals used to disinfect the swimming pool water are responsible for the development of BHR among the competitive swimmers.

In the third chapter, we established the prevalence of exercise-induced asthma (EIA) in the same group of swimmers from the lower mainland using a standard exercise challenge test in the laboratory and a tethered swimming protocol in the swimming pool. We also determined whether there were differences in the prevalence of EIA among competitive swimmers in the Case and Control Groups and compared their results with the Non-Swimming Control Group. In addition, we determined whether a prolonged exercise challenge test in the swimming pool resulted in the development of respiratory symptoms and significant changes in pulmonary mechanics.

The prevalence of EIA among lower mainland competitive swimmers was 9.8%. This value was within the 3-11% prevalence reported for other competitive athletes, and was similar to the 6.3% that was observed for the non-swimming athletes in our study. The prevalence of EIA among the swimmers was also higher in the laboratory (9.8%) when compared to the swimming pool (3.6%). Our results are in agreement with those of other researchers who have shown the lower asthmogenicity of swimming when compared to land-based activities. The mechanisms for this protective effect are not clear and, in our study, do not appear to be related to respiratory heat loss (RHL) or to differences in $\dot{V}E$ or the temperature and humidity of the inspired air. There were also no differences in the prevalence of EIA among competitive swimmers who have asthma or swimming-related symptoms (11.1%) and those who have neither asthma nor swimming-related symptoms (11.8%).

Finally, while continuous submaximal swimming for 45 minutes results in the swimmers complaining of many of the symptoms reported on our questionnaire, there were no significant pre- to post-exercise changes in FEV_1. However, the swimmers in the Case Group adopted a restrictive breathing pattern similar to that of athletes who are exposed to irritants such as SO_2, NO_2, and O_3 during exercise. It is possible that this might be an early indicator of respiratory distress.

In summary, these results provide us with substantial evidence that there is something about the swimming-related exposure that may cause a mild form of asthma in susceptible swimmers, causes non-specific BHR in 60% of swimmers whether or not they have asthma or swimming-related symptoms, but does not appear to incite EIA. In fact, there is a remarkable discrepancy between the prevalence of BHR and EIA among the competitive swimmers. This finding is associated with a number of other interesting results. The presence of normal lung

among those swimmers with physician-diagnosed asthma suggests that many of the swimmers are not currently atopic or symptomatic. There was also a higher prevalence of BHR in swimmers when compared to non-swimmers, a similar prevalence of EIA among swimmers and non-swimmers and, despite a low prevalence of EIA, there was a high prevalence of swimming-related symptoms among the swimmers. It is possible that individuals with unstable asthma or severe swimming-related symptoms that affect performance may not be able to participate in competitive swimming at the national or international level.

These findings suggest that the underlying mechanism responsible for the BHR is related to a heightened cholinergic excitatory mechanism that increases non-specific bronchial responsiveness to methacholine, but not to exercise. We speculate that chronic, low level exposure to the chemicals used to disinfect the pool water may damage the respiratory epithelium and expose bronchial irritant receptors and pulmonary C-fibers. This may trigger an axon reflex that results in the release of chemical mediators that enhance smooth muscle contraction, inflammation, and BHR. Swimmers who complain of symptoms during training may have been exposed to higher concentrations of these chemicals. Since the most common cause of asthma in young people is sensitization to inhaled allergens, there may be a relationship between atopy and the chemical irritants in the swimming pool. Knowing this relationship may have provided us with information about whether chemical irritants in the swimming pool increase the likelihood of becoming atopic or, conversely, whether atopic individuals are more likely to develop swimming-related symptoms. In retrospect, it would have been prudent to have assessed the atopic status of the subjects from the lower mainland.

Future studies of competitive swimmers need to document the relationship between the clinical findings in our study and exposure to the chemicals used to disinfect swimming pool water. This will need to be done using specific inhalation challenge tests with the chemical irritants found in the water. In addition, studies need to evaluate the prevalence of respiratory illnesses and symptoms, BHR, and EIA, longitudinally. These studies should attempt to establish these prevalences at the onset of the swimmer's career, and measure the change in prevalence at regular intervals during the competitive season and throughout the swimmer's career. Since a majority of swimmers feel that their symptoms improve if they do not exercise in the swimming pool for several days, it would also be interesting to monitor changes in their peak expiratory flow rates before and after training sessions and after prolonged periods away from the swimming pool. These studies may provide us with information about any long-term health-related problems associated with competitive swimming and establish whether the swimming-related exposure results in the development of irritant-induced occupational asthma or RADS.

APPENDIX A

Competitive Swimmer's Respiratory Health Questionnaire (27/04/91)

27/04/91

DEPARTMENT OF PHYSIOLOGY
FACULTY OF MEDICINE

UNIVERSITY OF BRITISH COLUMBIA

COMPETITIVE SWIMMER'S RESPIRATORY HEALTH QUESTIONNAIRE

NAME: _____
(Last) (First) (Middle)

ADDRESS: _____
(Street)

_____ _____
(City) (Province) (Postal Code)

_____
(Telephone Number)

DATE OF BIRTH: _____ _____ _____ **GENDER:** _____
(Year) (Month) (Day) (M/F)

SWIM CLUB: _____

COACH'S NAME: _____
(Last) (First)

COMPETITIVE CATEGORY:

7-10 year olds	_____
11-17 year olds (not a national qualifier)	_____
18-over (not a national/university qualifier)	_____
University (not a national qualifier)	_____
National Qualifier	_____

I.D. Number _____

Today's Date: _____ _____ _____
(Year) (Month) (Day)

AGE: _____ **GENDER:** _____

Did you complete this questionnaire by yourself _____ or with the help of someone else _____? If someone helped you complete this questionnaire, name that person: (please √ below)

(a) Mother _____
(b) Father _____
(c) Female Guardian _____
(d) Male Guardian _____
(e) Coach _____
(f) Other (specify) _____

COMPETITIVE CATEGORY:

7-10 year olds _____
11-17 year olds (not a national qualifier) _____
18-over (not a national/university qualifier) _____
University (not a national qualifier) _____
National Qualifier _____

TRAINING FACILITY: _____

(1) How many years have you been a competitive swimmer? _____

(2) On average, how many times do you train in the water each day? _____

(3) On average, how many days do you train in the swimming pool each week? _____

(4) On average, how many weeks do you train in the swimming pool each year? _____

(5) On average, how many metres do you swim each week? _____

(6) Are your training sessions early in the morning (5 am to 9 am) _____, mid-day (10 am to 2 pm) _____, or late afternoon/early evening (3 pm to 7 pm) _____? (please √ appropriate times)

(7) On average, how long are your training sessions?:

(a) early morning training sessions _____ hours
(b) mid-day training sessions _____ hours
(c) late afternoon/early evening training sessions _____ hours

I.D. Number _____

(8) During the past year, have you had any chest illnesses (pneumonia, bronchitis, asthma, colds, etc.) that have kept you from participating in your daily activities for 3 days or more? YES ☐ NO ☐

If you answered YES to (8), how many times did this occur during the past year? Number of illnesses _____

If you answered YES to (8), how many times did these illnesses last for 7 days or more? Number of illnesses _____

(9) On average, how many colds do you get each year? Number colds _____

(10) Do you usually have a cough with colds? YES ☐ NO ☐

(11) Do you usually have a cough apart from colds? YES ☐ NO ☐

(12) If you answered YES to (10) or (11), do you cough on most days (4 or more days each week) for as much as 3 months of the year? YES ☐ NO ☐

(13) Do you usually cough during or after <u>exercise other than swimming</u>?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (13), please indicate the number of years you have experienced this problem? Number of years _____

If you answered YES to (13), does this cough usually prevent you from continuing to exercise? YES ☐ NO ☐

(14) Do you usually cough during or after <u>exercise in the swimming pool</u>?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (14), please indicate the number of years you have experienced this problem? Number of years _____

I.D. Number _____

If you answered YES to (14), does this cough usually prevent you from continuing to exercise? YES ☐ NO ☐

If you answered YES to (11),(13) or (14), does this cough get better when you have not exercised in the swimming pool for several days? YES ☐ NO ☐

(15) Does your chest usually feel congested when you have a cold? YES ☐ NO ☐

(16) Does your chest usually feel congested apart from colds? YES ☐ NO ☐

(17) Does your chest usually feel congested during or after exercise other than swimming?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (17), please indicate the number of years you have experienced this problem? Number of years _____

If you answered YES to (17), does this chest congestion usually prevent you from continuing to exercise? YES ☐ NO ☐

(18) Does your chest usually feel congested during or after exercise in the swimming pool?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (18), please indicate the number of years you have experienced this problem? Number of years _____

If you answered YES to (18), does this chest congestion usually prevent you from continuing to exercise? YES ☐ NO ☐

If you answered YES to (16),(17) or (18), does this congestion get better after you have not exercised in the swimming pool for several days? YES ☐ NO ☐

(19) Do you usually bring up phlegm when you have a cold? YES ☐ NO ☐

I.D. Number _____

(20) Do you usually bring up phlegm apart from colds? YES ☐ NO ☐

(21) If you answered YES to (19) or (20), do you bring up phlegm on most days (4 or more days each week) for as much as 3 months of the year? YES ☐ NO ☐

(22) Do you usually sneeze when you have a cold? YES ☐ NO ☐

(23) Do you usually sneeze apart from colds? YES ☐ NO ☐

(24) Do you ever sneeze during or after <u>exercise other than swimming</u>?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (24), please indicate the number of years you have experienced this problem? Number of years _____

If you answered YES to (24), does this sneezing usually prevent you from continuing to exercise? YES ☐ NO ☐

(25) Do you ever sneeze during or after <u>exercise in the swimming pool</u>?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (25), please indicate the number of years you have experienced this problem? Number of years _____

If you answered YES to (25), does this sneezing usually prevent you from continuing to exercise? YES ☐ NO ☐

If you answered YES to (23),(24) or (25), does this congestion get better after you have <u>not exercised</u> in the swimming pool for several days? YES ☐ NO ☐

(26) Does your chest ever sound "wheezy" when you have a cold? YES ☐ NO ☐

I.D. Number _____

(27) Does your chest ever sound "wheezy" apart from colds? YES ☐ NO ☐

If you answered YES to (27), does your chest sound "wheezy" on most days or nights? YES ☐ NO ☐

If you answered YES to (27), please indicate the number of years that you have experienced this problem. Number of years _____

(28) Does your chest ever sound "wheezy" during or after exercise other than swimming?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (28), please indicate the number of years that you have experienced this problem. Number of years _____

If you answered YES to (28), please indicate whether this "wheezing" usually prevents you from continuing to exercise? YES ☐ NO ☐

(29) Does your chest ever sound "wheezy" during or after exercise in the swimming pool?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (29), please indicate the number of years that you have experienced this problem. Number of years _____

If you answered YES to (29), please indicate whether this "wheezing" usually prevents you from continuing to exercise? YES ☐ NO ☐

If you answered YES to (27),(28) or (29), does this "wheezing" usually get better after you have not exercised in the swimming pool for several days? YES ☐ NO ☐

(30) Do you usually have chest tightness with colds? YES ☐ NO ☐

(31) Do you usually have chest tightness apart from colds? YES ☐ NO ☐

I.D. Number _____

(32) Do you ever have chest tightness during or after exercise other than swimming?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (32), please indicate the number of years you have experienced this problem. Number of years _____

If you answered YES to (32), does this chest tightness usually prevent you from continuing to exercise? YES ☐ NO ☐

(33) Do you ever have chest tightness during or after exercise in the swimming pool?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (33), please indicate the number of years that you have experienced this problem. Number of years _____

If you answered YES to (33), please indicate whether this chest tightness usually prevents you from continuing to exercise? YES ☐ NO ☐

If you answered YES to (31),(32) or (33), does this chest tightness usually get better after you have not exercised in the swimming pool for several days? YES ☐ NO ☐

(34) Do you usually have difficulty breathing when you have a cold? YES ☐ NO ☐

(35) Do you usually have difficulty breathing apart from colds? YES ☐ NO ☐

(36) Do you ever have difficulty breathing during or after exercise other than swimming?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (36), please indicate the number of years that you have experienced this problem. Number of years _____

I.D. Number _____

If you answered YES to (36), does this difficulty breathing usually prevent you from continuing to exercise? YES ☐ NO ☐

(37) Do you ever have difficulty breathing during or after exercise in the swimming pool?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (37), please indicate the number of years that you have experienced this problem? Number of years _____

If you answered YES to (37), does this difficulty breathing usually prevents you from continuing to exercise? YES ☐ NO ☐

If you answered YES to (35),(36) or (37), does this difficulty breathing occur less frequently or with less intensity after you have not exercised in the swimming pool for several days? YES ☐ NO ☐

(38) Is your throat usually "raspy" or "ticklish" when you have a cold? YES ☐ NO ☐

(39) Is your throat usually "raspy" or "ticklish" apart from colds? YES ☐ NO ☐

(40) Is your throat ever "raspy" or "ticklish" during or after exercise other than swimming?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (40), please indicate the number of years that you have experienced this problem? Number of years _____

If you answered YES to (40), does this "raspy" or "ticklish" throat usually prevent you from continuing to exercise? YES ☐ NO ☐

I.D. Number _____

(41) Is your throat ever "raspy" or "ticklish" during or after exercise in the swimming pool?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (41), please indicate the number of years that you have experienced this problem? Number of years _____

If you answered YES to (41), does this "raspy" or "ticklish" throat usually prevent you from continuing to exercise? YES ☐ NO ☐

If you answered YES to (39),(40) or (41), does your throat feel better after not exercised in the swimming pool for several days? YES ☐ NO ☐

(42) Are your eyes usually itchy, watery, or puffy when you have a cold? YES ☐ NO ☐

(43) Are your eyes usually itchy, watery, or puffy apart from colds? YES ☐ NO ☐

(44) Are your eyes ever itchy, watery, or puffy during or after exercise other than swimming?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (44), please indicate the number of years that you have experienced this problem? Number of years _____

If you answered YES to (44), do itchy, watery, or puffy eyes usually prevent you from continuing to exercise? YES ☐ NO ☐

(45) Are your eyes ever itchy, watery, or puffy during or after exercise in the swimming pool?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (45), please indicate the number of years that you have experienced this problem? Number of years _____

I.D. Number _____

If you answered YES to (45), do itchy, watery, or puffy eyes usually prevent you from continuing to exercise? YES ☐ NO ☐

If you answered YES to (43),(44) or (45), do your eyes feel better after you have <u>not exercised</u> in the swimming pool for several days? YES ☐ NO ☐

(46) Do you usually experience headaches when you have a cold? YES ☐ NO ☐

(47) Do you usually experience headaches apart from when you have colds? YES ☐ NO ☐

(48) Do you ever experience headaches during or after <u>exercise other than swimming</u>?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (48), please indicate the number of years that you have experienced this problem? Number of years _____

If you answered YES to (48), do these headaches usually prevent you from continuing to exercise? YES ☐ NO ☐

(49) Do you ever experience headaches during or after <u>exercise in the swimming pool</u>?

(a) during exercise YES ☐ NO ☐

(b) after exercise YES ☐ NO ☐

If you answered YES to (49), please indicate the number of years that you have experienced this problem? Number of years _____

If you answered YES to (49), do these headaches usually prevent you from continuing to exercise? YES ☐ NO ☐

If you answered YES to (47),(48) or (49), do these headaches occur less frequently or with less intensity after you have <u>not exercised</u> in the swimming pool for several days? YES ☐ NO ☐

I.D. Number _____

(50) Have you ever had an ear infection? YES ☐ NO ☐

If you answered YES to (50), please indicate the average number of ear infections you get each year? Number per year _____

(51) Has a doctor ever told you that you have any of the following, and if you answer Yes, at what age were you when it was first diagnosed by the doctor?

(a) Asthma	YES ☐	NO ☐	Age _____
(b) Bronchitis	YES ☐	NO ☐	Age _____
(c) Croup	YES ☐	NO ☐	Age _____
(d) Pneumonia	YES ☐	NO ☐	Age _____
(e) Hay Fever	YES ☐	NO ☐	Age _____
(f) Eczema	YES ☐	NO ☐	Age _____
(g) Other (specify) _____			Age _____

(52) Has a doctor ever said that any member of your family (mother, father, brother(s), or sister(s)) has ever had any of the following?

(a) Asthma	YES ☐	NO ☐
(b) Bronchitis	YES ☐	NO ☐
(c) Emphysema	YES ☐	NO ☐
(d) Pneumonia	YES ☐	NO ☐
(e) Hay Fever	YES ☐	NO ☐
(f) Eczema	YES ☐	NO ☐
(g) Other (specify) _____		

(53) Has a doctor ever told you that you are allergic to any of the following, and if you answer YES, at what age were you when you were told?

(a) Dust	YES ☐	NO ☐	Age _____
(b) Pollen	YES ☐	NO ☐	Age _____
(c) Animals or Pets	YES ☐	NO ☐	Age _____
(d) Grasses	YES ☐	NO ☐	Age _____
(e) Molds	YES ☐	NO ☐	Age _____
(f) Tobacco Smoke	YES ☐	NO ☐	Age _____
(g) Air Pollution	YES ☐	NO ☐	Age _____
(h) Insect Bites	YES ☐	NO ☐	Age _____
(i) Food(s)	YES ☐	NO ☐	Age _____
(j) Medication(s)	YES ☐	NO ☐	Age _____
(k) Other (specify) _____			Age _____

I.D. Number _____

(54) Has a doctor ever said that any member of your family (mother, father, brother(s), or sister(s)) is allergic to any of the following?:

(a) Dust	YES □	NO □
(b) Pollen	YES □	NO □
(c) Animals or Pets	YES □	NO □
(d) Grasses	YES □	NO □
(e) Molds	YES □	NO □
(f) Tobacco Smoke	YES □	NO □
(g) Air Pollution	YES □	NO □
(h) Insect Bites	YES □	NO □
(i) Food(s)	YES □	NO □
(j) Medication(s)	YES □	NO □
(k) Other (specify) _____		

(55) Are you sensitive to things that come into contact with your skin?

(a) Underwrap	YES □	NO □
(b) Tape	YES □	NO □
(c) Sweat Bands	YES □	NO □
(d) Deodorants	YES □	NO □
(e) Cologne, Perfume, etc.	YES □	NO □
(f) Other (specify) _____		

(56) Have you ever smoked cigarettes (answer YES only if you have smoked more than 20 cigarettes in your lifetime)? YES □ NO □

If you answered YES to (56), at what age did you start smoking? Age _____

If you answered YES to (56), what is the average number of cigarettes you smoke/smoked each day? Number _____

(57) If you answered YES to (56), do you still smoke? YES □ NO □

If you answered NO to (57), at what age did you quit smoking? Age _____

I.D. Number _____

(58) Do you live with anyone who smokes (cigarettes, cigars, pipe, etc.) YES ☐ NO ☐

If you answered YES to (58), is that person your:

(a) Mother	YES ☐	NO ☐
(b) Father	YES ☐	NO ☐
(c) Brother(s)	YES ☐	NO ☐
(d) Sister(s)	YES ☐	NO ☐

(e) Other (please specify) _____

(59) Are you currently taking any prescription medication? YES ☐ NO ☐

If you answered YES to (59), list the medications that you are currently taking.

_____
_____
_____
_____
_____
_____
_____
_____

(60) Do you ever smell a strong chemical odor in the swimming pool when you exercise? YES ☐ NO ☐

If you answered YES to (60), do you usually have any of the following symptoms when you smell a strong chemical odor in the swimming pool?

(a) Coughing	YES ☐	NO ☐
(b) Chest Congestion	YES ☐	NO ☐
(c) Sneezing	YES ☐	NO ☐
(d) Wheezing	YES ☐	NO ☐
(e) Chest Tightness	YES ☐	NO ☐
(f) Difficulty Breathing	YES ☐	NO ☐
(g) "Raspy" or "Ticklish" Throat	YES ☐	NO ☐
(h) Itchy, watery, or puffy eyes	YES ☐	NO ☐
(i) Headaches	YES ☐	NO ☐
(j) Nausea	YES ☐	NO ☐

(k) Other (specify) _____

If you answered YES to (60), has this strong chemical odor ever prevented you from continuing to exercise? YES ☐ NO ☐

I.D. Number _____

APPENDIX B

Tables for Calculating the Cumulative Dose of Methacholine

Table 24: Calculation of the cumulative dose of methacholine for subjects with asthma or symptoms suggestive of asthma while exercising. These values were used to calculate the linear slope of the dose response curve for each of the subjects.

Concentration (mg/mL)	Nebulizer Output (mL/min)	Time (min)	Dose (mg)	Cumulative Dose (mg)
Saline	0.13	2	0	0
0.25	0.13	2	0.065	0.065
0.50	0.13	2	0.130	0.195
1.00	0.13	2	0.260	0.455
2.00	0.13	2	0.520	0.975
4.00	0.13	2	1.040	2.015
8.00	0.13	2	2.080	4.095
16.00	0.13	2	4.160	8.255

Table 25: Calculation of the cumulative dose of methacholine for subjects with no clinical history of asthma or symptoms suggestive of asthma while exercising. These values were used to calculate the linear slope of the dose response curve for each of the subjects.

Concentration (mg/mL)	Nebulizer Output (mL/min)	Time (min)	Dose (mg)	Cumulative Dose (mg)
Saline	0.13	2	0	0
1.00	0.13	2	0.260	0.260
2.00	0.13	2	0.520	0.780
4.00	0.13	2	1.040	1.820
8.00	0.13	2	2.080	3.900
16.00	0.13	2	4.160	8.060