

RELATIONSHIP BETWEEN BREASTFEEDING AND THE DEVELOPMENT OF
ASTHMA: A REVIEW OF THE LITERATURE

A RESEARCH PAPER

SUBMITTED TO THE GRADUATE SCHOOL
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE MASTER OF ARTS
FAMILY AND CONSUMER SCIENCES: NUTRITION OPTION

BY

JESSICA J. JOHNSON RD, LDN

BALL STATE UNIVERSITY

MUNCIE, INDIANA

May 2012

ABSTRACT

TITLE: Relationship between Breastfeeding and the Development of Asthma: A Review of the Literature

STUDENT: Jessica J. Johnson

DEGREE: Master of Arts

COLLEGE: Applied Sciences and Technology

DATE: May 2012

PAGES: 74

Asthma is one of the major common diseases seen in children of all ages. Past research has noted that breastfeeding has a protective effect against the development of asthma, although the results remain conflicted. The purpose of this research paper was to conduct an extensive literature review to determine if sufficient evidence exists to identify a protective effect of breastfeeding on the incidence of asthma in children. Fourteen studies were reviewed to determine if current research literature solidifies a relationship between breastfeeding and asthma and/or wheeze. Nine of the 14 studies (64%) showed a protective effect of breastfeeding on asthma, 1 (11%) found that breastfeeding increased the risk for developing asthma in the absence of family history, and 3 (20%) noted both protective and non-protective effects, and one found no effect. Six (43%) demonstrated that the protective effect was influenced positively (n=3) or negatively (n=3) when a family history of asthma was present. Overall, more studies demonstrated a protective effect of breastfeeding, with the impact varying by family history. Results continued to be conflicted as evidenced by the current literature review.

ACKNOWLEDGEMENTS

I would like to extend a sincere “thank you” to Dr. Carol Friesen for supporting me throughout the completion of this paper. I am extremely grateful that she chose to work with me and I appreciate her knowledge and expertise in the field of nutrition and research. I’ve been able to learn a lot from this experience and it would not have been possible without her guidance.

Secondly, I would like to thank the Ball State University Department of Family and Consumer Sciences professors for their dedication to the department. Completing my graduate degree would not have been possible without their support and leadership. They have helped shaped me into an educated professional and for that I am thankful.

TABLE OF CONTENTS

	PAGE
ACKNOWLEDGEMENTS.....	ii
TABLE OF CONTENTS.....	iii
CHAPTER 1: INTRODUCTION.....	1
Problem Statement.....	3
Purpose Statement.....	3
Research Hypotheses.....	4
Rationale.....	4
Assumptions.....	5
Definitions.....	5
Summary.....	7
CHAPTER 3: METHODOLOGY.....	9
Methods.....	9
Instruments.....	10
Data Analysis.....	11
Summary.....	11
CHAPTER 3: REVIEW OF LITERATURE.....	13
Introduction.....	13
Asthma.....	13
Prevalence of Asthma.....	13
Causes of Asthma.....	15
Protective Effects.....	15

	PAGE
Diagnosis.....	16
Treatment of Asthma	17
Summary.....	18
Breastfeeding	18
Benefits of Breastfeeding.....	19
Goals.....	20
Incidence... ..	20
Composition.....	21
Motivating Factors... ..	23
Breastfeeding & Working Women... ..	23
Breast Milk & Immune System... ..	25
Relationship between Breastfeeding and Asthma.....	26
Summary.....	46
CHAPTER 4: RESULTS/DISCUSSION	48
CHAPTER 5: CONCLUSION AND RECOMMENDATIONS	56
REFERENCES	69

CHAPTER 1

INTRODUCTION

Asthma is the leading cause of chronic illness in children and is a major cause of childhood disability (Akinbami & Schoendorf, 2002). According to the Global Initiative for Asthma (GINA) in their report “Global Strategy for Asthma Management and Prevention, asthma is defined as “a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role (GINA, 2006). The chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, making it difficult to breathe. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment (Bateman et al., 2008).

During 2006–2008, an estimated 7.8 percent of the U.S. population had asthma. Current asthma prevalence is higher among children (9.3%) than among adults (7.3%) (Moorman, Zahran, Truman, & Molla, 2011). Asthma prevalence was higher among low-income children, with 21 percent of multi-racial children being affected compared to 10.1 percent of low-income non-Hispanic white children (Moorman et al., 2011).

According to the American Dietetic Association's Position Paper on Breastfeeding (James & Lessen, 2009), exclusive breastfeeding provides optimal nutrition and health protection for the first 6 months of life. Breastfeeding is a strategy for improving infant and child morbidity and mortality, while helping to control healthcare costs. Factors such as socioeconomic status and geographic location can influence initiation, duration, and exclusivity of breastfeeding (James & Lessen, 2009). The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) recommend that every infant should be exclusively breastfed for the first 6 months of life, with breastfeeding continuing up to the age of 2 years (James & Lessen, 2009).

Human milk is specifically designed to meet the needs of infants. There are two types of human milk: colostrum, which is present in the first few days postpartum and mature milk (James & Lessen, 2009). Human milk provides adequate amounts of carbohydrates, essential fatty acids, saturated fatty acids, medium-chain triglycerides and cholesterol. Human milk contains over 100 milk oligosaccharides that are thought to have a protective effect against respiratory diseases. However, studies on the effects of breastfeeding on the development of asthma aren't as clear. Some studies have shown a moderate protective effect, while others don't. Children without a strong family history of asthma who are breastfed at least three months have been shown to have a 27 percent reduction in the risk for asthma. When a family history of asthma is present, a 40 percent chance reduction has been shown when breastfed at least 3 months (James & Lessen, 2009).

Healthcare experts give many reasons why the rates for asthma are increasing. One factor thought to play a role in the development of asthma is the reduction in the

number of exclusively breastfed infants. In 2006, 74 percent of infants were “ever breastfed” (HP2020, 2010). At six months, 43.5 percent of infants were still being breastfed, below the HP 2010 goal of 50 percent. At one year, 22.7 percent of infants were still being breastfed, below the 2010 goal of 25 percent. Only 33.6 percent of infants born in 2006 were exclusively breastfed through 3 months and only 14.1 percent were breastfed exclusively breastfed through 6 months. The decreased rate of continued exclusive breastfeeding prevents important immune building substances from being passed from the mother to the infants developing immune system.

In an effort to increase breastfeeding rates, Healthy People 2020 (United States Department of Health and Human Services [HHS], Healthy People 2020, 2011) has established the following goal rates: “ever breastfeeding” 81.9 percent, 3 month exclusive breastfeeding 46 percent, and 6 month exclusive breastfeeding 25.5 percent. A significant public health effort will have to be made if these goals are to be achieved.

Problem

Whether breastfeeding plays a role in the development of asthma remains unclear. Compounding the interaction is the impact of the duration and frequency of breastfeeding on the incidence of asthma. A thorough examination of the literature to explore these variables is warranted.

Purpose

The purpose of this research paper is to conduct an extensive literature review to determine if sufficient evidence exists to identify a protective effect of breastfeeding on the incidence of asthma in children five years of age or younger.

Research Questions

The research questions examined in this paper include:

1. Is there sufficient evidence in the scientific literature to clearly indicate a relationship between breastfeeding and the incidence of asthma in children five years of age and younger?
2. Is there sufficient evidence in the scientific literature to clearly indicate a relationship between the incidence of asthma and the duration and/or frequency of breastfeeding?

Rationale

Asthma is the leading cause of chronic illness in children and is a major cause of childhood disability (Akinbami & Schoendorf, 2002). Past research has noted there is a link between breastfeeding and development of asthma, however results remain controversial. Some studies support the presumption of a decreased risk of asthma due to breastfeeding while others have not been able to prove a protective effect (Pohlabein, Muhlenbruch, Jacobs, & Bohmann, 2010). Despite no proven results, breastfeeding is noted to be beneficial to a mother and an infant in many other ways

As with any disease, managing asthma and allergies can be financially taxing, not to mention a burden on a child and family. These factors greatly influence quality of life and billions of dollars continue to be spent on the disease each year. With the prevalence rate increasing the cost annually is sure to rise too.

With all of these factors influencing research it is necessary to continue to look at the link between breastfeeding and an infant's developing immune system. If future

research proves that there is a positive impact from breastfeeding on the infants developing immune system then many of these problems may be somewhat avoided and/or less severe.

Health care workers can gain insight on the relationship between duration of breastfeeding and its influence on the development of asthma. The information presented in this study may be useful to professional health educators, physicians, dietitians, and nurses to make recommendations and improve length of breastfeeding. This study could also reveal where gaps in research are so that future research needs can be recognized.

Assumptions

The researcher makes the following assumptions in the implementation of the study and in the interpretation of the data:

1. The literature analyzed for this research paper was presented in an unbiased manner.
2. The literature was current, peer reviewed, comprehensive, and accurate.
3. The researcher correctly interpreted the content of the peer-reviewed articles examined in this paper.

Definitions

For the purpose of this study, the following definitions will be used:

1. Cytokines: A small protein released by cells that has a specific effect on the interactions between cells, on communications between cells or on the behavior of cell (Snijders, Damoiseaux, Penders, Kummeling, Stella, et al., 2006)

2. Exclusive breastfeeding: when the infant only receives breast milk without any additional food or drink (World Health Organization [WHO], 2009).
3. Incidence: measurement of rate of occurrence of new cases of a disease or condition (Roe & Doll 1995).
4. Prevalence: a measurement of how much disease or condition there is in a population at a particular point in time (Roe & Doll, 1995).
5. Neutrophil granulocytes: most abundant type of leukocytes. They make up 50-70 percent of all white blood cells (Segal, 2005).
6. Natural Killer cells: large lymphocyte cells that are part of the natural immune system (Caligiuri, 2008).
7. Atopic disease: eczema, asthma, and rhinoconjunctivitis. Atopic disease occurs when the immune system is dysregulated, resulting in inflammation (Gold & Kemp, 2005).
8. FVC (forced vital capacity)/spirometry: the amount of air you can exhale with force after you inhale as deeply as possible (WebMD, 2011).
9. Lactoferrin: Lactoferrin is a non-heme iron binding glycoprotein produced during lactation and by epithelial cells at mucosal surfaces. The protein is a prominent component of the first line of mammalian host defense and its expression is upregulated in response to inflammatory stimuli (Adlerova, Bartoskova & Faldyna, 2008).
10. TGF- β 1: performs cell functions. It controls cell growth, cell division, cell differentiation, and cell death (Rigotti, et al., 2006).

11. IL-10: Small protein that regulates the immune system. Two major functions include: inhibition of cytokine production by macrophages and inhibition of cytokine production by macrophages and inhibition of the accessory function of macrophages during t-cell activation. This plays an anti-inflammatory role in the immune system (Rigotti, et al., 2006).
12. Colostrum: Colostrum is the first stage of breast milk and 2 to 4 days after birth. Colostrum is high in protein, fat-soluble vitamins, minerals, and immunoglobins (La Leche League, 2006).
13. Mature milk: final milk produced. Ninety percent is water to maintain hydration and the other 10% is composed of CHOs, proteins, and fats. There are two types of mature milk: foremilk and hind milk (American Pregnancy Association, 2004).

Summary

Past research has noted a potential link between breastfeeding and development of asthma; a compilation of current published evidence will help examine the adequacy of the evidence that links these two concepts. If the body of evidence suggests there is a positive impact from breastfeeding on the incidence of asthma, this information can be used by public health professionals as one more reason to encourage new mothers to breastfeed.

CHAPTER 2

METHODOLOGY

The purpose of this research paper is to conduct an extensive literature review to determine if sufficient evidence exists to identify a protective effect of breastfeeding on the incidence of asthma in children five years of age or younger. This chapter will describe the methods used to identify the articles included in the comprehensive literature review.

Methods

The data collection for this research paper was done by review of journals identified through four online medical databases (e.g., Cinahl, Academic Search Premier, PubMed, and the American Dietetic Association (ADA) Evidence Analysis Library). Studies were selected from years 2000-2011. Search criteria include combination of the following keywords: breastfeeding, asthma, and infant immunity. The aim of this review was to conduct a thorough examination of the scientific literature to determine if a relationship between breastfeeding and asthma could be established and to identify gaps that need to be further addressed in future research endeavors. Table 1 displays the number of articles found when searching using the key terms “breastfeeding,” “asthma,”

and “infant immunity” in various combinations which resulted in the 14 studies examined in this research paper.

Table 1. Number of Cited Articles using various Key Word Combinations.

TERM SEARCHED	ARTICLES: Cinahl	ARTICLES: PubMed	ARTICLES: Ac. Search Premier
Asthma	18,724	123,641	34,802
Breastfeeding	5,608	31,300	7,243
Infant Immunity	12	12,635	122
Asthma, Breastfeeding	56	411	185
Asthma, Infant Immunity	12	116	1
Asthma, Breastfeeding, Infant Immunity	0	14	0

Instruments

To aid in the analysis and comparison of the studies, the researcher developed a chart to review the information found in the selected articles used in the paper (Appendix A). The chart consisted of article details: author, year, database, design, subjects, and what relationship, if any, existed between asthma and breastfeeding. Key points from the chart will be included in the literature review in Chapter 3 of this research paper.

Data Analysis

No formal statistical analyses were used to compose this paper. An overall summary of studies used will be stated in the form of percentages (i.e., 5 out of 10 sources found significant results of 50 percent of studies reviewed).

Summary

The purpose of this research paper was to analyze current research to find trends in breastfeeding, breastfeeding practices, and development of the infant immune system by reviewing the literature published in 2000 through 2011. Data collection was organized in a table that provided key points from each articles' results that indicated whether or not there was a protective effect of breastfeeding on the incidence of asthma. The goals of this research paper were to identify the relationship between breastfeeding and asthma, to find trends that could be used to make recommendations in practice, and to illustrate current gaps in research.

CHAPTER 3

REVIEW OF LITERATURE

The purpose of this research paper is to conduct an extensive literature review to determine if sufficient evidence exists to identify a protective effect of breastfeeding on the incidence of asthma in children five years of age or younger. This chapter will present a review of the literature that describes asthma, breastfeeding, and the relationship, if any, between asthma and breastfeeding.

Asthma

Asthma is defined as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role (Bateman et al., 2008). The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment. The constriction of the airway makes it difficult to breathe.

Prevalance of Asthma

Asthma is the leading cause of chronic illness in children and is a major cause of childhood disability (Akinbami & Schoendorf, 2002). In 2009, the prevalence of asthma was at 8.2 percent with 7.1 million children affected (Akinbami, Moorman, & Liu, 2011). The prevalence of asthma is higher among children (9.3 percent) than among adults (7.3 percent) (Moorman, Zahran, Truman, & Molla, 2011). Among children, the prevalence of asthma is higher among males (9.3%) than females (7.8%), higher among the poor (11.7%) compared to the near poor (9.9%) and the non-poor (8.2%), and higher among Hispanics (18.4%), Multiracial (13.6%), and black, non-Hispanics (14.6%) than white, non-Hispanics (8.2%) (Moorman et al., 2011). Pediatric cases of undiagnosed asthma range from 3 percent to 20 percent (McCloud & Papoutsakis, 2011).

Although the reasons for the disparities in the prevalence of asthma are unclear, observed differences in asthma prevalence among certain demographic and socioeconomic groups (e.g., females, children, non-Hispanic blacks, Puerto Rican Hispanics, and the poor) might be indicators for underlying differences in genetic factors, higher levels of exposure to environmental irritants (e.g., tobacco smoke or air pollutants), and environmental allergens (e.g., house dust mites, cockroach particles, cat and dog dander, and mold) (Moorman et al., 2011).

The prevalence of asthma is increasing in most countries, especially within the younger population. Factors that have been speculated to influence the risk of developing asthma include: diet, urbanization (air pollution), exposure to both indoor/outdoor allergens, tobacco smoke exposure, respiratory infections, receipt of an antibiotic during

the first two years of life, small birth size, attendance at day care, having few siblings, and lower socioeconomic status (McCloud & Papoutsakis, 2011).

Akinbami & Schoendorf (2002) have referred to the term “diagnostic transfer” as another possible explanation for the increasing prevalence of asthma. Diagnostic transfer is a term in which other respiratory issues are labeled as asthma rather than what they actually are. The effect of diagnostic transfer on the prevalence of asthma has not been definitively established.

Causes of Asthma

Environmental exposures have been shown to stimulate interactions that accelerate the development of airway inflammation and airway hyperresponsiveness among those at higher risk for asthma (genetically predisposed) (McCloud & Papoutsakis, 2011). Emerging research has concluded that developmental aspects, including maturation of the immune response during the first years of life, are important factors that modify the risk of asthma in a person that is more susceptible genetically (Bateman et al., 2008).

Protective Effects of Asthma

The evidence supporting the protective effect of breastfeeding on prevalence of asthma remains inconclusive. Breastfeeding allows important immune building substances to be passed from the mother to the infants developing immune system. There are two types of human milk: colostrum, which is present in the first few days postpartum and mature milk (ADA, 2009). Human milk provides adequate amounts of carbohydrates, essential fatty acids, saturated fatty acids, medium-chain triglycerides and cholesterol.

There are also over 100 milk oligosaccharides that are thought to have a protective effect against respiratory diseases (James & Lessen, 2009).

Multiple studies have looked at the connection between specific nutrients (those affecting immune status) and development of asthma. A meta analysis supports a protective role of Vitamins A and C in decreasing asthma risk. Fish oil or fish consumption has not been consistently shown to have a protective effect, while an adequate intake of Vitamin D during pregnancy has been associated with having a protective effect against asthma and wheezing outcomes in children up to five years of age (McCloud & Papoutsakis, 2011).

Diagnosis of Asthma

Asthma is usually diagnosed based on the presence of characteristic symptoms, including wheezing, coughing, chest tightness. Methods used to determine an asthma diagnosis are a detailed medical history and a physical examination of the respiratory tract, chest, and skin (McCloud & Papoutsakis, 2011). Patients' lung function can be measured to check for the degree of airway constriction. However, some of these types of tests can only be performed on patients that are greater than five years old. One such test is called forced expiratory volume in one second (FEV_1). This test measures the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation (Bateman et al., 2008).

Another important diagnostic tool is a peak expiratory flow (PEF), which measures the maximum speed of expiration testing the airflow of the bronchi. Measurements can be made using a hand held peak flow meter. Measurements from the

FEV₁ and PEF are not interchangeable as the values obtained from each tool vary and the range of predicted values is too wide (Bateman et al., 2008).

Diagnosing asthma can be challenging, especially when children are involved. Diagnosing asthma in children is based largely on clinical judgement and a thorough assessment of symptoms and physical findings (Bateman et al., 2008). Since wheezing can be an indicator of multiple illnesses it's important to rule out other causes. The symptoms highly suggestive of a diagnosis of asthma are frequent episodes of wheezing, activity-induced cough or wheeze, coughing at night during a period without infections, and symptoms that persist after the age of three (McCloud & Papoutsakis, 2011).

When diagnosing asthma in children, a detailed nutrition assessment can be a beneficial at baseline and over time as treatment regimens are trialed. Nutrition assessments are useful in monitoring drug nutrient interactions that may occur over time. Medication changes can influence nutritional status. Asthma related medications can interfere with normal absorption of protein, calcium, Vitamin D, potassium, sodium, Vitamin A and Vitamin C (McCloud & Papoutsakis, 2011). Obtaining weight, height, and BMI and plotting it on the Centers for Disease Control (CDC) growth charts can provide evidence of steroid-induced weight gain and its impact on growth delays. An assessment of bone mineral density can monitor for corticosteroid induced osteoporosis in children receiving the therapy (McCloud & Papoutsakis, 2011).

Treatment of Asthma

With all the advances in medical therapy, many treatments are available to help control asthma so that a normal life may be led. Asthma treatments differ slightly from

adults to children; treatments are also very individualized. Inhaled therapy is generally preferred as a treatment for children. Some considerations when choosing an inhaler are cost, ease of use, and efficacy of drug delivery. A spacer is generally preferred with children to ensure the drug gets into the lungs (Bateman et al., 2008). Asthma medications can be classified as controller medications or short acting rapid medications. The medications include: inhaled and systemic glucocorticosteroids, leukotriene modifiers, long acting inhaled B₂-agonists, theophylline, and cromones (Bateman et al., 2008; McCloud & Papoutsakis, 2011). Controller medications are used over a longer period of time to achieve control of asthma symptoms. Rapid acting oral Beta2-agonists are used to get immediate relief from asthma symptoms.

Asthma Summary

Asthma can cause a great burden on a child and their family. Asthma is a major cause of childhood disability that can lead to premature death, however morbidity can be decreased if patients and families are educated. Early diagnosis of asthma and implementing appropriate therapy can improve a patients' quality of life. Treating asthma can be very costly and access to quality health care is a key component to managing the disease (Akinbami & Schoendorf, 2002). Scientific advances and modern technology have improved our understanding and our ability to manage this chronic disease (Bateman et al., 2008).

Breastfeeding

Breastfeeding is an unequalled way of providing ideal food for the healthy growth and development of infants; it is also an integral part of the reproductive process with

important implications for the health of mothers (World Health Organization [WHO], 2011). Breast milk is the natural first food for babies; it provides all the energy and nutrients that the infant needs for the first months of life, and it continues to provide up to half or more of a child's nutritional needs during the second half of the first year, and up to one-third during the second year of life (WHO, 2011).

Benefits of Breastfeeding

Breast milk promotes sensory and cognitive development, and protects the infant against infectious and chronic diseases. Exclusive breastfeeding is associated with a plethora of health impacts to include: 1) reduction in infant mortality from common childhood illnesses such as diarrhea or pneumonia; 2) decreased likelihood of contracting middle ear infections, cold, and flu bugs; 3) reduced risk of childhood onset diabetes; 4) decreased risk of asthma and eczema; 5) decreased dental problems; 6) decreased risk of obesity later in life; 7) lowered risk of Sudden Infant Death Syndrome (SIDS); and 8) increased intelligence (WHO, 2011), (James & Lessen, 2009), (Ruowei, Fein, Chen & Grummer-Strawn, 2008). In addition, breastfeeding contributes to the health and well-being of mothers by: 1) helping to space children, 2) reducing the risk of ovarian cancer and breast cancer, and 3) increasing family and national resources as it is a secure way of feeding that is safe for the environment (WHO, 2011; James & Lessen, 2009).

The American Dietetic Association recommends exclusive breastfeeding for the first six months of life to provide optimal nutrition and health protection for the beginning six months of life, (American Dietetic Association, [ADA], 2009).

Breastfeeding offers health benefits into and after toddlerhood. Not being breastfed is

associated with an increased risk of infectious morbidity including: risk of childhood obesity, type 1 and type 2 diabetes, infant allergies and asthma, respiratory illness, sudden infant death syndrome, and hypertension, among others.

Breastfeeding Goals

Healthy People 2020 (USDHHS, Healthy People 2020, 2011) is an ambitious ten year agenda for improving the health of the nation. Healthy People 2020 strives to identify nationwide health improvement priorities; increase public awareness and understanding of the determinants of health, disease, and disability and the opportunities for progress; provide measurable objectives and goals that are applicable at the national, State, and local levels; engage multiple sectors to take actions to strengthen policies and improve practices that are driven by the best available evidence and knowledge; and identify critical research, evaluation, and data collection needs (USDHHS, 2011).

HP2020 objective MICH-21.1 aims to have a least 81.9 percent of mothers initiate breastfeeding at birth; MICH objective 21.2 aims to have at least 60.6 percent of mothers continuing to breastfeed their child for six months; and MICH objective 21.3 aims to have at least 34.1 percent of mothers who continue to breastfeed their child until they are at least one year of age. HP2020 also established goals for exclusive breastfeeding, with the aim to have 46.2 percent of infants exclusively breastfed at 3 months (MICH 21.4) and 25.5 percent exclusively at 6 months (MICH 21.5) (USDHHS, 2011).

Incidence of Breastfeeding

Of all infants born in 2006, data from the National Immunization Survey (NIS), CDC, NCIRD, and NCHS indicated 74.0 percent were “ever breastfed,” below the goal

of 81.9 percent established by HP 2010. At six months, the rate of breastfed infants had dropped to 43.5 percent, compared to the goal of 60.6 percent established by HP2010. At one year of age, only 22.7 percent of infants born in 2006 were breastfed, compared to the goal of 34.1 percent (USDHHS, 2011).

Including the concept of “exclusively” breastfeeding, only 33.6 percent of infants born in 2006 were breastfed exclusively through 3 months as reported in 2007–09, far below the goal of 46.2 percent; only 14.1 percent of infants born in 2006 were breastfed exclusively through 6 months as reported in 2007–09, again far below the goal of 25.5 percent. Meeting the *Healthy People* objectives could lead to a significant decrease in health care costs associated with these increased infant morbidity risks. (Position Statement: American Dietetic Association, 2009).

Composition of Breast Milk

It is a well-known fact that an infants’ immune system functions very differently than an adults. During the prenatal stage, little antigen exposure occurs; naturally the postnatal stage is a time of rapid development as the infant is in contact with microbial agents (Fields, 2005). Breast milk contains a variety of antimicrobial substances, which provide protection to the immature infant immune system as well as to the mothers’ mammary gland. An infants’ resistance to infection depends on the protective factors found in human milk as well as the infants’ ability to develop immunity (Fields, 2005). There are many components of breast milk that enable an infant to do so.

Macrophages derived from breast milk affect infant T and B cell function as they express activation markers, show phagocytic activity, and secrete immune-regulatory

factors. Neutrophils are another component, however little is known on their role. Research suggests that they play a role in maternal protection (Fields, 2005). Lymphocytes are a major component, mostly T-cells. It is thought that these cells T cells (maternal origin) make up for the immature function of neonatal T cells. Activated antigen mature lymphocytes may compensate for the low antigen presenting capacity of macrophages (Fields, 2005). Some research suggests that a decrease in CD4 and CD* cells and an increase in natural killer cells (NK) is seen after exposure to maternal milk. Human milk also contains a large amount of cytokines, including TGF, IL-4, IL-5, IL-13, etc. Cytokines generally influence the maturation and development of infant immune cells, more specifically producing cells that mature the infants developing intestinal system. Many hormones (cortisol, progesterone, thyroid hormones, insulin, leptin, etc), growth factors, polyunsaturated fatty acids, and partially digested milk peptides have been found in human milk (Fields, 2005). These components have been shown to influence the immune development in infants. Breast milk also contains nucleotides, which promote lymphocyte proliferation, NK activity, and macrophage activity (Fields, 2005).

Human milk is specifically tailored to meet the nutrition needs of human infants (James & Lessen, 2009). The nutrients within the milk are well balanced, highly bioavailable, and easily digested. The contents in the milk change as a newborn grows into an infant. The milk contains proteins, carbohydrates, minerals, essential fatty acids, saturated fatty acids, medium chain-triglycerides, long-chain poly-unsaturated fatty acids, and cholesterol (James & Lesson, 2009). The protein is mostly alpha-lactalbumin (whey protein) that is easily digestible and provides a limited amount of nitrogen. This is

important, as infants' kidneys are still immature. Breast milk also contains over 100 milk oligosaccharides (carbohydrates) that remain undigested as they pass through the infants' intestinal system. It is suspected that these oligosaccharides intervene with the pathogens binding to host cell receptors, helping to reduce infection. Minerals found in breast milk include: sodium, calcium, phosphorous, magnesium, and iron. These substances are mostly protein bound so that availability is enhanced (James & Lesson, 2009). Dietary n-6 and n-3 polyunsaturated fatty acids (PUFAs) have been suggested to participate in immune development. It is noted that PUFAs have the ability to alter production of cytokines and eicosanoids, both of which act with the body's immune system to regulate the body's response to disease and infection (Fields, 2005).

Motivating Factors to Breastfeed

Despite the evidence indicating that breastfeeding is better than formula feeding, some women choose to forgo breastfeeding or just initiate it for short period of time. Some women supplement with formula feeding while breastfeeding. Multiple factors may play a part in the mothers' decision including: lack of support in the hospital setting, lack of knowledge, lack of family support, and personal beliefs (James & Fields, 2009). Reasons cited by women who stop breastfeeding after initiation include: uncertainty of producing enough milk, nipple problems, embarrassment, going back to work, and mother/infant not liking the feeding (Ahluwalia et al., 2005).

Breastfeeding and Working Women

Healthy People 2020 objective MCH22 recommends the proportion of employers that have worksite lactation support programs should increase from the current 25 percent

of employers who provide an on-site lactation/mother's room to 38 percent (USDHHS, 2011). Currently, the only law related to maternity leave in the United States is the Family Medical Leave Act, which gives 12 weeks of unpaid leave, continued insurance and a guarantee of your job (James & Lessen, 2009). However, the federal law in the United States does not require additional paid maternity leave. Five states (i.e., California, Hawaii, New Jersey, New York, and Rhode Island) have selected to go beyond FMLA and offer temporary disability insurance. The disability insurance can be funded by the employee, employer, or both (James & Lessen, 2009). Legislation providing rights for breastfeeding mothers in public and in the workplace has been enacted in many states. The International Lactation Consultant Association recommends strategies to protect breastfeeding in the workplace including: providing an environment where mother and infant can be together (work from home or infant to workplace) and adequate breaks and workplace facilities specifically dedicated to expressing milk at work (James & Lessen, 2009).

Chuang et al., (2009) examined the relationship between continuing breastfeeding when mothers returned to work. Approximately 20,000 postpartum women completed a home interview at 6 and 18 months. The authors reported the initial rate of breastfeeding was 83 percent. Postpartum women who returned to work up to one month after delivering had the lowest initiation of breastfeeding at 77 percent. Overall, at six months, 25 percent of women were still breastfeeding and at 12 months, only 12 percent of women were still breastfeeding. Results indicated women with maternal leave of less than 6 months stopped breastfeeding earlier than those that did not return to work after 6

months. Overall, the authors reported early maternal return to work (within 6 months) was a barrier to the initiation and continuation of breastfeeding.

Breast Milk and the Immune System

Breast milk contains natural antibodies and lymphocytes that help protect against infections (Rigotti et al., 2006). These substances all act to boost and stimulate the development of the immature immune system and neonatal organ systems. It has been hypothesized that these substances in breast milk might provide a protective effect against many immunological diseases, including asthma. It has also been hypothesized that when a mother is exposed to specific antigens that these can be passed to an infant, therefore exposing the infant to those antigens, providing the infant with a protective effect.

Oddy et al., (2006) examined the physiological pathway associated with the transfer of antigens through breast milk of mice. Results indicated airborne allergens could be transferred from mother to newborn through breast milk. This exposure could induce antigen specific tolerance in the offspring providing protection against allergic airway disease. The authors concluded that the transfer of an antigen and TGF to the infant during breastfeeding provides the protective effect.

Breastfed infants are noted to have fewer infections than those children who are formula fed because components in human milk give a high bioavailability of nutrients as well as influence the maturation of natural and adaptive immunity (Andersson et al., 2009). These authors examined immune cell composition in formula fed vs. breastfeed infants. Immune cells are thought to provide the protective effect in the development of

asthma. The study randomized participants into an exclusive breastfeeding group, a control group, and two groups fed two different formulas with various protein concentrations. Results indicated that the white blood cell (WBC) –especially the lymphocytes and the neutrophil granulocytes – in exclusively breastfed infants (EBF) increased marginally over time. The significant increase in these types of cell was not seen in formula fed infants over the six months. However, the proportion of T cells in formula fed infants increased significantly with age and was significantly higher than in breastfed infants at four and six months. In contrast, natural killer cells decreased significantly in the formula groups and were significantly lower than in the breastfed group at four and six months. The authors hypothesized that lactoferrin, known to enhance NK and T cell proliferation and function, and IL-2 and immune modulating factors could provide the breastfed infant with important signals during those important stages of T cell development (Andersson et al., 2009). The authors noted, however, that it cannot be concluded if these findings are clinically significant.

Relationship between Breastfeeding and Asthma

It has been speculated for quite some time that a positive relationship between breastfeeding and risk of developing asthma and or wheeze exists. It has yet to be proven that a protective effect exists. In fact, some studies conclude that breastfeeding can actually increase the risk of asthma. A thorough review of literature is examined in the current section.

Ogbuanu et al., (2009) conducted a longitudinal study in which participants were recruited between January 1989 and February 1990. At birth, weight was measured and

extensive questionnaires were collected on asthma and family history of allergy, as well as smoking habits. Breastfeeding practices and duration were assessed at birth and all follow up visits 1 and 2 years. At 1, 2, 4, and 10 years, the original questionnaire information was updated, a physical exam was completed, and signs and symptoms of asthma and allergic diseases were recorded. Skin prick test were done at 4 and 10 years. At 10 years lung function was performed on all consenting children. Breastfeeding was categorized into not breastfed, breastfed for less than 2 months, breastfed for more than 2, but less than four, and breastfed for at least four months. Results indicated that, compared with children who were not breastfed, those who were breastfed for at least 4 months had FVC values that were larger than those who were not breastfed. Children who were breastfed for four months or longer had significantly higher PEF compared to those breastfed for less than 4 months who did not show any significant beneficial effects on lung function. When testing to see if lung function varied with maternal history, the authors did not see any significance effect in this cohort of children.

Kull et al., (2010) studied 4089 newborn children from cities in Stockholm County from 1994-1996. Data on family history was collected from parental questionnaires when the children were two months of age. Other questionnaires focusing on diet, parental tobacco smoke, and other variables were given when the child was one, two, four and eight years old. Information on breast-feeding was assessed by a questionnaire at age one. By age eight, all of the children who had completed questionnaires (2370) were invited to a clinical investigation including lung function and blood testing. Lung function was measured with peak expiratory flow. This study defined partial breastfeeding as human milk consumption as well as infant formula or solid food.

This study, did define specific health outcomes. Recurrent wheeze meant the child had three episodes in the last 12 months at 1, 2, 4, or 8 years. At 1 and 2 years asthma was defined as at least 3 episodes of wheeze and signs of bronchial hyper reactivity or 1 combination of wheeze in combination with inhaled corticosteroids. The authors analyzed the length of breastfeeding from participants. The mean duration of EBF was 5.1 months and partial was 3.5 months. Eighty percent of children were EBF for the first 4 months and 5 percent received breast milk and formula from the start. They also analyzed factors associated with shorter breastfeeding. Children exclusively breast-fed for 4 month or more had an overall reduced risk of asthma during the first 8 years of life with similar results for recurrent wheeze compared with children breast-fed less than 4 months. At follow up 1, 2, 4, and 8 years asthma and recurrent wheeze were less prevalent in children who were EBF for 4 months or longer.

Like Ogbuanu et al., (2009), Kull et al., (2010) conducted follow-up surveys. The authors examined trends over time by classifying children with asthma (between 3 months and 8 years) into transient (asthma during 1-4 years, but not later, late onset (after 4 years), and persistent asthma (age 1-4 years and after 4 years). The effect of breastfeeding for 4 months or more was significant for children with transient and persistent asthma, but not late onset asthma. Similar to the findings of Ogbuanu et al., (2009), the effect of breastfeeding did not differ when considering family history. The authors attempted to differentiate between the length of EBF and partial breastfeeding, grouping it into 3 categories (0 to <2 months, 2 to <4 months, and >4 months. For recurrent wheeze, a reduced risk was seen in children breastfed for 2-4 months. For asthma a reduced risk was “suggested” among children EBF for 2 months or more, however

significance was seen at 4 months or more. Similarly to Ogbuanu et al., (2009) Kull et al., (2010) found that children who were EBF for 4 months or more had significantly better lung function at 8 years when measuring with PEF. Similar results were seen with FEV, but they were not significantly significant.

Between 1997 and 2001, Silvers et al., (2009) recruited children representative of New Zealand for the Asthma and Allergy Cohort Study prospective birth cohort. A total of 1011 children were available through beginning of study to 15 months. Soon after birth questionnaires were given about infant feeding; the questionnaire was repeated at 3, 6, and 15 months, which was more frequent than Kull et al., (2010) and Ogbuanu et al., (2009) who assessed feeding practices at birth and 1 year and 1 year only, respectively. Breastfeeding in this study was assessed in two ways: the duration of exclusive breastfeeding (age when infant formula, food, or other liquids were introduced) or “any” breastfeeding (age when breastfeeding was stopped). Additional breastfeeding was also a category (duration of any breastfeeding minus the duration of exclusive breastfeeding). These categories are more vague than the categories used by Kull et al., (2010) and Ogbuanu et al., (2009). Silvers et al., (2009) identified health outcomes via parental report to document a doctor’s diagnosis of asthma, ever wheezing, every used an inhaler, a combination of all three. Current asthma was defined as a doctor’s diagnosis of asthma and if even wheezed or used an inhaler by 15 months. In this study, the median duration of EBF was 1.4 months, compared with 5 months in the study done by Kull et al., (2010). The duration of any breastfeeding was 9 months. Longer duration of exclusive breastfeeding was associated with a significant reduction in the risk of adverse respiratory outcomes at 15 months. After adjustment for confounders, results indicated that for each

month the child was EBF, the risk of doctor-diagnosed asthma was reduced by 20 percent, wheezing by 12 percent, inhaler use by 14 percent, all three categories by 24 percent, and current asthma by 21 percent (Silvers et al., 2009). Similar to the studies above, when considering maternal history of asthma, no significant changes in results were seen. It was associated with outcomes, but not significant.

Pohlabeln et al., (2010) studied the frequency of allergic diseases in 2-year-old children in relationship to parental history of allergy and breastfeeding. Similar to Silvers et al., (2009), this study was conducted with children up to two years of age. Mothers were recruited and initially assessed for family history of allergic disease, lifestyle, and education, similar to the protocol used by Silvers et al., (2009), Kull et al., (2010) and Ogbuanu et al., (2009). Interviews were conducted at 6 months, 12 months, and 2 years with questions of breastfeeding behavior and symptoms of allergic disease. A total of 1685 mothers completed the baseline and 3 follow up interviews. Results indicated that 23 percent of the children had evidence of allergic disease at age two, 70 percent had symptoms of eczema, and one-third had physician-diagnosed asthma. These results were strongly influenced by paternal predispositions. Similar to many other studies, this breastfeeding was associated with social class, with lower class having high numbers of not breastfeeding. This study also noted that depending on the social class, if a family history was known, the breastfeeding duration was likely to increase for > 4 months. (Pohlabeln et al., 2010). When looking at allergic symptoms in children without genetic predisposition (notice this study did not have clearly defined definitions), a higher number of children were found with “allergic” symptoms in the breastfed groups vs the never breastfed. Those without a genetic predisposition who were EBF for >4 months,

showed a significant increase in developing atopy. However, in those with genetic predisposition, the “appearance” of allergic disease was less common in breastfed children. In contrast to other researchers in this field, Pohlabeln et al., (2010) analyzed the results by source of genetic predisposition. Results indicated that individuals whose mother was the only parent with a history of asthma had a “considerably” higher risk for asthma if they were EBF for more than four months than if they were not breastfed. However, if the father had asthma, the child had a ‘significantly’ decreased risk of developing asthma if they were EBF for more than four months. Breastfeeding for less than four months had no influence on asthma risk, even when parental disposition was considered (Pohlabeln et al., 2010). The study noted that results of the parental history influence were based on a very small number of subjects. The authors noted that, in future studies, it may be helpful to differentiate between paternal history of allergic diseases so that breastfeeding duration and other aspects of heredity can be investigated on the development of childhood allergies.

Nagel et al., (2009) conducted a cross sectional study for The International Study of Asthma and Allergy in Childhood (ISAAC) Phase II. Similar to Kull et al., (2010) and Ogbuanu et al., (2009), the authors examined the relationship between breastfeeding and its effect on lung function and bronchial hyper reactivity. Unlike Kull et al., (2010), Pohlabeln et al., (2010), Ogbuanu et al., (2009), and Silvers et al., (2009), Nagel et al., (2009) chose children aged 9-11 as subjects rather than studying children from birth. This large-scale study had 54, 943 participants, ranging from age 8-12 years, from 20 different countries. The parental questionnaire from ISAAC I was used to collect data on allergies and asthma. Parents were asked questions about breastfeeding duration (categorized into

never, breastfed for <6 months or >6 months), which is in contrast to the majority of asthma-breastfeeding studies which have used the four-month breastfeeding time period as their cut point. Parents were also questioned about the exclusiveness of breastfeeding without adding foods or juices (<2 months, 2-4 months, 5-6 months or >6 months). The time spent exclusively breastfeeding was also categorized into <2 months, 2-4 months or >4 months, similar to other studies, but more descriptive than the studies that only examined women who EBF for <4 month or > 4 months. The authors stratified subsamples for skin prick testing (SPT), lung function measurements and bronchial hyper reactivity. The subsamples were chosen according to their wheezing status during the past year (example, 100 wheezers and 100 non-wheezers per center. The centers were divided by Gross National Income into affluent and non-affluent countries. The diagnosis of “asthma” was self-reported, not based on a physician diagnosis. Results indicated breastfeeding was inversely associated with wheeze in both affluent and non-affluent countries. No significant effect was found on duration of breastfeeding in affluent countries; however, the opposite is true for non-affluent countries, where exclusive breastfeeding for >2 months and > 4 months was inversely associated with wheeze. In all countries, any breastfeeding was associated with reduced lifetime prevalence of asthma. When considering maternal influence, in affluent and non-affluent countries, breastfeeding and wheeze wasn't affected by maternal history. In both affluent and non-affluent, breastfeeding was inversely related to bronchial hyper reactivity; however this was not proven to be significant. The study did not examine the relationship between breastfeeding duration and lung function, which would have been helpful in this large study where asthma was self-reported rather than with a doctor's diagnosis.

Rothenbacher et al.,(2005) studied a specific human gene in breast milk and risk of asthma in early childhood. Subjects in this study were examined during their first two years of life. Data from 1066 families was collected. At baseline, mothers underwent interviews about demographics, housing, and family history. The family history questions were based off of a physician diagnosis of asthma. Follow up exams and parental questionnaires were completed at 12 and 24 months. Medical information from pediatricians was obtained at one and two years of age to confirm the diagnosis of atopic disorder and asthma. Interviews for evaluating breastfeeding were done at baseline, 6 weeks and 6 months postpartum. Mothers were asked if they were currently breastfeeding and, if not, how long they continued breastfeeding. All women who were still breastfeeding 6 weeks post-partum had milk collected (by a trained nurse) and frozen until analysis. A total of 803 mothers and children were included in the final analysis. Overall, physicians reported 157 of the 1066 (15%) children were diagnosed with asthma. The incidence of atopic diseases was higher in children with a maternal history of atopic disease. A protective effect of duration of breastfeeding on asthma was seen, both overall and in children with no family history, after adjustment for maternal history of AD. The authors also looked at the concentration of sCD14 in breast milk. They noted that children breastfed for >6 month, the incidence of asthma was “tentatively” lower in children whose mothers had a sCD14 concentration in the upper ranges, when comparing those mothers in the lower ranges. In children who were breastfed for > 6 months, the odds ratio was also lowest in those that had the highest sCD14 levels in the breast milk. Overall, this study found an inverse association between duration of breastfeeding and risk of asthma, which was more so in children of mothers without a history of atopic

disease. This effect seemed to relate with the sCD14 concentrations in milk. It is noted that these levels were only measured in the 6-week milk samples and concentrations may vary at different points of the lactation period. They also did not test the sCD14 levels in the serum of the children. Unlike any of the studies noted thus far, Rothenbacher et al., (2005) appears to be the first to test a certain component of breast milk, giving a potential explanation of what components of breast milk provide the protective effect.

Sears et al., (2002) followed a cohort of 1037 children who were assessed within a month of their birth into their adult years. Subjects were assessed at ages 3, 5, 7, 9, 11,13,15,18, 21, and 26 years. Skin testing was done in 714 of children at age 13 and in 885 subjects at age 21 years. Initiation and duration of breastfeeding was documented via interview when the children were age 3. Newborns and infants were assessed by a nurse via home visits and clinic visits until the child was 2-3 years old. When the child was seven years old, it was determined whether the child had ever had asthma, wheezing, hay fever, bronchitis, or allergies. At both seven and 18 years of age, the adult was asked about family history of asthma, hay fever, and allergies. At age 9, interviewers used a comprehensive questionnaire to record the occurrence and frequency of symptoms of wheezing, diagnoses of asthma and hay fever, drugs, clinical characteristics, admissions, and environmental exposures. At ages 18, 21, and 26 years, participants also completed questions derived from questionnaires from the American Thoracic Society. Asthma was defined as a positive response to the question, "Do you have asthma?" Spirometry was done at every assessment from ages 9-26 years. Results indicated that, at age 9 years, more children who were breastfed had been diagnosed with asthma, had current asthma, and had current wheeze, that those who were not breastfed. The effect identified with

current asthma persisted at all ages to 26 years. Among the children with daily wheezing at age 9 years, seven of the eight had been breastfed. . The relationship with breastfeeding remained strong when airway hyper-responsiveness was needed to confirm the diagnosis of asthma, or that wheezing was due to asthma. Children who were breastfed were more likely to have current asthma with airway hyper-responsiveness than those that were not. Any breastfeeding for longer than 3 weeks raised risk of asthma. NO duration of exclusive breastfeeding had a protective effect against development of asthma in later childhood. Sears et al., (2002) did note in the beginning of the study that many of the children in the study who were breastfed received a nightly formula feed for about 3-4 days to let the mother rest, thus indicating none of the infants were TRULY exclusively breastfed. Nonetheless, these results are inconsistent with most research studies that have examined the relationship between breastfeeding and asthma. Sears et al., (2002) noted that the small dosage of formula biased their findings as the breastfed subjects recorded more asthma than those who were not breastfed.

Kramer et al.,(2007) conducted a cluster-randomized trial to study the effect of prolonged exclusive breast-feeding on risk of allergy and asthma. This study used a strategy to target prenatal women who were already planning to breastfed. The goal was to promote exclusivity and increase duration; this strategy was called the promotion of breastfeeding intervention trial (PROBIT). The experiment was based on the baby hospital initiative developed by the World Health Organization and the United Nations Children's Fund (UNICEF to promote breast-feeding (Kramer et al, 2007). The control group was the hospitals that continued their normal practices and policies in effect (Kramer et al, 2007). The trial results came from a total of 17, 046 healthy breastfed

infants, all of who were born at term. The infants were followed in the first year at 3, 6, 9, and 12 months. Pediatricians did the interviews and exams at age 6. Allergy symptoms and diagnosis were ascertained with international study of asthma and allergy questionnaire. The pediatricians also did skin prick tests to five different antigens: dust mite, cat, birch pollen, northern grasses, and *Alternaria* (fungi). A total of 13889 children were seen in follow up. Results indicated that, in the experimental groups, 11 percent of the population “ever” had wheezing, vs. 9.6 percent in the control group; 3.4 percent in the experimental group had wheezing in the past 12 months, vs. 2.8 percent in the experimental group. An estimated 1.4 percent of the children who ever had asthma were in the experimental group vs. 1 percent in the control group. The authors noted that the experimental intervention to promote breastfeeding did not reduce the risk of asthma, hay fever, or eczema at age 6.5 years, but noted that the experimental intervention did lead to a difference in duration of breastfeeding through the first year. At 3 months, 72.7 percent were still breastfeeding, vs. 60 percent in the control group. At 6 months, 49 percent vs 36.1 percent in the control and at 1 year, 19.7 percent vs. 11.4 percent. At 3 months, the numbers exclusively still breastfeeding was sevenfold higher; however EBF was low in both groups at 6 months. Their results conflict with previous studies, suggesting breastfeeding reduced the risk of asthma. However, Kramer et al., (2007) only used one questionnaire to obtain asthma results and the primary focus of this study was on allergies as they administered skin prick tests (SPT) rather than asthma and lung function was not measured which reduces the comparability of this study to the others in the field..

Midodzi et al.,(2010) studied factors associated with physician-diagnosed asthma in 8499 preschool children between the ages of 2 to 5, all of whom had no prior history of

asthma, using longitudinal data from the Canadian Early Childhood Development cohort, conducted as part of Canadian Longitudinal Study of Children and Youth (NLSCY). The cohort was selected in “panels”, of which were based off of the NLSCY cycles. Panel 1 was followed from 1996/97 to 2000/01 and Panel 2 was followed from 1998/99-2002/03. The panels, at the time of recruitment, selected children under the age of 2. The questionnaire was completed in the respondent’s home by the mother (or guardian) via computer-assisted personal interviews. The main outcome was the incidence of physician-diagnosed asthma at preschool age. Prenatal, perinatal, and postnatal factors that were considered in the study included: maternal smoking, presence of pregnancy health problems, delivery method, low birth weight, breast feeding (never, 0-3 months of >3 months). Early childhood factors included history of early wheezing (occurring in the previous 12 months), history of childhood allergy (dx by a health professional), and history of nose or throat infection, early daycare attendance at age 2, maternal age at birth, and gestational age. Parental atopy, history of asthma and allergies in either parent was also obtained. Results concluded a higher incidence of physician diagnosed asthma occurred in the preschool years for children with a history of early wheezing. A factor that was associated with reduction in the risk of developing asthma included breastfeeding. Although, they noted breastfeeding as a protective factor, no thorough discussion took place regarding duration of breastfeeding categories and/or exclusivity of breastfeeding. This study concluded that 20.3 percent of children who had wheezing before 2 years of age developed physician-diagnosed asthma from age 2-5 compared to 9.2 percent of the children who had no history of wheeze at all.

Strassburger et al., (2010) evaluated the impact of exclusive breastfeeding and introduction of cow's milk in the first year of life on the diagnosis of asthma, wheezing, and atopy in children aged 3-4. This randomized trial examined the effectiveness of the dietary guidelines in the first year of life that emphasize the importance of exclusive breastfeeding until six month of age that were recommended by the Brazilian Ministry of Health (2002). In the study, one group received guidance on the benefits of exclusive breastfeeding and information and guidance was not given to the control group. Children were chosen by nutrition school students at the hospital nursery in the city of Sao Leopoldo based on certain criteria. Trained undergraduate students collected the data at home visits at ages 6 months, 12 months, and between three and four years of age. The students collected information about exclusive breastfeeding, age at introduction of fresh fruit and fruit juice, and age when cow's milk was introduced. Exclusive breastfeeding was defined as the use of breastfeeding as the only food offered to the child, with no offer of tea and water or any other item. The variables used were duration of breastfeeding, divided into two ages, 4 and 6 months, introduction of cow's milk, introduction of fruit or fruit juice, and salty pureed foods. These were cut off at age 4 months. Asthma and wheezing were assessed by a questionnaire at age 3-4 years using the ISAAC questionnaire. Asthma was defined as a positive combination of "Has your child had wheezing in the past 12 months?" and "Has your child ever had asthma?". Information on the medical and family history of disease was also taken. A total of 354 children participated. Results indicated one third of children were EBF beyond four months and in 40 percent of children, cows milk had been introduced by 4 months. Children of parents with a history or asthma were more likely to have wheezing. At age 4, early introduction

of cow's milk and fruit juice or EBF up to 4 or 6 months of age was not associated with wheeze. Children fed cow's milk before 4 months were significantly more likely to have asthma. The risk was also four times greater for children of mothers with a history of asthma. The authors conclude that because they were fed cow's milk early, the length of time the children were exclusively breastfed was shortened, therefore increasing asthma.

The authors note the culture in Brazil is different and that in the first 2 years of life, children are fed milk products, flour and sugar are added to milk formulas and these are introduced before 6 months of life. It is well-known in the United States that cow's milk should not be introduced until 1 year of age. The government funded program, Women, Infants, and Children (WIC) places high emphasis on educating the participants on this. The study does note a major limitation in that the diagnosis of asthma in children under 5 was not confirmed (Strassburger et al., 2010). The study also did not discuss the results of their "guidance" on exclusive breastfeeding. They did not include statistics on the experimental groups or control group. This would have been an appropriate discussion to see if such interventions might have had potential to increase the amount of children who were exclusively breastfed in a underprivileged city, such as Sao Leopoldo, Brazil.

Guilbert et al., (2007) conducted a population based cohort study of infants enrolled in the children's Respiratory Study in Tucson, Arizona. Children were followed up to age of 11 and 16. The study looked at the effect of breastfeeding on lung function in children by maternal asthma and atopy. Feeding practices were assessed based on forms completed by the child's pediatrician and at well child visits at ages 2, 4, 6, and 9 months. Breastfeeding was categorized into 3 groups: breastfeeding for <1 month, 2 to < 4

months, and breastfeeding for >4 months. The caregiver completed respiratory questionnaires at age 6, 11, and 16. Wheeze was ascertained during the first 3 years of life based on physician report. The doctor completed a form when a child was seen for signs or symptoms of respiratory infections. Parental asthma was determined by asking the parent on the initial questionnaire if they had ever had physician-diagnosed asthma. Severity of maternal asthma was defined further by asking about frequency of wheeze in the past year either active (1 + episodes of wheeze) or inactive (wheeze, but not in past year). Lung function testing was performed at 11 years of age and 16 years of age. Forced vital capacity (FVC) and Forced expiratory volume (FEV) were measured. Results indicated longer breastfeeding was significantly associated with an increased FVC. Longer breastfeeding also altered FVC at age 16 when considered in relation to early formula introduction. FVC was increased by 4.5 percent at age 11 for participants with longer breastfeeding when compared with those that had early formula introduction. There was no relation between infant feeding and FEV through age 16. Relations were different when the analysis was stratified by maternal asthma and atopy. The longer breastfed children with maternal history or asthma had a FVC that was not improved (increased). These results did not change when the severity of maternal asthma was taken into consideration. Longer breastfed children with atopic, non-asthmatic mothers had a FVC that was significantly higher. These results were similar to Ogbuanu et al.,(2009) who concluded that when comparing those who were not breastfed-FVC was increased in children who were breastfed for at least 4 months. Unlike Guilbert et al.,(2007) Ogbuanu et al.,(2009) put a length of duration when doing testing. In both studies in which FVC improved significantly with longer duration of breastfeeding, the children were similar in

age (10 and 11). Ogbuanu et al.,(2009) also measured lung function with peak expiratory flow- as did Kull et al., (2010). Both concluded that in children ages 8 and 10, those breastfed for 4 months or longer had better lung function when measured with peak expiratory flow. All three studies concluded that breastfeeding enhances lung volume (growth) in children. However, Ogbuanu et al., (2009) and Guilbert et al.,(2007) noted different findings when adjusting for family history. Guilbert et al.,(2007) noted that when maternal asthma was present, longer breastfeeding was associated with decreased airflows (Guilbert al., 2007). Inversely, Ogbuanu et al., (2009) said that in their sample population, the effect of breastfeeding duration on lung function measurements was not changed by maternal history of asthma (Ogbuanu et al., 2009). It is noted that one study states “presence” of maternal asthma while the other study noted “history of maternal asthma”. It appears terms and conditions differ among several studies.

Elliot et al., (2008) used a large birth cohort called the Avon Longitudinal Study of Parents and Children to examine the relationship between breastfeeding and later asthma and allergy. The original ALSPAC sampled consisted of 14062 live births, with 13,978 alive at one. Data on breastfeeding was obtained like most of the studies reviewed, via questionnaires. These were sent to mothers’ during the first four years of life. They assigned duration to never, < 1 months, 1 to < 3 months, 3 to < 6 months and 6+ months. Health outcomes, specifically asthma, were questioned at 7.5 years. Asthma was clearly defined as current asthma doctor diagnosed, plus either wheeze or the use of asthma medications within the past 12 months. The authors collected this data on 8, 131 children. Lung function and bronchial hyper –responsiveness were assessed at 8 years. The number of children completing the bronchial challenge was 6, 551. Results indicated

breastfeeding had a small inverse association with wheeze within the first 3-year. After adjustment for confounders, breastfeeding still was seen to be protective for early wheeze. They found no evidence of effect modification of the association between breastfeeding and confounders including maternal asthma. The authors compared EBF for >4 months with EBF for < 4 months and did not find an increased risk of asthma among atopic children with asthmatic mothers in those that were breastfed less. Overall, no evidence that breastfeeding increased the risk of wheeze was found; inversely, the authors found a slight protective effect of breastfeeding on wheeze. Elliot et al., (2008) failed to discuss the relationship between duration of breastfeeding and bronchial hyper-responsiveness. It appears the author's main goal was to argue the fact that breastfeeding does not increase incidence of asthma and wheeze, rather than to support breastfeeding's supposed protective effects.

A multidisciplinary review of literature conducted by van Odijk et al, (2003) focused on objectives similar to the current review of literature. This review questioned if breastfeeding protected against development of atopic disease and allergic manifestations, and if so, how long should breastfeeding continue. The authors focused on high-risk population to see if results varied in this group. A Medline search for articles published prior to 10/2001 was conducted; a total of 56 studies were reviewed for results. Similar to findings done in this review, a number of different definitions of breastfeeding existed throughout the articles. Studies were categorized into 4 groups. Twenty-six studies examined the relationship between breastfeeding and atopic manifestations. Half of those studies reported that breastfeeding reduced the risk of asthma, wheezing, atopic dermatitis, and cow's milk allergy, while three-quarters examined the impact of any

breastfeeding. Results indicated a protective effect of breastfeeding on asthma that persisted for 5 years or more and increased with up to 4 months duration of breastfeeding. These results are consistent with studies examined in this literature review. In two of their studies, breastfeeding was reported as a risk factor for eczema and hay fever-neither examined in this review. Six of their studies stated no effect was seen with breastfeeding. This is not noted in the current review: all studies examined yielded some type of result. Another category was breastfeeding and atopic manifestations in children with atopic heredity. Nineteen studies were reviewed. Out of those, all, but one, concluded breast milk provided a protective effect up to at least 1-3 years. The other categories examined included studies on formula feeding and atopic manifestations and cow's milk exposure and atopic manifestations. Neither of these subjects was discussed in the current review of literature. It appears, according to the majority of the studies that were examined, an overall consensus of the protective effect of breastfeeding is noted, especially among children with atopic hereditary.

A clinical report conducted by Greer et al. (2008) examined several studies and a meta-analysis to find a relationship between breastfeeding and asthma. Wright et al., (2001) authored one such study included in the clinical report. The data was taken from the Tucson Children's Respiratory Study-infants and families were enrolled at birth from 1980 to 1984-described in detail elsewhere. Information on parental asthma was also obtained. Feeding practices were assessed at health surveillance visits when the physician recorded information on if child was being breast fed or getting formula. Information was also obtained by questionnaire at year two about age when formula was introduced. Breastfeeding was categorized into the following groups: never breastfed, breast fed

exclusively <4 months, breastfed for exclusively > 4 months. At age 2, 3, 6, 9, 11, and 13 parents asked if the child ever had asthma, whether a doctor said the child had asthma, whether symptoms were present in the past year. Recurrent wheeze was defined as wheezing > 4 times the past year. Asthma was defined as physician diagnosed asthma and wheeze or asthma symptoms reported on 2 or more questionnaires at 6 and 13. By age 13, 14.3 percent of children had asthma. There was no significant relationship between asthma by age 13 and duration of exclusive breastfeeding. In children with non-asthmatic mothers, the percentage of asthma by 13 wasn't related to duration of breastfeeding, but in those with a maternal history of asthma there was a relationship between duration of breastfeeding and asthma. Exclusive breastfeeding was related to significant lower odds of recurrent wheeze before age 2 and by the age of 3. Inversely, exclusive breastfeeding was associated with higher odds of recurrent wheeze at age 6 through 13. Overall, the study noted that breastfeeding caused increased risk when maternal asthma was present. But, longer exclusive breastfeeding regardless was associated with lower rates of wheeze in the child. Guilbert et al., (2007) found similar results, however testing lung function, which Wright et al., (2001) did not do. Guilbert et al., (2007) found that longer breastfed children with asthmatic mothers had a FVC that was not increased when comparing with children that had early formula introduction. The ages were also similar at 13 and 16. These studies support the stated hypothesis that those children who have a maternal history of asthma are at an increased risk for the development of asthma resulting in decreased lung function if breastfed for a longer duration.

Summary

Overall, results are mixed with regard to the connection between duration of breastfeeding, infant immunity and the development of asthma. It appears the development of asthma may further be complicated by the mother's own asthmatic status. This paper explored the research to give better insights, provide direction and knowledge to support groups, clinics, and hospitals in hopes of encouraging breastfeeding and reducing risk of infections or development of allergies/asthma. Unfortunately, the inconclusive results obtained do not allow a definitive statement to be made at this time.

CHAPTER FOUR

RESULTS AND DISCUSSION

The purpose of this research paper was to conduct an extensive literature review to determine if sufficient evidence exists to identify a protective effect of breastfeeding on the incidence of asthma in children five years of age or younger. This chapter will discuss the results of literature reviewed.

A total of 14 studies were thoroughly reviewed to see if the current research literature demonstrates a protective effect of breastfeeding on asthma and/or wheeze. Results remained varied; some studies found a protective effect on breastfeeding, while others did not. Certain studies also found that the protective effect was conditional, i.e. only seen with a family history or with increased duration. Sixty four percent (9 of 14) of the studies reviewed showed a protective effect of breastfeeding on asthma (Nagel et al., 2009), (Kull et al., 2010; Ogbuanu et al., 2009; (van Odijk et al., 2003; Silvers et al., 2009; Rothenbacher et al., 2005; Elliot et al., 2008; Midodzi et al, 2010; Strassburger et al., 2010), seven percent (1 of 14) found that breastfeeding increased risk for developing asthma (Sears, et al., 2002), twenty percent, (3 of 14) noted both protective and non-protective conditionally (Wright et al., 2001; Pohlabein et al, 2010; Guilbert et al., 2007), and seven percent, 1 of 14 (Kramer, et al., 2007) found no protection of breastfeeding on reduction of asthma/wheeze.

Out of these studies, 43 percent (6 of 14) demonstrated that the protective effect was influenced positively or negatively when a family history of asthma was present (van Odjik et al., 2003; Wright et al., 2001; Guilbert et al., 2007; Pohlabein et al., 2010; Sears et al., 2002). If an effect was present, it appeared to depend on the duration and differentiation between maternal and paternal history of disease. Only one of six studies demonstrated a protective effect when considering maternal history. In fact, about half (three of six) stated that maternal history increased the risk (Guilbert et al., 2007; Pohlabein et al., 2010; Wright et al., 2001). Sears et al., (2002) stated breastfeeding effects were not influenced by any paternal history. The protective effect, even with maternal history, was seen in a study by Rothenbacher et al., (2005). The study considered the soluble CD14 concentration in breast milk. They concluded that a protective effect of duration of breastfeeding with cumulative incidence of asthma was evident and reached statistical significance even after adjustment for maternal history of atopic disease (Rothenbacher et al., 2005). When looking at the duration of exclusive breastfeeding, they observed a similar pattern – e.g., if a child was breastfed, the duration of EBF was associated with a decreased risk for asthma, even after adjusting for maternal history of disease (Rothenbacher et. al., 2005).

One of six studies showed a protective effect of breastfeeding when a paternal history of asthma was documented. Pohlabein et al., (2010) conducted a study based on initial questions containing detailed questions on family history of allergic disease and a range of lifestyle related aspects. Mothers completed follow up interviews, collecting information about breastfeeding, at 6, 12 months and again at 2 years. The authors concluded that in 2 year old children with a family history of atopy, appearance was less

common in breastfed children when compared with non-breastfed children. Children with a paternal only predisposition had a significantly decreased risk if they had been breastfed for greater than four months, while maternal- only predisposition had a higher risk of symptoms at age 2. However, the maternal findings were not significant. Breastfeeding for less than 4 months seemed to have no influence on increased or decreased risk in children with either a paternal or maternal history of disease. The study noted that these results are based on very small numbers, so they should be interpreted lightly.

Greer et al., (2008) completed a clinical review and found that exclusively breastfeeding for at least 3 months was protective against the development of asthma between 2 and 5 years of age and this effect was stronger when the analysis was limited to those with a family history. However, when the authors-analyzed the data of Wright et al., (2001), the researchers found that infants whose mothers' had asthma were at greatest risk of developing asthma by age 13, if they were breastfed for greater than four months. van Odijk et al., (2003) reported breast milk seemed to provide a protective effect for asthma up to at least 1-3 years in children with atopic heredity, although when reporting results, the author used terms such as "seemed" and "different, but not significant" indicating no statistical results were obtained. The study analyzed less than fifty percent of the studies selected as the remaining studies were regarded as inconclusive.

Three of the six studies examined in this review had solid, significant evidence that most children with family history, especially maternal, had a significant increase in asthma symptoms and/or actual clinical diagnosis when they were breastfed. This may suggest that genetic makeup will most likely not be altered by breastfeeding. Seven

percent of the studies showed no protective effect of breastfeeding on asthma (Kramer et al., 2007). A large cluster randomized trial conducted by Kramer et al., (2007) focused on taking initiative to increase duration of breastfeeding. The authors found similar results in regards to duration. Despite a large increase in exclusive breastfeeding at 3 months and a significantly higher prevalence of any breast feeding at all ages up to and including 12 months results showed that no reduction in risk of developing asthma, hay fever or eczema at age 6.5 years. No increase in protective effect of breastfeeding was seen in those with a family history. Similarly, seven percent of these studies showed that breastfeeding actually increased a child's risk of developing asthma.

Sears et al., (2002) conducted a longitudinal study from 9- 26 years of age and found that more children who were breastfed reported current asthma at each assessment between age 9 and 26 years of age. The relationship with breastfeeding remained strong when airway hyper-responsiveness was used to confirm the diagnosis of asthma. Children who were breastfed were more than 2 times as likely to have asthma with airway hyper-responsiveness or current wheeze with airway hyper-responsiveness at all ages up to 21 years (Sears et al., 2002). The study also found that no duration of EBF had a protective effect against development of atopy and asthma in later childhood. None of the studies were able to prove that no relationship between the two variables existed.

Greater than 50 percent of the studies reviewed, concluded that breastfeeding had a protective effect on the development of asthma (Nagel et al., 2009; Kull et al., 2010; Ogbuanu et al., 2009; van Odijk et al.,2003; Silvers et al., 2009; Rothenbacher et al., 2005; Elliot et al., 2008; Midodzi et al, 2010; Strassburger et al., 2010). All of the studies took duration into account. Kull et al., (2010) found that breastfeeding exclusively for 4

months or more reduced risk of asthma during the first 8 years of life. At age 8, reduced risks of sensitization and asthma combined with sensitization were seen within the children who were exclusively breastfed for 4 months or more. These children had better lung function when measuring with the peak expiratory flow. The study done by Rothenbacher et al., (2005) found lowest incidence of atopic disease when children were breastfed for > 6 to < 9 months and exclusively breastfed for > 3 months.

The remainder of the studies noted similar results with protective effects noted with 3 months of breastfeeding (exclusive, not noted), 4 months of breastfeeding (exclusive-not noted), and 6 months of exclusive breastfeeding. Silvers et al.,(2009) found that longer durations of exclusive and any breastfeeding were associated with a significant reduction in adverse respiratory outcomes. After adjusting for confounders, Silvers et al., (2009) found that each month of exclusive breastfeeding reduced the risk of doctor diagnosed asthma by 20 percent, wheezing by 12 percent, and inhaler use by 14 percent. Silvers et al., (2009) also noted that risk was reduced by 7 percent, 8 percent and 8 percent, respectively in those with any breastfeeding noted. Only the study by Silvers et al., (2009) compared percentages from exclusive breastfeeding to any breastfeeding. That particular study did show that exclusive breastfeeding reduced the percentage of diagnosed asthma, wheeze, and inhaler use more that just any breastfeeding. It appears breastfeeding exclusively for at least 3 months and continuing with any breastfeeding beyond 3 months could have the greatest benefits for a child.

Many limitations were seen and were consistent throughout the studies. Breastfeeding duration was often self-reported during follow up assessments through questionnaires. The type of breastfeeding (exclusive, partial, supplemental) was also self-

reported and the definition criteria of breastfeeding varied from study to study (i.e., not breastfed, <2 months, somewhat breastfed >2 and <4). This can be a limitation to the studies when comparing duration with increased or decreased risk of asthma. Another common trend throughout the studies is different definitions and criteria for presence of asthma. Many of the studies referred to wheeze and atopic disease. Some of the studies reviewed did not require a physician diagnosis of asthma.

Strengths of this literature review include adjustment for confounding variables. A typical variable adjusted for was family history of atopic disease. Others included: smoking status, socioeconomic status, gender, and ethnicity. Over half of the studies reviewed objective measures including, lung function (via spirometry), skin prick tests, and measurement of immune building helper cells. These types of measurements are influenced as atopic disease manifests. Comparing these to breastfeeding status can provide insight on the relationship between the two. Over half of the studies reviewed did conclude a protective effect, however many noted results were not significant and/or the protective effect was only to a certain extent (i.e., the first 1-2 years of life).

Oddy & Peat (2003) conducted an Epidemiological Review of Literature in which the primary objective was to assess the evidence of whether breastfeeding protects asthma and atopic disease. Their results yielded similar conclusions regarding the protective effect of breastfeeding. The review included several studies: The Finnish Study, Tucson Children's Respiratory Study, The Isle Of Wight Studies, The Dundee Infant Feeding Study, The Western Australian Pregnancy Cohort Study, National Longitudinal Survey of Children and Youth, and Swedish Study.

The Tuscon Children's Respiratory Study (Oddy & Peat, 2003) was designed to look at risk factors for lower respiratory tract illness. The study included 1246 infants in whom feeding patterns were recorded at well-child visits and from parental reports. In total 29 percent of mothers stopped breastfeeding by 4 months, percent stopped between 4 and 6 months, and 40 percent stopped thereafter. If the infant was breastfed for less than 1 month than the prevalence of wheeze was 12 percent; if breastfed for 1-3 months the prevalence was 8 percent; and for 4 or more months, the prevalence was 5 percent. After adjusting for maternal education, smoking, ethnic origin, gender, parental history of respiratory illness and type of day care, bottle-feeding remained significantly associated with more wheezing illness at 4 months of age. Further analysis of the Tuscon data was done when the study population was at 6 years of age. At this age, recurrent wheeze was less common in non-atopic children who were breastfed in infancy when compared with those who were not breastfed. At age 11, an association between breastfeeding and asthma was differentiated by the mothers' asthmatic status: 9 percent of those who developed asthma were never breastfed, 36 percent for children breastfed under 3 months and 57 percent for those breastfed for greater than 4 months, however breastfed children were significantly less likely to wheeze at age 6, 9, or 11 years if they hadn't been diagnosed with asthma. The study also concluded that children whose mothers were in the higher range of IgE, breastfeeding for greater than 4 months was associated with higher IgE levels in the child when compared with those breastfed for less than 4 months, signifying that there is an relationship between maternal asthma status and the effect of breastfeeding duration.

The Isle of Wright Study was a cohort of 843 infants. The study investigated the effect of breastfeeding on allergic disease at 1 year of age. Allergic disease was characterized as eczema, chronic rhinitis, asthma, or bronchitis. The incident of allergic disease was greater in infants' started on formula than those who were started on breastfeeding. Children were followed at 2 and 4 years of age. At age 4, breastfeeding was found to have no association against recurrent wheeze, but in children with a paternal history of asthma, 9 percent who were breastfed has asthma in comparison of 11 percent of children that had asthma with mixed feeding (Oddy & Peat, 2003).

A second birth cohort began from this study, which included 1456 infants who were followed to age 4. This study included similar diagnostic criteria but the end of exclusive breastfeeding was defined with introduction of formula. Children introduced to formula before 3 months had significantly more asthma at 4 years of age (Oddy & Peat, 2003).

The Dundee Infant Study assessed 674 children who were followed from birth. The study was designed to review the relationship between breastfeeding and infant illness until 2 years of age. Breastfeeding was categorized as full breast feeding (13+ weeks), partial breastfeeding (breastfed with supplements introduced), early weaners (stopped before 13 weeks, and formula fed (bottle fed immediately following birth) (Oddy & Peat, 2003). Full or partial breastfeeding was associated with a reduction in respiratory infections in children up to 24 months of age. After adjusting for father's social class, maternal age, and parental smoking, respiratory infections in bottle fed children were significantly higher than in partial or full breastfeeding (Oddy & Peat, 2003).

These children were also followed up again at age 7 and the prevalence of wheeze, shortness of breath, or cough at age 7 was significantly lower if the child had been EBF for at least 15 weeks. The prevalence for respiratory symptoms was 17 percent for EBF, 31 percent for partial and 32 percent for bottle-feeding (Oddy & Peat, 2003).

The Western Australian Pregnancy Cohort Study investigated the relationship between duration of EBF and development of asthma at age 6. The study had 2187 participants. After adjusting for confounders, the introduction of formula milk before 4 months was a significant risk factor for doctor-diagnosed asthma, wheeze 3 or more times since 1 year, or wheeze in the past year. In this study, a significant reduction in risk of childhood asthma was seen at age 6, if EBF was continued for at least 4 months (Oddy & Peat, 2003).

The Swedish Study chose 4089 infants to participate in their study. The parents filled out questionnaires regarding exposures, allergic symptoms, and feeding at 2 months, 1 and 2 years of age. Children exclusively breastfed for 4 months plus had less asthma, less atopic dermatitis, and less suspected allergic rhinitis at age 2 when compared to those exclusively breastfed for a shorter period of time. A significant risk reduction for asthma was seen when looking at breastfeeding during 6 months or more. The study concluded that those with a parental history of asthma benefited the most from breastfeeding (Oddy & Peat, 2003).

A meta-analysis of nine studies, some of which were included in this review showed that children breastfed for at least 3 months of age were significantly protected from the development of asthma (Oddy & Peat, 2003). Other meta-analyses concluded a protective effect between 26 percent and 30 percent from EBF during the beginning 3

months of life against developing asthma, allergic rhinitis, and atopic eczema during childhood (Oddy & Peat, 2003).

Summary

Overall, the review noted that mothers' should be encouraged to breastfeeding related to the benefits breastfeeding provides. The review and analysis indicated the majority of the studies have found that breastfeeding has a protective effect on asthma. However, the continuing protective effect of breastfeeding on asthma later in adolescence and adulthood has not been confirmed. At this time, no definitive conclusive recommendation can be made regarding the relationship between breastfeeding and asthma.

CHAPTER 5

CONCLUSIONS, LIMITATIONS, AND RECCOMENDATIONS

Overall, results are mixed with regard to the connection between duration of breastfeeding, infant immunity and the development of asthma and, as such, no definitive recommendation can be made at this time. Some studies continue to show that breastfeeding provides a protective effect; while others show that breastfeeding actually increases risk of developing atopic disease (asthma). However, it seems that there is most definitely some type of relationship that exists between the two variables as > 95 percent of the studies reviewed revealed some type of relationship, either protective or non-protective. The results do indicate the rate of atopic disease continue to rise, while the rate of breastfeeding lags below the suggested levels.

Despite the lack of a definitive answer to the relationship between asthma and breastfeeding, healthcare professionals should continue to encourage breastfeeding in any amount to expectant mothers' as there are numerous documented benefits of breastfeeding to both the mother and the baby. Professionals should be aware of the Healthy People 2020 (HHS, Healthy People 2020, 2011) goal for breastfeeding and a concerted effort should be made to reach these goals. If breastfeeding rates rise, the scientific community will be watching to determine if there is a concomitant decrease in

the rate of atopic disease nationwide. Additional research will be needed to answer this critical question.

Limitations

The results of this study are limited by the following factors:

1. The studies reviewed in this paper may not fully represent the general population.
2. Some of the studies reviewed in this paper do not follow infants into later childhood; therefore the duration of some studies may not be long enough to produce statistically significant results.
3. Studies used in this paper may not take into account other variables that may influence the relationship between two variables.
4. Literature used for the review was limited to that available on the Ball State University Library database.

Recommendations for Future Research

Future recommendations for studies include providing a more tightly controlled environment, monitoring breastfeeding practices over an extended period of time more closely, and assuring both duration and frequency are considered. This type of study, however, may be unrealistic and the scientific community will need to rely on changes in breastfeeding atopic disease rates in a “natural” experiment to identify any link between the variables. Studies should also test components of breast milk closely and more frequently to see if the makeup of breast milk changes as duration increases. All researchers should be encouraged to examine both maternal and paternal asthma history, rather than focusing exclusively on maternal history.

Summary

Based on the studies discussed in this literature review, the results do not support a definite protection of breastfeeding on the development of asthma in children of all ages. The studies reviewed in this literature examined children at age 2, as well as up to 10, 11, and early 20s. Contrary to providing a protective effect, it has been suggested that breastfeeding, especially when maternal history is present, increased the risk of asthma in children. At this point, the protective effect breastfeeding may provide, cannot be claimed on the current body of evidence.

References

- American Pregnancy Association (2004). Breastfeeding: Overview.
<http://www.americanpregnancy.org/firstyearoflife/breastfeedingoverview.htm>
Accessed on January 2, 2012.
- Adlerova, L., Bartoskova, A., Faldyna, M. (2008). Lactoferrin: a review. *Veterinarni Medicina*, 2008, 457-468.
- Ahluwalia I.B., Morrow, B., Hsia, J. (2005). Why do women stop breastfeeding? Findings from the pregnancy risk assessment and monitoring system. *The American Academy of Pediatrics*, 116, 1408-1412.
- Akinbami, L.J., & Schoendorf, K. C. (2002). Trends in childhood asthma: Prevalence, health care utilization, and mortality. *The American Academy of Pediatrics*, 110, 315-322.
- Akinbami, L.J., Moorman, J.E., & Liu, X. (2011). Asthma prevalence, health care use, and mortality: United States, 2005-2009. *National Health Statistics Reports*, 32, 1-15.
- Andersson, Y., Hammarstrom, M., Lonnerdal, B., Graverholt, G., Falt, H., & Hernell, O. (2009). Formula feeding skews immune cell composition toward adaptive immunity compared to breastfeeding. *The Journal of Immunology*, 183, 4322-4328.
- Bateman, E.D., Hurd, S.S., Barnes, P.J., Bousquet, J., Drazen, J.M., FitzGerald, M., ...Zar, H.J. (2008). Global strategy for asthma management and prevention: GINA executive summary. *European Respiratory Journal*, 31, 143-178.
- Caligiuri, M.A. (2008). Human natural killer cells. *Journal of the American Society of Hematology*, 112, 461-469.
- Chuang, C., Chang P., Chen, Y., Hsieh, W., Hurng, B., Lin, S., ...Chen, P. (2010). Maternal return to work and breastfeeding: A population-based cohort study. *International Journal of Nursing Studies*, 47, 461-474.
- Demir, A. H., Celikel, S., Karakaya, G., & Kalyoncu, F. (2010). Asthma and allergic diseases in school children from 1992 to 2007 with incidence data. *Journal of Asthma*, 47, 1128-1135.

- Elliot, L., Henderson, J., Northstone, K., Chiu, G., Dunson, D., & London, S. (2008). Prospective study of breastfeeding in relation to wheeze, atopy, and bronchial hyperresponsiveness in the Avon Longitudinal Study of Parents and Children (ALSPAC). *Journal of Allergy and Clinical Immunology*, 122, 49-54.
- Field, Catherine (2005) The immunological components of human milk and their effect on immune development of infants. *Journal of Nutrition*, 135, 1-4.
- Gold, M.S., & Kemp, A.S. (2005). Atopic disease in childhood. *Med J Aust*, 182, 298-304.
- Greer, F.R., Sicherer, S. H., & Burks, A.W. (2008). Effects of early nutritional interventions on the development of atopic disease in infants and children: The role of maternal dietary restriction, breastfeeding, timing of introduction of complimentary foods, and hydrolyzed formulas. *The American Academy of Pediatrics*, 121, 183-191.
- Guilbert, T. W., Stern, D.A., Morgan, W.J., Martinez, F.D., & Wright, A.L. (2007). Effect of breastfeeding on lung function in childhood and modulation by maternal asthma and atopy. *American Journal of Respiratory and Critical Care Medicine*, 176, 843-848.
- James, D. C. S., & Lessen, R. (2009). Position of the American Dietetic Association: Promoting and supporting breastfeeding. *Journal of the American Dietetics Association*, 109, 1926-1942.
- Karmaus, W., Dobai, A. L., Ogbuanu, I., Arshard, S. H., Matthews, S., & Ewart, S. (2008). Long-term effects of breastfeeding, maternal smoking during pregnancy, and recurrent lower respiratory tract infections on asthma in children. *Journal of Asthma*, 45, 688-695.
- Kramer, M. S., McGill, J., Matush, L., Vanilovich, I., Platt, R., Bogdanovich, N., ...Mazer, B. (2007). Effect of prolonged and exclusive breast feeding on risk of allergy and asthma: Cluster randomized trial. *BMJ Journal*, 1-6.
- Kull, I., Melen, E., Alm, J. Hallberg, J., Svartengren, M., van Hage, M., Bergstrom, A. (2010). Breast-feeding in relation to asthma, lung function, and sensitization in young schoolchildren. *Journal of Allergy and Clinical Immunology*, 125, 1013-1019.
- La Leche League International (2006). What is colostrum? How does it benefit my baby? <http://www.llli.org/faq/colostrum.html>. Accessed January 2, 2012.

- McCloud, E., & Papoutsakis, C. (2011). A medical nutrition therapy primer for childhood asthma: Current and emerging perspectives. *Journal of American Dietetics Association*, 111, 1052-1064.
- Midodzi, W.K., Rowe, B. H., Majaesic, C. M., Saunders, L. D., Senthilselvan, A. (2010). Early life factors associated with incidence of physician-diagnosed asthma in preschool children: Results from the Canadian Early Childhood Development Cohort Study. *Journal of Asthma*, 47, 7-13.
- Moorman, J. E., Zahran, H., Truman, B. I., & Molla, M. T. (2011). Current asthma prevalence: 2006-2008. Centers for Disease Control and Prevention, National Health Interview Survey (NHIS), 60, 84-86.
- Nagel, G., Buchele, G., Weinmayr, G., Bjorksten, B., Chen, Y-Z., ... Weiland, S.K. (2009). Effect of breastfeeding on asthma, lung function, and bronchial hyperreactivity in ISAAC Phase II. *European Respiratory Journal*, 33, 993-1002.
- Oddy, W. H., & Peat, J. K. (2003). Breastfeeding, asthma, and atopic disease: An epidemiological review of the literature. *Journal of Human Lactation*, 19, 250-261.
- Oddy, W. H., Pal, S., Kusel, M. M. H., Vine, D., de Klerk, N.H., Hartmann, P. ... Landau, L. L. (2006). Atopy, eczema, and breast milk fatty acids in a high-risk cohort of children followed from birth to 5 year. *Pediatric Allergy and Immunology*, 17, 4-10.
- Ogbuanu, I.U., Karmaus, W., Arshad, S.H., Kurukulaaratchy, R.J., & Ewart, S. (2009). Effect of breastfeeding duration on lung function at age 10 years: A prospective birth cohort study. *National Institute of Health*, 64, 62-66.
- Pohlabeln, H., Muhlenbruch, K., Jacobs, S., & Bohmann, H. (2010). Frequency of allergic diseases in 2-year-old children in relationship to parental history of allergy and breastfeeding. *Journal of Investig Allergol Clinical Immunology*, 20, 195-200.
- Rigotti, E., Piacentini, L. G., Ressa, M., Pigozzi, R., Boner, A.L., & Peroni, D. G. (2006). Transforming growth factor- B1 and interleukin-10 in breast milk and development of atopic disease in infants. *Clinical and Experimental Allergy*, 36, 614-618.
- Roe, B., & Doll, H. (1995). Information Point: Prevalence and incidence. *Journal of Clinical Nursing*, 9, 178-188.

- Rothenbacher, D., Weyermann, M., Beermann, C., & Brenner, H. (2005). Breastfeeding, soluble CD14 concentration in breast milk and risk of atopic dermatitis and asthma in early childhood: Birth cohort study. *Clinical and Experimental Allergy*, 35, 1014-1021.
- Ruowel, L., Feln, S.B., Chen, J., Grummer-Strawn, L. M. (2008) Why mothers stop breastfeeding: mothers' self-reported reasons for stopping during the first year. *American Academy of Pediatrics*, 122, S69-S76.
- Sears, M. R., Greene, J. M., Willan, A. R., Taylor, R. D., Flannery, E. M., Cowan, J.O., ...Poulton, R. (2002). Long-term relation between breastfeeding and development of atopy and asthma in children and young adults: A longitudinal study. *The Lancet*, 360, 901-907.
- Segal, A.W. (2005). How Neutrophils kill microbes. *Annu Rev Immunol.* 23, 197-223
- Silvers, K. M., Frampton, C. M., Wickens, K., Epton, M.J., Pattemore, P.K., Ingham, T... Town, G. I. (2009). Breastfeeding protects against adverse respiratory outcomes at 15 months of age. *Maternal and Child Nutrition*, 5, 243-250.
- Snijders, B.E., Damoiseaux, J.G., Penders, J., Kummeling, I., Stelma, F.F., van Ree, R., ...Thijs, C. (2006). Cytokines and soluble CD14 in breast milk in relation with atopic manifestations in mother and infant (KOALA study). *Clin Exp Allergy*, 36, 1609-1615.
- Strassburger, S. Z., Vitolo, M. R., Bortolini, G. A., Pitrez, P. M., Jones, M. H., & Stein, R. T. (2010). Nutritional errors in the first months of life and their association with asthma and atopy in preschool children. *Jornal de Pediatria*, 86, 391-399.
- Takemura, Y., Sakurai, Y., Honjo, S., Kusakari, A., Hara, T., Gibo, M...Kugai, N. (2001). Relation between breastfeeding and the prevalence of asthma. *American Journal of Epidemiology*, 154, 115-119.
- United States Department of Health and Human Services (USDHHS), Healthy People 2020. (2011, June 29).*Maternal Infant and Child Health Objectives*. Retrieved from <http://healthypeople.gov/2020/topicsobjectives2020/objectiveslist.aspx?topicId=26>
- van Odijk, J., Kull, I., Borres, M. P., Brandtzaeg, P., Edberg, U., Hanson, L. A., ...Wille, S. (2003). Breastfeeding and allergic disease: A multidisciplinary review of the literature (1966-2001) on the mode of early feeding in infancy and its impact on later atopic manifestations. *Allergy*, 58, 833-843.
- WebMD Medical Reference (2011). Lung function tests. <http://www.webmd.com/lung/lung-function-tests>. Accessed January 2, 2012

World Health Organization (WHO) (2012). Nutrition: Exclusive Breastfeeding. http://www.who.int/nutrition/topics/exclusive_breastfeeding/en/. Accessed January 2, 2012.

Wright, A.L., Holbert, C.J., Taussig, L.M., Martinez, F.D. (2001). Factors influencing the relation of infant feeding to asthma and recurrent wheeze in childhood. *Thorax*, 56, 192-197.

APPENDIX A

Summary Table of Research Articles

Table 2. Summary of Peer Reviewed Studies that Examined the Relationship between Breastfeeding and Asthma in Children less than 5 years of age..

Author/Year	Database	Relation BF:Asthma	Subjects	Design	Results
Rothenbacher Weyermann, Beerman, Brenner 2005	PubMed Academic Search Premier	Yes	803 women, their offspring, partners and pediatricians	Researchers measured sCD14 concentrations in breast milk samples collected at 6 weeks postpartum from 803 women. Women German w/ mean age 31.5 years who came to the University of Ulm Dept. of OBGYN between Nov 2000-Nov 2001 to deliver. During the 2-year follow up, incidence of asthma was recorded. Data was collected at baseline with interviews of parents. At 12 and 24 months, parents filled out questionnaires and the MD provided medical info.	Overall, asthma diagnosed in 19.6% of children (n=157) by 2 years of age. A protective effect of breastfeeding was found when the duration of breastfeeding was considered, with the cumulative incidence of asthma-statistically higher among children who had no family history (hx) of atopic disease and after adjustment for family hx. Children breastfed for more than 6 months had a lower incidence of asthma when mothers had a higher sCD14 concentration compared to those with a lower concentration. The duration of exclusive breast feeding was associated with decreasing risk of asthma after adjustment for maternal history of atopic disease. In children without a hx of atopic dz- the risk of asthma decreased with increasing duration.
Pohlabeln, Muhlenbruch, Jacobs, Bohmann 2010	PubMed	Mixed	1685 participants-mothers/children up to 2 years of age.	1685 participants-completed a baseline questionnaire and one at 6, 12, and 2 years postpartum. Questionnaires at 6/12 months included breastfeeding duration – only mothers who had EBF were included in the breastfeeding categories. Differentiated for never, < 4 months, and > 4months. Family hx was an important confounding variable. Analyzed for children with and without a parental hx of atopic disease- further categorized into paternal/maternal sides.	Approx 23% of children (n=393) had evidence of an allergic disease; of these, 70% had eczema and a third of were dx with asthma. Symptoms were influenced by fam hx with maternal predisposition having a slight stronger influence. When analyzing association between prevalence of allergic symptoms in children without a predisposition a higher portion of children with symptoms in the breastfed groups vs. nonbreastfed group was seen. When analyzing between prevalence of allergic symptoms in children with a family hx, the prevalence was less common in breastfed children vs. never breastfed. Children without a genetic predisposition breastfed exclusively for >4 months had a higher risk for developing atopic disease. Results varied depending on parental predisposition. Maternal only: higher risk of disease symptoms if EBF for >4 months vs never. Paternal: significantly decreased risk if breastfed >4 months vs. never Breastfeeding for < 4 months had no influence on

Author/Year	Database	Relation BF:Asthma	Subjects	Design	Results
					in/dec risk with either side.
Midodzi, Rowe, Majaesic, Saunders, Senthilselvan 2010	PubMed Academic Search Premier	Yes	8499 children; Canadian Early child Development study (ECD Panel 1). Followed from '96-97 to '00- 01; panel 2 from '98-99 to '02-03. Studied for 5 yrs	The ECB used questionnaires to gather information- data was obtained using computer assisted personal interviews in the home. At baseline- the children used had no history of reported asthma. Main study outcome was incidence of dx asthma at preschool age. Risk factors were obtained at baseline, one factor was breastfeeding, never, <3 months, or > 3months. No information on if BF was exclusive or not was discussed.	Of 8499 children, 27.4% had family hx of asthma in either parent and 57.2% were breastfed for more than 3 months. A higher incidence of dx asthma occurred in the preschool year in children with a hx of early wheezing. Study found that breastfeeding was associated with a significant reduction in the risk of developing asthma. Parental hx of atopy had a significant interaction with early wheezing and breastfeeding in regards to incidence of asthma. Results also similar in those w/out a family hx. In those never breastfed: 1844 (20.3% of sample), 17.6% had incidence of asthma. <3 months 1908 (22.6% of sample), 13.4% incidence of asthma and 3 months 4548 (57% of sample), 12.4% incidence of asthma
Kull, Melen, Alm, Hallberg, Svartengren et al 2010	PubMed	Yes	The Children Allergy milieu Stockholm an Epidemiologica l Study was used. It's a study of unselected pop based cohort study to assess for risk factors.- children enrolled from 94-96. 4089 subjects	At 2 months data on family hx of allergic dz was obtained. Follow up questionnaires on symptoms were done at 1,2,4, and 8. Information on breast feeding and age for into of complementary feeding was asked at 1 year. Children with answered questionnaires at 8 were asked to a clinical investigation, looking at lung function and blood samples. A total of 2370 were analyzed for IgE antibodies, inhalant allergens, and food allergens.	80% were EBF during first 4 months of life, 5% received breast milk in combo with formula at birth. Mean duration of EBF was 5 months, partial was 3.5 months. Children EBF for 4 months or more had an overall reduced risk of asthma during first 8 years of life. At each follow up the asthma was less prevalent. They also classified children with asthma into categories: 1-4 (not after) was transient late onset was after 4, and persistent 1-4 and after 4. Effect of BF was significant for kids with transient and persistent asthma, but not late onset. Breastfeeding effects did not differ in relation to parental hx. The duration of EBF and PBF was also categorized: 0 to <2, 2 to <4, and >4. For asthma, a reduced risk was "suggested" among children exclusively breast fed for 2 months or more, but stats significantly associations were consistently seen only for at least 4 months of EBF. Children who were EBF for 4 months or more had better lung function at 8 years

Author/Year	Database	Relation BF:Asthma	Subjects	Design	Results
Elliott, Henderson, Northstone, Chiu, Dunson et al 2008	PubMed	Yes	Prospective data from the Avon Longitudinal Study of Parents and Children that enrolled 14000 pregnant women and followed children through late childhood.	Data on breastfeeding was obtained from questionnaires about dietary and feeding habits included in 6 questionnaires sent to mothers during first 4 years of life. Breastfeeding duration was assigned to never, <1 month, 1 to <3 months, 3 to < 6 months, and 6+ months. Testing was done on bronchial hyper responsiveness as well	25% of children in this cohort were never breastfed, 25% were breastfed for at least 6 months and approximately 8.5% were breastfed for at least 4 months. Wheezing in the first three years of life was reported among 51% of questionnaire respondents with breastfeeding and covariate data-at 7.5 years of age it was at 10.5% of children. When adjusting for confounders' breastfeeding had a protective effect for early wheeze. The analysis comparing EBF for 4+ months with EBF for < 4 months does not suggest an increased risk among atopic children with asthmatic maternal hx. Also numbers were small in study-were only 6 asthmatic children among the 198 who were eBF for > 4 months. Children with wheeze reported by 3 months of age appeared to be breastfed for longer than children without early wheeze. Mean duration of breastfeeding for those without early wheeze was 6.6 months, those compared with 8.9 months for children with wheeze. Found evidence for a modest protective effect of breastfeeding on wheeze in first few years of life. Protective effect did not extend into later life
Kramer, McGill, Matush, Vanilovich, Platt et al 2007	PubMed Cinahl Academic Search Premier	No	Total of 170466 mother infant pairs were selected and 13889 were followed up at 6.5 years	Randomized cluster controlled trial-randomized to an intervention that promotes breastfeeding-specifically in promoting exclusively and duration among mothers who have already made decision to breastfeed. 2 randomized groups experimental/clinical were similar in social/clinical aspects. Experimental intervention was based on baby hosp initiative, developed by WHO to promote bfeeding. The control maternity hosp continued practices and policies in effect at the time of randomization	Experimental intervention led to a large difference in duration: 72.7 vs. 60% were still feeding at 3 months. 49.8% vs. 36.1% at 6 months. 36.1 vs 24.4 at 9 months and 19.7 vs. 11.4 at 12 months.

Author/Year	Database	Relation BF:Asthma	Subjects	Design	Results
Odijk, Kull, Borres, Brandtzaeg, Edberg et al 2003	Academic Search Premier PubMed	Mixed	Review of literature: Selected 132 studies for review, but 56 were thrown out.	Used a lit search from Medline articles published before October 2011. Words included for searches were breast-feeding, bronchial asthma, infant feeding, atopy, atopic disease, human milk. The researcher presented each article with comments from assessor, and the articles were discussed and evaluated by entire panel on certain criteria. Randomized controlled trials were used.	The group that studies breastfeeding and atopic manifestations in cross sectional population included 26 studies. Half of the studies reported that breastfeeding reduced risk of asthma. 3 out of 4 that focused on “any breastfeeding” indicated a decreased risk of recurrent wheeze, asthma-protective effect reported to persist for 5 plus years and increased with duration of breastfeeding up to at least 4 months. 2 out of 6 studies reported no effect of breastfeeding on asthma. . Another 5 of 6 studies noted a protective effect of breastfeeding. One problem is mothers who breastfed might be ones that have hx of asthma/atopic dz themselves, could mask the protective effect as they are already genetically predisposed.
Strassburger, Vitolo, Bortolini, Pitrez, Jones et al 2010	PubMed	Yes	397 children were followed 1 st yr of life. A age 3 and 4, 354 of those were reassessed. Subjects picked from a hospital nursery	Cohort study, randomized trial. One group received guidance on benefits of exclusive breastfeeding –while the control group did not receive guidance. Study took place in brazil. Home visits from trained profs were conducted at 6, 12 months and between ages 3 & 4. AT 6 months info was collected on EBF. At 12 months food s that had been introduced were reviewed. Important variables were included-esp that of duration of breast-feeding .To evaluate for asthma a questionnaire was given on wheezing and asthma. No medical dx.	354 were assessed initially in second phase- of those 347 answered questions adequately. In last 12 months prior to home visit prevalence of wheezing was 21.3% and asthma was 5.5 % . Only 1/3 of children were EBF beyond 4 months. Crudes odd ratio showed that those with genetic predispositions had higher chances of wheezing. Ebf up to 4-6 months of age was not associated with wheeze at 4 y/o- only maternal h/o of rhinitis was associated with wheeze. Only found that children given cows milk before 4 months were significantly more likely to have asthma. In crude bivariate analysis- asthma at 4 was 4 times greater for children with maternal hx.

Author/Year	Database	Relation BF:Asthma	Subjects	Design	Results
Nagel, G., Buchele, G., Weinmayr, B., et al 2009	PubMed	Yes	54, 943 children aged 8-12 were included	Cross sectional studies were performed in 27 health centers in 27 countries. Information was collected by questionnaire. Data on breastfeeding was conducted retrospectively, with categorization of breastfeeding in place. Exclusiveness of breastfeeding was also assessed. Skin prick tests and spirometry was performed. These tests were performed in full samples or sub samples.	Breastfeeding was inversely associated with wheeze during the psat year, in affluent and no affluent countries. In nonaffluent countries breastfeeding for > 6 months was associated with less wheeze. In affluent countries EBF for 2-4 was significantly inversely associated with wheeze.. Any breastfeeding was related to a reduced lifetime prevalence of asthma in affluent countries and similarly in nonaffluent countries. The association between any breastfeeding and wheeze were not affected by maternal atopy in affluent countries. Breastfed children tended to have better lung function in affluent countries.
Greer, Sicherer, Burks 2008	PubMed Academic Search Premier Cinahl	No	Meta analysis of 12 prospective studies	Meta Analysis.	2001 meta-analysis of 12 prospective studies found that EBF for at least 3 months was protective against development of asthma between 2 and 5 years of age. Effect of bf was stronger when analysis was limited to those with family hx of asthma. However, a 2002 cochrane review found no benefit of EBF beyond 3 months on incidence of asthma. Another study found that infants who had maternal hx of asthma were at greatest risk of developing asthma when EBF for >4 months. An increased risk of developing asthma was not found in breastfed children without a maternal hx. However same study found that EBF was significantly associated with lower rates of wheezing in infancy. Another study found that breastfeeding for more than 4 weeks significantly increased the risk of developing asthma at 9 years and 21 years. – summary: it is not possible to conclude that EBF protects against development of asthma.

Author/Year	Database	Relation BF:Asthma	Subjects	Design	Results
Sears, Greene, Willan, Taylor, Flannery 2002	Cinahl PubMed Academic Search Premier	No	Subjects included 1037 children born between 72 and 73.	Longitudinal study. 2 groups: breastfed and non-breastfed were created. Children were assessed q 2-5 years from age 9-26 with respiratory questions, pulmonary function, and bronchial challenge. h/o breastfeeding recorded in early childhood via interviews at 3 years of age. These interviews were verified with the New Zealand Plunket Nurse program. This program required newborns and infants to be assessed through home and clinic visits until 2-3 year of age. Family hx was asked to caregiver (usually mom) who was with child at 7 and then again obtained at 18 years. During adult years this study used questionnaires derived from American Thoracic Society. Spirometry was done on assessments from 9-26	Of 1037 in the study, 45% were not breastfed. 7% of children were breastfed for <4 weeks- these children were included in non breastfed group. Total 51% of children not breastfed. Mean duration of BF in comparison group (49%) was 21 weeks, however not necessarily EBF. At age 9 year, more children who were breastfed had been dx with asthma, currently had asthma, and had current wheeze compared with those not breastfed. This persisted with all ages to 26 years. Relationship with BF remained strong when airway hyper-responsiveness was needed for a confirmation of dx of asthma-or that the wheezing was caused by asthma. Therefore those breastfed were more than twice as likely to have wheeze with AHR or current asthma with AHR. More children with a parental history of asthma developed asthma; effects of BF were not influenced by family hx. They did not find a sig effect of EBF and protective effect, but the incidence of EBF could not be firmly documented.
Guilbert, Stern, Morgan, Martinez, Wright 2006	Cinahl PubMed Academic Search Premier	Yes	679 participants -infants	Population based cohort. Feeding practices were assessed prospectively based on forms completed by the child's pediatrician at age 2,4,6 and 9 months. Categorized into 3 groups: BF for less than or equal to 1 month, BF for 2 to <4 months, and BF for 4+ months. Detailed respiratory questionnaires were completed by caregiver for child at age 6, 11, and 16, parental hx of asthma also obtained. Lung function tests were performed at age 11 and 16	Longer breastfeeding was associated with significantly increased FVC and decreased FEV/fvc ratio at age 11 and similarly at age 16. Relationship changed when adjusting for maternal asthma-among longer breastfed children with mothers with asthma, FVC was not increased and ratios were significantly decreased at age 16. Children with early introduction of formula had decreased FVC when compared with the children with longer breastfeeding. However, breastfeeding was not associated an improvement in airflow. Breastfeeding to lung function was influenced by maternal hx.

Author/Year	Database	Relation BF:Asthma	Subjects	Design	Results
Ogbuanu, Karmus, Arshad, Kurukulaaratchy, Ewart 2009	PubMed Academic Search Premier	Yes	Children from 89-90 children were selected. A total of 1456	Prospective cohort study. BF practices and duration were prospectively assessed at birth and at 1 & 2 years of age. At ages 1,2,4, 10 a study physician performed physical exams on children and symptoms of asthma were recorded. Age 10 lung function tests were recorded. Questionnaires collected including info on asthma and family hx of asthma. Breastfeeding duration put into 4 groups; never BF, BF for <2 months, BF for >2, but <4, BF for at least 4 months.	Those who were breastfed for at least 4 months had FVC values that were larger than those who weren't breastfed. FVC- forced vital capacity. Children who were breastfed for 4 months of longer had sig higher PEF-peak expiratory flow. In all models, BF for <4 months did not show significant beneficial effects on lung function. They did not find any relationship between maternal history and asthma.
Silvers, Frampton, Wickens, Epton, Pattermore et a 2009		Yes	Used the New Zealand asthma and Allergy Cohort Study. Expectant mothers (1105 children) sought between 97-01	Prospective Cohort study. Detailed information about infant feeding was collected using questionnaires after birth and at 3, 6, and 15 months. Duration was categorized into exclusive or any breastfeeding. 16.8% were BF up until the 15 month mark. Mothers were asked about respiratory outcomes several regarding asthma and wheezing. Parental hx of asthma was included in a separate analysis.	Of 1105 enrolled, 1011 were included in study results. EBF data was restricted to 987 r/t uncompleted questionnaires. Mean duration of EBF was 1.4 months and any breastfeeding was 9 months. Longer durations of both were associated with significant reduction in the risk of adverse respiratory outcomes. After adjustment for cofounders- each month of EBF reduced risk of dx asthma by 20%, wheeze by 12%-wheeze, dx asthma, and inhaler use by 24% and current asthma by 21%. Study demonstrates that children with lowest risk are those that were EBF for at least 3 months