

Delayed Administration of Diphtheria, Pertussis, Tetanus Vaccine and Risk of Development of Childhood Bronchial Asthma

Thesis

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Presented By

Engy Mahmoud Mahmoud Mustafa Hamza

M.B., B.Ch.

Supervised By

Prof. Mohamed Nasr El-Din El-Barbary

Professor of Pediatrics

Faculty of Medicine, Ain Shams University

Dr. Rania Ibrahim Hossni Ismail

Lecturer of Pediatrics

Faculty of Medicine, Ain Shams University

**Faculty of Medicine
Ain Shams University
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List of Abbreviations

AIA	Aspirin-Induced Asthma
AIT	Allergen immunotherapy
BA	Bronchial Asthma
BCG	Bacille de Calmette et Guérin vaccine
BHR	Bronchial Hyper-responsiveness
BTS	British Thoracic Society
CDC	Centers for disease control and Prevention
DTP	Diphtheria, Tetanus and Pertussis vaccine
EIA	Exercise-induced asthma
FEV	Forced Expiratory Volume
FVC	Forced vital capacity
GERD	Gastroesophageal Reflux Disease
GM-CSF	Granulocyte Monocyte-colony Stimulating Factor
GSK159797	GlaxoSmithKline 159797
HR	Hazard Ratio

HS	Highly significant
ICS	Inhaled Corticosteroids
IFN	Interferon
IL	Interleukin
ISAAS	International Study of Asthma and Allergies in Childhood
LABAs	Long Acting β 2 Agonists
LBW	Low Birth Weight
LTRAs	Leukotriene Receptor Antagonist
mAPI	Modified asthma predictive index
MMR	Measles, Mumps, Rubella vaccine
NHIS	American National Health Interview Survey Immunization Supplement
PAMP	Pathogen-associated molecular patterns
PEF	Peak Expiratory Flow
PEFR	Peak Expiratory Flow Rate
P _a CO ₂	Arterial Carbon dioxide
PFTs	Pulmonary function tests

PaO ₂	ArterialOxygen
RAST	Radioallergosorbent test
SABA	Short Acting β 2 Agonists
SIGN	Scottish Intercollegiate Guidelines Network
SpO ₂	Peripheral capillary oxygen saturation
SPSS	Statistical package for social science
Tdap	Acellular pertussis vaccine
Th1	T-helper 1
Th2	T-helper 2
TLR	Toll-like receptors
WHO	World Health Organization

Introduction

Asthma is a chronic inflammatory disorder of the airways characterized by an obstruction of airflow, which may be completely or partially reversed with or without specific therapy. Airway inflammation is the result of interactions between various cells, cellular elements, and cytokines. In susceptible individuals, airway inflammation may cause recurrent or persistent bronchospasm, which causes symptoms that include wheezing, breathlessness, chest tightness, and cough, particularly at night (early morning hours) or after exercise. Airway inflammation is associated with airway hyperreactivity or bronchial hyperresponsiveness (BHR), which is defined as the inherent tendency of the airways to narrow in response to various stimuli (eg, environmental allergens and irritants) (**National Heart, Lung, and Blood Institute, 1995 & Bateman et al., 2011**).

The prevalence of asthma is about 13% of the world's population, and this prevalence is still rising (**National Heart, Lung and Blood Institute, 2005 & Bateman et al., 2011**).

Childhood asthma is one of the most common childhood diseases in the developed world. The rising prevalence of asthma in many industrialized countries over the last quarter century has occurred alongside improvements in hygienic standards and immunization.

Several studies have suggested either a provocative or protective effect of immunization depending on the specific vaccine, the target population, and the age at which the vaccine was administered and vaccination delays (**Mullooly et al. , 2002 & McDonald et al., 2008**).

Recent evidence indicates that the association with childhood asthma is dependent on the timing of exposure to microbes. Different schedules for immunization may explain the discrepant findings of an

association with asthma reported in observational studies of vaccinated children (**Williams et al.,2005**).

There are two proposed mechanisms by which immunization may influence the development of allergic disease. The first is that vaccination could have a direct impact on the immune system, and there is evidence that pertussis vaccine enhances humans' response to histamine (Sen et al., 1974) and leads to raised immunoglobulin E levels (Odelram et al., 1994). The evidence that early childhood immunizations promote the development of asthma is based on the detection of an IgE response to vaccine antigens in the sera of children vaccinated with diphtheria/tetanus, and the IgE response to vaccine antigens is more pronounced among atopic individuals (**Dannemann et al.,1996 & Nilsson et al.,1998^a**).

The second potential mechanism is commonly known as the hygiene hypothesis (**Strachan,1989 & Karmaus and Botezan, 2002**).