INTRODUCTION

The prevalence of atopic asthma, allergic rhinitis and atopic dermatitis had exhibited over a 3-fold rise over the past 25 years in many countries Worldwide. This had been attributed to a variety of factors including environmental pollution ***(Cookson, 2008).***

Mesquites belong to the Fabaceae (legume) family. The genus Prosopis L. contains 44 species. Mesquite species are found in arid regions of North and South America (especially Argentina), South Africa and tropical Africa and Asia. Mesquite (Prosopis juliflora) is a major cause of allergic disease in the southwestern United States ***(Novey et al.,2000; Bieberdorf and Swinny, 2001)***, Mexico ***(Bessega et al.,2000)***, Saudi Arabia, South Africa ***(Al-Frayh et al.,2000; Ezeamuzie et al.,2000)***, Kuwait ***(Davis, 2000)***, United Arab Emirates (UAE) ***(Bener et al., 2002)***, and India ***(Thakur, 2003).*** Prosopis juliflora is a legume with several variations ***(Bieberdorf and Swinny, 2001)*** that has been used for the reclamation of desert lands and as a wood resource ***(Al-Frayh et al.,2000; Thakur, 2003)***, with the end result that its easily dispersed and its far-traveling pollen is an abundant and significant source of allergens In addition to pollen exposure, the burning of mesquite wood and its resulting smoke may be another source of exposure to some of these same allergens ***(More et al.,2002; Johns et al.,2001).***

Allergen immunotherapy has been used for the treatment of allergic diseases since 1911 as a result of the pioneering clinical work of Noon ***(Noon, 1911)*** and Freeman. This therapy involves injection of specific allergens that alter the immune system's responses and decrease sensitivity to those allergens. The practice of immunotherapy has changed substantially over the last two decades

Specific cluster immunotherapy with relevant allergy vaccines using standardized extracts consistently results in the amelioration of symptoms, significant reduction in the cost of medications and the complete resolution of allergic manifestations in a considerable number of cases ***(Portnoy, 2001; Larche, 2000; Theodoropoulos and Lockey, 2000).*** Moreover, specific Immunotherapy is the only therapeutic modality of allergic diseases that has a potential of inducing complete cure ***(Creticos, 2001; Bousquet et al., 2001).***

AIM OF THE WORK

The aim of the present study is to study the prevalence of sensitization to Mesquite tree pollens among Egyptian children with different allergic diseases (bronchial asthma, allergic rhinitis, atopic dermatitis and atopic conjunctivitis) and the efficacy of specific cluster immunotherapy against Mesquite pollens.

1. PEDIATRIC BRONCHIAL ASTHMA

Definition

Asthma is a chronic inflammatory condition of airways resulting in episodic airflow obstruction. Other associated histopathologic abnormalities of the airways characteristic asthma include epithelial damage, subepithelial collagen deposition, membrane thickening, and mucus gland smooth muscle hypertrophy ***(Lieu et al., 2004).***

Asthma may have its onset at any age, 30% of patients are symptomatic by age of one year, whereas 80-90% of asthmatic children have their first symptoms before 4-5 years of age ***(Sly, 2005).***

Although most cases begin before the age of 25 years asthma may develop at any time of life ***(Drazen, 2006).***

Worldwide prevalence of asthma:

Over the past 30 years, the prevalence of asthma has increased to epidemic proportions in developed countries, and asthma is the most common chronic diseases in children ***(Arroda et al., 2006).***

Risk factors for asthma and atopy:

Genetic factors:

Asthma is a complex genetic disorder with variable phenotypes, largely attributed to the interactions of the environment and multiple genes ***(Arroda et al., 2006).***

Numerous loci and candidate genes have been reported to show linkage and association of asthma and asthma associated phenotypes, atopy, elevated IgE levels, and bronchial hyper-responsiveness, to alleles of microsatellite markers and single nucleotide polymorphism (SNPs) within specific cytokine, chemokine and Ig E regulating genes; however, only a few genes conferring significant risk have been mapped ***(Vercelli et al.,2003).***

The clinical implications of the genetic variations within these genes remain undetermined ***(Hershey, 2004).***

Familial factors of asthma:

The familial aggregation in asthma has provided support for a genetic component. The presence of aggregation among related individuals may indicate either shared genes or a common household environment. A study of monozygotic twins showed higher concordance rates than in dizygotic twins ***(Arroda et al., 2006).***

A history of asthma in the mother is associated with a larger increase in asthma risk. It is feasible that maternal effects on the developing immune system are confined not only to the fetal period but might also influence the postnatal period through breast milk and environmental conditions ***(Kuyucu et al., 2004).***

Gender and asthma:

Male sex is a risk factor for asthma up to the age of puberty. This explanation for this difference is not very clear.

Boys have lower maximal expiratory flows a given lung volumes than girls. Probably, in the first year of life, immune factors (boys are more sensitized and atopic) and lung- specific factors are both important. The prevalence of asthma in boys and girls changes during puberty and hormonal changes have been implicated in the reversal of sex ratio, probably including early menarche. Also, airways size increases more rapidly in boys than in girls ***(Osman, 2003).***

Maternal effects:

Children born from parents with asthma or atopic disorders present an increased risk of developing similar disease, maternal factors, placental factors, or both may an impact on perinatal allergic sensitization ***(Arroda et al., 2006)***

Exclusive breast feeding for at least 6 months has been associated with protection for development of asthma or atopic diseases ***(Oddy, 2004),*** but other studies have failed to demonstrate this protection by breast milk ***(Sears et al., 2002)***

Atopicdermatitis and allergic rhinitis as risk factors for asthma:

Most patients with asthma present symptoms in the first year of life. Prospective studies have aimed to identify predictive factors for asthma, and an asthma predictive index (API) has been developed ***(Guilbert et al., 2004).***

The API was determined on frequent wheezers, defined as those children who presented more than three episodes of

wheezing within a year, during the first 3 years of life. A positive API is met when a frequent wheezers has either one major criterion (physician- diagnosed atopic dermatitis or physician – diagnosed parental asthma) or two minor citeria (peripheral blood eosinophilia > 4%, wheezing apart from cold, or physician diagnosed allergic rhinitis). The API has a positive predictive values of 47.5% and a negative predictive value of 91.6% for the development of asthma at age of 6 years, and these values have not changed significantly with age, from ages 6 to 13 years ***(Guilbert et al., 2004)***.

The identification of allergic rhinitis as a risk factor for asthma was highlighted in the guidelines developed by the allergic rhinitis and its impact on asthma workshop ***(Bousquet et al., 2001).***

Perroni et al., (2003) showed that the presence of rhinitis was a risk factor for physician – diagnosed asthma, asthma symptoms, atopic dermatitis and allergic sensitization in preschool children, using the International Study of Asthma andAllergies in Childhood **(ISSAC)** protocol.

Atopic dermatitis which is the first manifestation of atopic march, has been identified as a risk factor for development of asthma ***(Perroni et al., 2003).***

The September epidemic of asthma exacerbations in children:

Epidemics of asthma exacerbation requiring hospitalization of children during the month of September have been reported in many northern hemisphere countries, including Canada, the United States, the United Kingdom, Mexico, Israel, Finland and Trinidad ***(Johnston et al., 2005).***

Between 20% and 25% of all asthma exacerbations of children requiring hospitalization in Canada occur in September ***(Jonathan et al., 2003).***

Viral respiratory tract infections, particularly of rhinoviruses, are associated with exacerbations of asthma in children ***(Chauhan et al., 2003)*** and adults ***(Corne et al., 2002).***

In the northern hemisphere, descriptive studies have identified peaks in asthma hospitalization after school return, particularly after the summer vacation, and have linked these to coincident higher rates of respiratory tract infection, but have not established a causal relation of the 2 phenomina ***(Johnston et al., 2005).***

Rhinovirus infections are the predominant cause of respiratory infections in children in the early fall ***(Gern and Busse, 2007).*** Between 80% and 85% of children with acute wheezing episodes test positive for respiratory viruses, predominantly rhinovirus, in both hospital ***(Thumerelli et al., 2003)*** and community settings.

The peak periods for rhinovirus infection are quite distinct from those for influenza virus, occurring in the early fall and to a lesser extent in the spring. Rhinovirus infections have been demonstrated to increase in frequency in September a few days after school return ***(Johnston et al., 2005***).

Etiology of asthma

Asthma can be triggered by many agents, including allergens, viral infection, and airways irritants, that induce inflammation and both airway hyper-responsiveness and airflow obstruction. airflow obstruction in asthma results from one of a number of events, including acute broncho-constriction, airway oedema, mucus plug formation and airway remodeling ***(Solomon, 2003)***.

Pathogenesis:

The pathologic changes linked to persistent airways inflammation and hyper-responsiveness underlie the chronic basis of asthma ***(Liu et al., 2004)***. Airway obstruction results in increased resistance to airflow and premature closure of the smaller airways. These changes lead to a decrease ability to expel air and result in hyperinflation ***(Barnes, 2003).***

Airway inflammation is a characteristic feature of asthma and contributes significantly to many features of this disease. many inflammatory cells contributes to airway inflammation in asthma including activated mast cells, lymphocytes, particularly the TH2 sub-population of cells, which release a family of pro-inflammatory cytokines including IL-4, IL-5 and IL-13 ***(Lemanske and Busse, 2003).***

Cell involved in the pathogenesis of asthma:

1- Mast cells:

Although the classic role of IgE–induced mast cell release of preformed mediators of inflammation (e.g. histamine) in causing acute bronchospasm and airway edema has been long recognized, mast cells also contribute to the maintenance of mucosal inflammation via release and new synthesis of proinflammatory mediators. Mast cells contain a number of proteases.

Mast cells can be classified according to the contents of their granules into; cells that contain tryptase (MCT) and their growth and proliferation are primarily regulated by interleukin-6 (IL-6) and interleukin-9 (IL-9), cells contain chymase (MC ct) as well and they are mostly influenced by fibroblasts growth factors and stem cell factors, these substances probably play a role in chronic asthma ***(Kercsmar, 1999)***.

2- T-lymphocytes:

Lymphocytes may play a key role in the complex inflammatory reaction in asthma. Although both T,B lymphocytes are found in the airways, most of the lymphocytes are of T cells, with the CD4+ population predominating, particularly in the airways of atopic asthmatics, CD8+ Tcells may also be increased in patients with asthma specially in non atopic subjects ***(Azzawi et al., 2000).***

3- Eosinophils:

Eosinophils are known to play a vital role in asthma. Airway inflammation, infiltration of eosinophils into the

distinctive features of asthma, these bronchial changes involve four steps–namely, enhanced eosinophil production, recruitment of lung tissue, activation of eosinphil, and release of mediators ***(Jang et al., 2003).***

4- Basophils:

Increased number of basophils have been found in the blood and sputum of asthmatic patients during clinical exacerbations of the disease. Upon activation, basophils release a number of mediators including both preformed and newly formed molecules, preformed mediators include histamine and chondrotine sulphate ***(Kaplan et al., 2001).***

5- Macrophages:

Macrophages are found in the airways and bronchi of asthmatic patients. They take up foreign protein (such as allergen), to process these allergens, to present them to sensitized T cells that bear the appropriate α β T –cell receptor, and to activate these cells to proliferate and produce cytokines., macrophages have secretory products, these include bioactive lipids such as leukotriens and cyclooxgenase products and platelet activating factors, reactive oxygen intermediates, and nitric oxide and nitrites, hence they may have important effects on vascular smooth muscle tone and on bronchial epithelial cells. Therefore it is clear that macrophages can have the capability of playing a significant role in airway inflammation ***(Rosen et al., 2006).***

6-Neutrophils:

There is increase evidence that neutrophils may play a role in acute severe asthma. Prominent neutrophilic inflammation has been demonstrated in fatal asthma of sudden onset. Neutrophil numbers and activation are also increased in the airways of subject with status asthmatics and during exacerbations of asthma ***(Jatakanon et al., 2006).***

Table (1): Showing triggers of asthma.

- Common viral infections of respiratory tract
- Aeroallergens in sensitized asthmatics
- Animal dander
- Indoor allergens
  - Dust mite
  - Cockroaches
  - Molds

* Seasonal aeroallergens
  - Pollen (grasses, trees, weeds).
  - Seasonal molds

* Environmental tobacco smoke
  - Ozone
  - Sulfur dioxide
  - Particulate matter
  - Wood or coal – burning smoke
  - Dust

Table (1): Continued

* Strong or noxious odours or fumes
- Perfumes, hairsprays
- Cleansing agents
* Occupational exposures
Farm and barn exposures
Formaldehyde, cedar, paint fumes
* Cold hair, dry air
* Exercise
* Crying, laughter, hyperventilation
* Co-morbid conditions
- Rhinitis
- Sinusitis

(Lieu et al., 2004)

Table (2): Showing classification of asthma.

	Symptoms	Nighttime symptoms	Lung function
Severe persistent	• Continual symptoms • Limited physical activity • Frequent exacerbations	Frequent	FEV, or PEF≤60%
Moderate persistent	• Daily symptoms • Daily use of inhaled Short-acting β 2 agonist • Exacerbations affect activity • Exacerbations ≥ 2 times a week; may last days	>1 time a week	FEV or PET >60% <80 predicted
Mild persistent	• Symptoms >2 times a week but <1 time a day • Exacerbations may affect activity	>2 times a month	FEV, or PEF≥80% predicted
Mild intermittent	• Symptoms ≤2 times a week. • Asymptomatic and normal PEF between exacerbations • Exacerbations brief (from a few hors to a few days); intensity may vary	≤2 times a month	FEV, or PEF≥80% predicted

(Wilmott et al., 2002)

Table (3): Showing diagnosis of asthma can be considered if any of the following signs or symptoms are present.

- Wheezing-high-pitched whistling sounds when breathing out especially in children (a normal chest examination does not exclude asthma).
- History of any of the following:
  - Cough, worse particularly at night
  - Recurrent wheeze.
  - Recurrent chest tightness (Note: eczema, hay fever or a family history of asthma or atopic disease are often associated with asthma).
- Symptoms occur or worsen at night, awakening the patient
- Symptoms occur or worsen in the presence of:
  - Animal with fur
  - Aerosol chemicals
  - Changes in temperature
  - Domestic dust mites
  - Drugs (aspirin, β-blockers)
  - Exercise
  - Pollen
  - Respiratory (viral) infection
  - Smoke
  - Strong emotional expression
- Reversible and variable airflow limitation-as measured by using a spirometer (FEV1) or a peak expiratory flow (PEF) meter, when using a peak flow meter, consider asthma if:
  - PEF increases more than 15 percent 15 to 2) minutes after inhalation of a rapid – acting β 2-agonist, or
  - PEF varies more than 20 percent from morning measurement upon arising to measurement 12 hours later in patients taking a bronchodilators (more than percent in patients who are not taking a bronchodilators).
  - PEF decrease more than 15 percent after 6 minutes of sustained running of exercise.

(GINA, 2002)