

**Sensitization To Aeroallergens In
Patients With Chronic Urticaria Without
Allergic Respiratory Symptoms**

Thesis

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Contents

	<u>Page</u>
List of abbreviation	I
List of graphs	III
List of figures	IV
List of tables.....	V
Introduction.....	1
Aim of the work	2
Review of literatures	
I. Allergic diseases	3
II. Chronic urticaria	34
III. Inhaled allergens	99
Patients and methods.....	112
Results	122
Discussion	145
Summary	158
Conclusion and recommendations	161
References.....	162
Arabic summary	

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List of Abbreviations

Ach E	: Acetylcholinestrase
AHR	: Airway hyperresponsiveness
APC	: Antigen presenting cells
BHR	: Bronchial hyper-responsiveness
C1INH	: C1 inhibitor
CLD	: Chronic liver disease
CRF	: Chronic renal failure
CU	: Chronic urticaria
DM	: Diabetes
DPU	: Delayed pressure urticaria
EIA	: Exercise induced anaphylaxis
FSU	: Fixed solar urticaria
HAE	: Hereditary angioedema
HD	: House dust
HTN	: Hypertension
IgE	: Immunoglobulin E
IL	: Interlukin
INF	: Interferon
ISHD	: Ischemic heart disease
IVIG	: Intravenous immunoglobulins
MCT	: Mast cell tyrptase
MCTC	: Mast cell tyrptase chymase
MM	: Mixed molds
MP	: Mixed pollens

List of Abbreviations (Cont.)

N	: Number
PG	: Prostaglandin
PIT	: Phagocytic inhibition test
Pt	: Patient
RASP	: Radio-allergisorbant procedure
RAST	: Radio-allergisorbant test
SCIT	: Subcutaneous immunotherapy
SD	: Standard deviation
SLIT	: Sublingual immunotherapy
SPT	: Skin prick test
Tcyt	: T cytotoxic
TGF- β	: Transforming growth factor $-\beta$
Th1	: T helper cells 1
Th2	: T helper cells 2
TNF	: Tumor necrosis factor
Treg	: T regulatory
TSLP	: Thymic stimulation lymphopoietin
UV	: Urticarial vasculitis
UVB	: Ultraviolet B waves
VEGF	: Vascular Endothelium Growth factor

List of Tables

	<u>Page</u>
Table 1: Classification of urticaria.	43
Table 2: Comparison between skin test and blood tests.	70
Table 3: Antihistaminics and their duration of action.	75
Table 4: Distribution of the patients according to etiology:	122
Table 5: Master sheets (Study group).	124
Table 6: Master sheet (control group).	127
Table 7: Shows the number of individuals tested positive only to aeroallergens in study and control group	128
Table 8: Comparison between both group (study & control) as regards general data (n=30).....	129
Table 9: Shows distribution of study group as regards disease duration	130
Table 10: Compare the study and control as regards sensitization to single or multiple inhaled allergens according to skin test results:	131
Table 11: Prevalence of the allergens in study group according to skin test results:	133
Table 12: Distribution of allergens in control group according to skin test results	135
Table 13: Distribution of studied cases according to skin test results	136
Table 14: Prevalence of allergens according to PIT results	137
Table 15: Distribution of studied cases as regards PIT results:.....	138
Table 16: Distribution of studied cases as regards results total IgE(n=30).	139
Table 17: Comparison between SPT results versus PIT in relation to specific IgE among studied cases	140
Table 18: Comparison between USS score levels before and after immunotherapy among studied cases: (n=12)	141
Table 19: Comparison between total IgE level before and after immunotherapy among the studied.....	143
Table 20: Comparison between specific IgE levels of mite before and after immunotherapy among the studied cases:	144

List of Figures

	<u>Page</u>
Figure 1: Response of mast cells on exposure to allergens.....	7
Figure 2: Eosinophils activation and mediators release.....	12
Figure 3: Basophils Netter's Essential Histology	13
Figure 4: Eosinophils Netter's Essential Histology	13
Figure 5: Mast cells Netter's Essential Histology immune cells.....	13
Figure 6: Regulation of lung eosinophil responses	22
Figure 7: Molecular and cellular control of the major atopic diseases.....	23
Figure 8: Different urticarial lesion.....	37
Figure 9: Angiodema.....	37
Figure 10: Dermographism	37
Figure 11: Solar urticaria	54
Figure 12: Cholinergic urticaria.....	54
Figure 13: Diagnostic approach in patients of urticaria.....	57
Figure 14: Skin test on the forearm in our allergy clinic.....	61
Figure 15: Patch skin test	65
Figure 16: The binding of serum IgE to the high affinity IgE receptor on basophil granulocytes and mast cells.....	92
Figure 17: Chimeric antibody made of both mouse and human antibody.....	92
Figure 18: Dust mites	103
Figure 19: Dust mites by light and electron microscopy	103
Figure 20: Pscoptera (book louse).....	103
Figure 21: Domestic coacrach.....	104
Figure 22: Asprigellous.....	107
Figure 23: Penicillium.....	107
Figure 24: Rhizopus.....	107
Figure 25: Mucor.....	108
Figure 26: Birch pollen tree	110
Figure 27: Birch pollen under light and electron microscopy	110

List of Graphs

	<u>Page</u>
Graph 1: Causes of choronic urticaria	123
Graph 2: Number of individuals tested positive in both study and control group	128
Graph 3: Distribution of the patients as regard disease duration.....	130
Graph 4: Comparison between study and control group as regards number of allergens detected by skin test	132
Graph 5: Prevalence of allergens in study group according to skin test results.....	134
Graph 6: Distribution of allergens in control group according to skin test results	135
Graph 7: Distribution of studied cases according to skin test results	136
Graph 8: Prevalence of allergens according to PIT results.....	137
Graph 9: Distribution of studied cases as regards results total IgE (n=30).....	139
Graph 10: Comparison between USS score levels before and after immunotherapy among studied cases: (n=12)	142
Graph 11: Comparison between total IgE level before and after immunotherapy among the studied	143
Graph 12: Comparison between specific IgE levels of mite before and after immunotherapy among the studied cases.....	144

Introduction

The etiology of chronic urticaria and angioedema remains uncertain in most of patients. There are several agents and factors including medications, foods, food additives, infections contact ants, physical factors and autoimmunity that are implicated in provoking urticaria symptoms.^[227]

In addition, the possible role of inhalant or aeroallergens has been considered in few reports,^[228] further more, urticaria as a sole clinical manifestation in inhalants allergy sensitive patients is unusual (airborne urticaria).

A possible association of house dust mite sensitivity with chronic urticaria was described by **Mahesh et al.**^[233]. Also, urticaria was statistically significantly associated with sensitization to pollens^[252].

Stokli and Bricher^[287] described patients with urticaria provoked by tobacco inhalation. The same observation was described by **Heudorf et al.**^[288] as a significant association between dermal symptoms and passive smoking in children was found.

In practice, skin test positive to aeroallergens is found in some cases of chronic urticaria, this can be due to concomitant respiratory allergy.^[81]

Aim of the Work

The aim of this study is to investigate the possible role of aeroallergens in provoking chronic urticaria in patients without allergic respiratory diseases.

I - Allergic diseases

The term (allergy) was introduced in 1906 by Von Pirquet, who recognized that in both protective immunity and hypersensitivity reactions, the term (Atopy) (from the greek atopos, meaning out of place) is often used to describe IgE mediated diseases.

The clinical symptoms of allergy are caused by cellular (IgE-triggered) responses to an allergen. Effector cells of allergy include eosinophil and basophil granulocytes, as well as tissue mast cells. Growth and accumulation, as well as IgE-dependent and independent functions of these cells are regulated by distinct proteohormones and peptides.^[1]

Cells Involved in Allergic Responses:

Basophil leukocytes and tissue mast cells are inflammatory cells that are found in virtually all human tissues. They appear to be involved in the pathogenesis of such allergic diseases as allergic rhinitis, bronchial asthma, anaphylaxis, atopic and contact dermatitis, chronic urticaria, and hypersensitivity pneumonitis. By releasing a variety of chemical mediators, they could also play a role in the pathophysiology of a wide range of inflammatory disorders of the joints, and of intestine, lung, coronary, and myocardial diseases.^[2]

Basophils and mast cells are effector cells in allergen/IgE-mediated immune responses. They induce type 1

immediate immune response in airway or other organ, resulting in bronchial asthma and other allergic diseases. However, they also play a critical role in host defense against infection with helminthes.^[2]

Upon linkage of FcεRI with a complex of allergen and IgE, basophils and mast cells release a large amount of Th2 cytokines and chemical mediators. Therefore these responses are "acquired allergic responses" and induce allergic diseases, such as bronchial asthma.^[3]

Although these two cell types are similar in several aspects, striking differences have also been observed. Moreover, human mast cells from different anatomical sites and within an individual tissue synthesize different mediators and have different release mechanisms.^[2]

Mast Cells:

Mast cell (or mastocyte) is a resident cell of connective tissue that contains many granules rich in histamine and heparin.^[4]

Mast cells were first described by Paul Ehrlich in his 1878 doctoral thesis on the basis of their unique staining characteristics and large granules. These granules also led him to the mistaken belief that they existed to nourish the surrounding tissue, and he named them "Mastzellen" (from the Ancient Greek *masto*, "I feed").^[4]

Mast cells are very close to basophil granulocytes (a class of white blood cells) in blood; the similarities between

mast cells and basophils has led many to speculate that mast cells are basophils that have "homed in" on tissues.^[4]

However, current evidence suggests that they are generated by different precursor cells in the bone marrow. Nevertheless, both mast cells and basophils are thought to originate from bone marrow precursors expressing the CD34 molecule. The basophil leaves the bone marrow already mature, whereas the mast cell circulates in an immature form, only maturing once in a tissue site. The tissue site an immature mast cell chooses to settle in probably determines its precise characteristics.^[4]

Two types of mast cells are recognized, those from connective tissue and mucosal mast cells. The activities of the latter are dependent on T-cells.^[5] Immunocytochemical studies have shown the presence within the tissues of two mast cell phenotypes distinguishable by their neutral protease content, the MC T(mast cell tryptase) phenotype containing only tryptase and the MC TC MC T(mast cell tryptase chymase) phenotype containing both tryptase and chymase.^[6]

IgE Initially, these respective subtypes were suggested to be the equivalents of the "mucosal" and "connective tissue" previously described in experimental animals. However, it is now realized that variable amounts of both mast cell subtypes are present within any given tissue; their relative abundance changes with disease (e.g., in allergy or fibrosis).^[6]

However, some rules are becoming apparant, Thus MC T phenotypes appear to be “immune system–related” mast cells with a primary role in host defense, whereas MC TC phenotypes appear to be “non-immune system–related” mast cells with functions in angiogenesis and tissue remodeling rather than immunologic protection. However, it should be remembered that both phenotypes express FcεRI and may therefore participate fully in IgE-dependent allergic or parasitic reactions.^[6]

The production of a wide range of cytokines by mast cells in response to activation by allergen places the mast cell in the center of the allergic inflammatory response.^[7] These cytokines may lead to eosinophil, basophil, and T cell recruitment. Coordinated production of IL-4 and IL-5 by TH2 helper cells enhanced IgE responsivity, thus perpetuating the allergic inflammatory response.^[7]

In the asthmatic airways, mast cells may stimulate the release of IL-6 and IL-8 from fibroblasts through the release of various pre-formed and newly generated mediators, and contribute to processes of inflammation and tissue remodeling.^[8] Mast cells play a role in Th polarization and that mast cell degranulation leads to more Th2 and less Th1 responses.^[9]