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Patterns of Hypersensitivity among Yemeni patients attending Elaj Medical Center

A graduation Project submitted to the Faculty of Medicine and Health Sciences as a Partial Fulfillment for requirement of Bachelor's Degree in Laboratory Medicine

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Dedication

We have no valuable and sufficient words to express our feeling and thanks, but we would to lovingly dedication this research to our respective parents and families, to the hundreds of people in community who are in pursuit of a healthy living, to our university, doctors, friends, and all supporters who were a backbone to us.

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Abbreviation	Meaning
NCDs	non -communicable diseases
Ig-G	immunoglobulin G
Ig-E	immunoglobulin E
MHC	major histocompatibility complex
HLA	Human lecuosit antigen
NIAID	National Institute of Allergy and Infectious Diseases
NK	natural killer
ILC-2	. Interleukin cells2
APT	atopy patch test
SPT	SKIN PRICK TEST
EBV	Ebstein Barr virus
EPD	An enzyme potentiated desensitization
LMICs	low - and middle -income countries
Th1	T helper 1
Th2	T helper 2

SPSS	Social Package of Statistical Science
Yrs	Years old
Mm	Millimeter
USA	United States of America
WHO	World Health Organization
HDMs	House Dust Mites
D. farina	Dermatophytes farina
D.PT	Dermatophytes metro nsens

Abstract

Background: Allergic diseases is a hypersensitivity reaction against external contact agents and continues to increase throughout the world. If left untreated; it can cause symptoms of allergic rhinitis, asthma, chronic urticaria, drug allergy, atopic/contact dermatitis, allergic conjunctivitis, and chronic rhinosinusitis, so that it can interfere with the quality of life. This study was conducted to investigate the patterns of hypersensitivity reaction among Yemeni patients at Elaj Medical Center in Sana'a city, Yemen during 2023.

Aim of the study: To highlight the importance of routine screening allergic diagnostic tests skin prick test or serum Ig-E and skin patch test before any specific allergy management and treatment.

Patients & Methods: Retrospective study to investigate patch test and skin prick test reactivity among patients with clinical diagnosis of Delayed or Immediate hypersensitivity reactions-contact /atopic dermatitis who were referred to the Elaj Medical Center in Sana'a city, Yemen during 2023. All patients subjected to patch testing and skin prick testing. Results had read, interpreted and analyzed.

Result: Among 82 cases studied who reacted positively to one or more allergens, 61 (74.4%) were reacted positively with skin prick tests had immediate hypersensitivity reactions-atopic dermatitis. While 21 (25.6%) were reacted positively with patch tests had delayed hypersensitivity reaction- contact dermatitis. Females had more affected than males with delayed and immediate hypersensitivity reactions with age range of 31-40 years, accounting to 33%.

In case of immediate hypersensitivity reactions, the most common allergens in our study were *D. farina* and *D.PT* with frequency 41 & 40, while less allergens with *Candida albicans*, *Composite*, and *Hores* with frequency 1**%** among males and females. The study found that there was a significant association between allergen (*Mimosa*) and gender with P= 0.0286 and X^2 =4.792 among patients with Immediate Hypersensitivity. Regarding delayed hypersensitivity reactions, the most common allergens were *Paraphenylenediam*, and *Potassium bichromate* but *Neomycin Sulphate* was the least allergen. The study found that there was no significant association between allergen and gender among patients with Delayed Hypersensitivity.

Conclusions: *D.farina* and *D.PT* was the dominant allergen in patients with atopic dermatitis- immediate hypersensitivity reactions while *Paraphenylenediam*, and *Potassium bichromate* was the dominant allergen in patients with contact dermatitis- delayed hypersensitivity reactions. Therefore, that skin prick test and patch test is recommended to be performed in the management of patients with immediate and delayed hypersensitivity reactions in order to detect the allergen because it has significant clinical relevance. We believe that there is a need for studies in different centers and at different time intervals to obtain more and more accurate information about the most common allergens in our country. This is why we want share this study that we conducted in Sana'a/Yemen.

Chapter one

Introduction

1.1 Introduction

The concept “allergy” was originally introduced in 1906 by the ,Viennese Pediatrician Clemens Von Pirquet after he noted that some of his patients were hypersensitive to normally innocuous entities such as dust, pollen ,or certain foods (**Pirquet, *et al.*,1906**). Historically, all forms of hypersensitivity were classified as allergies, and all were thought to be caused by an improper activation of the immune system. Later, it became clear that several different disease mechanisms were implicated, with the common link to a disordered activation of the immune system. Philip George, Houthem Gell and Robert Royston Amos Coombs categorized the main different reaction patterns into four categories: Immediate (type I hypersensitivity), Cytotoxic (type II hypersensitivity), Immune complex-mediated (type III hypersensitivity) and Delayed (type IV hypersensitivity) (**Coombs & Gell, *et al.*, 1963**).

The type I reaction, also known as the immediate hypersensitivity reaction, occurs because of Ig-E activation of mast cells in the skin as well as the gastrointestinal and respiratory mucosal linings. Food (e.g. seafood) drugs, transfusion products, insect venom , and environmental or inhaled allergens such as pollen, animal dander and house dust mites are common triggers. Previous exposure to the allergen is necessary for this reaction to manifest. The first exposure produces sensitization, and subsequent exposure to the same allergen triggers a cascade of events that produces a reaction within minutes (immediate reaction) and up to 1 to 3 days afterward (late phase reaction). This reaction may present as acute urticaria, pruritus, rhinitis, conjunctivitis ,bronchospasm, diarrhea, angioedema or anaphylaxis. Type-I allergic reactions are easier than type-IV reactions to diagnose because the offending allergens are often identified from a detailed history of the episode and preceding events (**Leelavathi & Adawiyah, 2021**).

The type IV reaction, also known as the delayed hypersensitivity reaction, is T-cell mediated and involves two phases. The initial sensitization phase occurs when contact is made with the allergen, which penetrates the skin. Repeated exposure to the same allergen triggers an inflammatory reaction manifesting as cutaneous lesions, usually within 12 to 48 hours of exposure, for weak allergens. This reaction commonly presents on the contact area (localized) as pruritic and erythematous papules, macules or vesicles that may spread through the systemic immune response and become generalized. This phenomenon is known as contact dermatitis with secondary generalization (or id reaction). Contact dermatitis, drug reactions (e.g. Stevens–Johnson syndrome), and allergic reactions to implants (e.g. joint or dental implants) are some examples of type IV reaction. (**Nosbaum *et al.,* 2009**). These reactions are more complicated because the temporal relationship between allergen exposure with clinical manifestation is often not clear. Morphology of the rash is commonly indistinguishable from endogenous eczema and symptoms, such as itch or erythema, and is highly influenced by environmental factors such as heat, sweat and dust **(Leelavathi & Adawiyah, 2021).**

Contact allergy is a delayed hypersensitivity type IV, T cell mediated reaction, CD4 and CD8 T cells activated by T cells ,secretes Lymphokines with fluid and phagocyte accumulation. Clinical syndrome mediated by type IV hypersensitivity are Tuberculin and contact dermatitis. Within the contact allergic reaction, two distinct phases are defined: the induction phase when the sensitization occurs and the elicitation phase when the allergic contact dermatitis develops. It is not clear whether individual co-factors such as genetic factors or co-morbidities confer a greater risk for development of contact allergy (**Johansen *et al.,* 2015**).

Patch test studies are often performed in a clinical setting among patients in dermatological specialist care, but studies in the general population are sometimes performed with simplified patch test procedures to ensure high participation and make the studies possible to perform in a population-based setting (**Alinaghi *et al.*, 2019**).

The patch test is also a necessary step in the diagnosis of allergic contact dermatitis. Early diagnosis is beneficial, and avoidance of harmful skin exposure to the skin sensitizing substance can reduce the risk of allergic contact dermatitis and hand eczema.Because the pathways for type I and type IV allergic reactions are different, the tests required to elicit these reactions also differ; the type I reaction is evaluated using either a skin prick test (in vivo) or a serologic test Ig-E (in vitro) while the type IV reaction is evaluated using a skin patch test (**Li JT, 2002**).

Allergic diseases are increasing in prevalence nowadays worldwide ,particularly in low and middle-income countries. Allergic diseases include food allergies, certain forms of asthma, rhinitis, conjunctivitis, atopic dermatitis (urticaria), indoor / insect According to World Health Organization, 300 million people suffered from asthma, 200 to 250 million people suffered from food allergies ,one tenth of the population suffers from drug allergies and 400 million from rhinitis worldwide allergies (**WHO, 2007**).

Allergic diseases include life-threatening anaphylaxis; asthma; rhinitis; drug, food, and insect allergies; eczema; and urticaria (hives); angioedema; and eosinophilic esophagitis. These diseases can cause long -term immune dysfunction and inflammation, which can form an underlying susceptibility for many other non -communicable diseases (NCDs), such as diabetes ,obesity and cardiovascular diseases (**Pawankar, 2014**).

In Yemen, few studies had conducted that concern with allergic diseases. Obaid *et al.* found that Early infant feeding, particularly with artificial milk, is a risk factor predisposing infants to the development of allergic respiratory disease presented with more clinical features of wheezing and asthma attack (**Obaid *et al*., 2022**).

Other studies found that House Dust Mites(HDMs) play as a main sensitizing allergen in allergic rhinitis in Taiz, Yemen, while allergic fungal rhinosinusitis can present clinically in different ways in Aden city (**Obaid & Waheed, 2019 & Alshaiby, 2021**).

1.2 Justification of the study:

Yemen Republic is one of developing countries that lacks data of many diseases including allergic diseases. Both the prevalence and the burden of allergic diseases are considerable exhibiting prevalence varying between 1 and 20% (**Dierick *et al.*, 2020**).

Appropriate treatment of allergic reactions along with allergen avoidance ensure a successful treatment outcome and prevent future reactions. So that allergy testing as a step in patient management & is a very important prerequisite for specific allergy treatment. Because of this reason, this study was conducted to detect the patterns of frequency/prevalence of allergic diseases both atopic & contact dermatitis in our country where very limited data are available.

1.2. 1. Rationale

To highlight the importance of routine screening allergic diagnostic tests skin prick test or serum Ig-E and skin patch test before any specific allergy management and treatment.

1.3 Aims of the study

1.3.1 General objective:

The objective of the study was detecting patterns of Hypersensitivity among Yemeni patients at Elaj Medical Center in Sana'a city, Yemen during 2023.

1.3.2 Specific objectives:

The specific aims of this study were to:

- detect the prevalence of Immediate Hypersensitivity and its allergens among Yemeni patients.
- detect the prevalence of Delayed Hypersensitivity and its inducers among Yemeni patients.

Chapter two

Literature review

2.1 Literature Review

Allergic diseases have been known for centuries, and allergic diseases such as asthma, urticaria and eczema were described in the ancient medical literature of China, Egypt, and Greece (**De Weck,1997**).

The first allergic individual in world history might have been the Egyptian pharaoh Menes, who – according to the hieroglyphs – died in the year 2,641 *B.C*. after a wasp sting **(Avenberg, *et al*., 1986).**

The first family history of atopy syndrome with asthma, rhinoconjunctivitis and atopic eczema can be found in the Julian-Claudian imperial family of Augustus, Claudius, and Britannicus (**20**). In the middle ages, "rose fever" with hay-fever-like symptoms was a well-known entity. Richard III of England was allergic against strawberries according to Shakespeare (**Blackley. 1873**).

The word "allergy" (from Greek "changed reactivity") was first used by von Pirquet in1906 for describing hypersensitivity reaction from the immune system and in 1923 Coca and Cooke used the word "atopy" (from Greek out "of place" or "strange disease") to describe the heredity syndrome of asthma and hay fever. In1967 the serum factor mediating classical allergy, Ig-E, was discovered (**Pirquet, 1906 & Johansson, 1967**). Historically, all forms of hypersensitivity were classified as allergies, and all were thought to be caused by an improper activation of the immune system. **(Coombs & Gell , 1963).** Today, the definition of allergy and allergic diseases is an abnormal adaptive immune response against innocuous , non-infectious external substances called allergens. In recent decades, the scientific community has discovered several different types of allergic diseases. **(Leelavathi & Adawiyah , 2021).**

The mechanism behind hypersensitivity reactions lie in the immune system. The immune system is a fascinating and complicated organization of cells and organs that are designed to protect the body from foreign invading organisms that are potentially harmful (**McKinley, O'Loughlin, & Bidle. 2016**).

2.2. The Role of the Immune System in Hypersensitivity

2.2. 1. Types of Antigens and Reactions:

Antigens that trigger allergic reactions are called **allergens**.These low-molecular-weight substances can enter the body by being inhaled, eaten, or administered as drugs. Allergens are a group of heterogenous soluble proteins (**Pomés**, **2008**) with varying biochemical structure and function. Generally, allergens are proteins with carbohydrate side chains of low molecular weight, which are highly soluble and mostly stable with the ability to stimulate T cells, containing peptides for antigen processing and presentation (**Murphy, *et al.*, 2008)**

Hypersensitivity reactions can occur in response to different types of antigen including **environmental substances**, **infectious agents**, **food**, and **self-antigens** harmful (**Turgeon, 2014**).

- Environmental Substances:

Environmental substances in the form of small molecules can trigger several types of hypersensitivity reactions. Dust can enter the respiratory tract, mimicking parasites, and stimulate an antibody response. An immediate hypersensitivity reaction associated with Ig-E, such as rhinitis or asthma, can result. If dust stimulates immunoglobulin G (Ig-G) antibody production, it can trigger a different type of hypersensitivity reaction, such as farmer's lung. If small molecules diffuse into the skin and act as haptens, a delayed hypersensitivity reaction, such as contact dermatitis, will result.

Drugs administered orally, by injection, or on the skin can provoke a hypersensitivity reaction mediated by Ig-E, Ig-G, or T-lymphocytes. Metals (particularly nickel) and chemicals can also cause type I hypersensitivity reactions. Low-molecular-weight chemicals usually act as a hapten by binding to body proteins or major histocompatibility complex (MHC) molecules- HLA molecules. The complex of antigen and MHC molecules is then recognized by specific T cells, which initiate the reaction. (**Turgeon , 2014**).

Infectious Agents:

Not all infectious agents are capable of causing hypersensitivity reactions. The influenza virus can cause hypersensitivity that results in damage to epithelial cells in the respiratory tract.Sometimes, an exaggerated immune response occurs. Influenza virus, for example, can trigger high levels of cytokine secretion or what is called a cytokine storm. In comparison, streptococci can cause a hypersensitivity reaction termed immune complex disease. (**Turgeon , 2014**).

- Self Antigens:

Very small immune responses to self antigens is normal and occur in most people. When these become an exaggerated response, however, or when tolerance to other antigens breaks down, hypersensitivity reactions can occur.

- Food Allergies:

According to the National Institute of Allergy and Infectious Diseases (NIAID), food allergy (FA) is an important public health problem that affects adults and children and may be increasing in prevalence. The prevalence of food allergy in Europe and North America has been reported to range from 6% to 8% in children up to the age of 3 years.

A recent U.S. study has estimated that 5% of children under 5 years of age and 4% of teens and adults have food allergies. Food allergy can cause severe allergic reactions and even death from food induced anaphylaxis.

Despite the risk, there is no current treatment for FA; the disease can only be managed by allergen avoidance or treatment of symptoms. The diagnosis of FA may be problematic because non-allergic food reactions, such as food intolerance, are frequently confused with FAs. The NIAID guidelines separate diseases defined as FA that include both Ig-E-mediated reactions to food (food allergies) non–Ig-E-mediated reactions to certain foods (e.g., celiac disease) and mixed Ig-E and non-Ig-E disorders (**Turgeon , 2014**).

Hypersensitivity reactions, allergic reactions, occur when the immune system identifies a particular protein as foreign to self and a potential danger. In food hypersensitivities, this happens when the immune cells within in the digestive tract identify a specific food protein as dangerous (**Grosvenor and Smolin, 2015**).

According to the Gell and Coombs Classification of allergic responses, allergic responses occur in four major ways, however, hypersensitive (allergic) disorders often involve more than one type. The brief overview of allergic reactions is summarized in **Table2-1**.

Table2-1: Immune reaction classification ((Turgeon M. 2014)

Parameter	Type of Reaction			
	I	II	III	IV
Reaction	Anaphylactic	Cytotoxic	Immune complex	T cell–dependent
Antibody	IgE*	IgG, possibly other immunoglobulins	Antigen-antibody complexes (IgG, IgM)*	None
Complement involved	No	Yes*	Yes*	No
Cells involved	Mast cells, basophils, granules (histamine)*	Effector cells (macrophages, polymorphonuclear leukocytes)*	Macrophages, mast cells	Antigen-specific T cells
Cytokines involved	Yes*	No	Yes*	Yes (T cell cytokines)*
Comparative description	Antibody mediated, immediate	Antibody dependent; complement or cell mediated	Immune complex mediated (immune complex disease)	T cell-mediated, delayed type
Mechanism of tissue injury	Allergic and anaphylactic reactions	Target cell lysis; cell-mediated cytotoxicity	Immune complex deposition, inflammation	Inflammation, cellular infiltration
Examples	Anaphylaxis Hay fever Asthma Food allergy	Transfusion reactions Hemolytic disease of newborn Thrombocytopenia	Arthus reaction Serum sickness Systemic lupus erythematosus	Allergy or infection Contact dermatitis

2.2.2. Types of Hypersensitivity Reactions:

According to Gell and Coombs, hypersensitivity reactions were classified into four types :type I: immediate (Ig-E-mediated), type II: cytotoxic (antibody and Fc receptor-mediated, cellular), type III: immune complex-mediated and type IV: delayed-type (T cell-mediated). **Table2-2, (Coombs, Gell, 1968).**

Table2-2: Types of Hypersensitivity (HS) and their Key Characteristics

(http://dx.doi.org/10.1016/B978-0-12-385245-8.00018-2)

Type	Type I HS	Type II HS	Type III HS	Type IV HS
Common name(s)	IgE-mediated HS Immediate HS Allergy, atopy	Direct antibody-mediated cytotoxic HS	Immune complex-mediated HS	Delayed type HS Cell-mediated HS
Primary immune system mediator	Antibody (IgE)	Antibody (IgG or IgM)	Antibody (IgG or IgM)	Effector T cells, macrophages
Time to symptoms	<1–30 min	5–8 hr	4–6 hr	24–72 hr
Mechanism	Allergens cross-link IgE bound on mast cells and basophils and induce degranulation	IgG or IgM bind to cell-bound antigen; cell is destroyed by phagocytosis, complement activation or ADCC	Immune complexes trigger complement activation; phagocyte FcR engagement leads to release of lytic mediators	Effector T cells produce IFNγ and other cytokines promoting macrophage hyperactivation
Examples	Asthma, hay fever, eczema, hives, food allergies, anaphylaxis	Hemolytic anemias, Goodpasture's syndrome	Arthus reaction, aspects of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE)	Lesions of TB and leprosy, poison ivy, farmer's lung

2. 2.2.1. Type-I reactions (Immediate or Ig-E-mediated reactions)

Type I reactions or immediate hypersensitivities or anaphylactic reactions are mediated by Ig-E antibodies. Allergen-specific Ig-E antibodies might be produced in response to allergens present in the environment (**Pawankar , *et al.,* 2014**), foods (**Zuberbier, *et al.* 2014**) and drugs (**Uzzaman & Cho SH, *et al.,* 2012**). Upon exposure to allergens, they bind to Ig-E antibodies, which are bound to a high-affinity receptor, called FcεRI, on mast cells and blood basophils. This activates the release of histamine, proteases and chemotactic factors, and synthesis of other mediators, such as prostaglandins, leukotrienes, platelet-activating factor and cytokines (**Uzzaman & Cho SH, *et al.,*.2012**).

The release of such mediator's results in vasodilation increased capillary permeability, mucus hypersecretion, smooth muscle spasm, and tissue infiltration with eosinophils, type 2 helper T (Th2) cells, and other inflammatory cells. On re-exposure, the allergen is recognized by Ig-E antibodies bound to mast cells and basophils, which leads to triggering of these cells, and an immediate hypersensitivity reaction with eosinophils, Th2 cells.

Common symptoms include one or more of the following symptoms; angioedema, urticaria ,bronchoconstriction, rhinitis, conjunctivitis and anaphylactic shock (**Delves . 2019**).

2.2. 2. Type-II reactions (antibody-dependent cytotoxic hypersensitivity)

Type-II reactions, i.e., antibody -dependent cytotoxic hypersensitivity, usually caused by IgG and IgM antibodies, takes place when antibodies bind to cell surface antigens, or a molecule bound to a cell surface. Such an antigen-antibody complex activates complements and cells such as natural killer (NK) cells ,eosinophils, macrophages, which participate in antibody-dependent cell -mediated cytotoxicity .This activation results in damaging cells and tissues. Type-II responses are associated with autoimmune diseases, adverse reactions to drugs and transplants. Disorders involving type-II reactions are Hashimoto thyroiditis Coombs-positive hemolytic anemias (**Delves*, et al.,* 2019**).

2.2. 3. Type-III reactions (Immune complex reactions- Toxic complex disease)

Type-III reaction is a response to antigen-antibody complexes deposited in vessels or tissue .Antigen-antibody complexes can activate the complement pathway, which leads to the release of inflammatory mediators. The activated complement components recruit and activate neutrophils, resulting in inflammation and tissue injury. Accumulation of

antigen -antibody complexes can be deposited in the tissues, such as renal glomeruli, blood vessels, synovial of joints causing systemic reactions (**Uzzaman & Cho SH, *et al.,* 2012**).

Examples of type III disorders are systemic lupus erythematosus, rheumatoid arthritis, leukocytoclastic vasculitis, cryoglobulinemia, acute hypersensitivity pneumonitis, and several types of glomerulonephritis. This reaction develops 4-10 days after exposure to antigen and continuous exposure to the can result in chronic. e.g ,.allergic asthma, Ig-E-mediated components of allergic bronchopulmonary aspergillosis (**Delves, *et al.,* 2019**). The primary target systems are the lungs, eyes, kidney, joints and the skin (**Descotes & Choquet-Kastylevsky, *et al.,* 2001**).

2.2. 4. Type-IV reactions (delayed hypersensitivity)

Type-IV reactions, also known as delayed hypersensitivity, are mediated by CD4+T helper cells, i.e., Th1 type of response (**Uzzaman & Cho SH, *et al.,* 2012**). Following the initial exposure to a specific antigen, T cells can be sensitized and activated by continuous exposure to the antigen. The tissue injury is mostly caused by lysosomal enzymes, reactive oxygen intermediates, and proinflammatory cytokines, secreted by activated macrophages. Disorders involving type-IV reactions include contact dermatitis (e.g, poison ivy), subacute and chronic hypersensitivity pneumonitis ,allograft rejection, the immune response to tuberculosis, and many forms of drug hypersensitivity (**Delves, *et al.,* 2019**).

2.3.The Clinical Manifestation of Allergy

2.3. 1. Signs and Symptoms:

Allergens are protein molecules found in various forms in a variety of substances. Multiple organ systems are affected by allergens, including the circulatory, cardiac, digestive, and respiratory systems. Allergens can produce edema, cutaneous reactions,

hypotension, bronchoconstriction, death, and coma depending on the sensitization rate and severity. The sudden, life-threatening, and extreme hyper-immune response is known as anaphylaxis and can cause death if not treated. Numerous allergenic compounds, such as latex, can cause skin rashes and irritations, resulting in angioedema contact and dermatitis. Allergens vary in nature and source, causing moderate to severe systemic and cutaneous symptoms depending on the exposure mechanism and route of sensitization. These can be inhaled, ingested, or exposed through skin contact. Many pollen and dust allergens are microscopic airborne particles (**Lei, & Grammer, 2019**).

These are easily inhaled and cause symptoms in organs exposed to the allergen, such as the nose, lungs, and eyes. Mucosal irritation, a runny nose, and sneezing are the most common symptoms of allergic rhinitis (hay fever). Swelling, irritation, and redness in the eyes are all possible side effects. Allergy particles inhaled into the lungs can cause bronchial hyper responsiveness. Particular airborne allergens can be inhaled in the lungs and induce asthmatic symptoms. Coughing, bronchoconstriction, and sneezing are caused by the narrowing of the airways. The increased mucus production restricts airflow to the lungs and thickens the airways, causing a shortness of breath (bronchial hyperresponsiveness, wheezing, and dyspnea). Allergic reactions can also be triggered by the ingestion of medications and food, allergen contact, drug administration, and insect bites (**Baldacci, *et al.,* 2015**).

Food and contact allergies symptoms include hives, itchy and swollen skin, edema, vomiting, gastrointestinal discomfort, and diarrhea. Food allergies rarely result in rhinitis or respiratory (asthmatic) reactions (**Turnbull, *et al.,* 2015**). Insect bites, drugs, medicines, and insect contact with venom lead to systemic allergic responses affecting several organs **(Table 2 -3)** (**Pramod, *et al.,* 2021**)

Allergies are seen in almost every organ. Most frequently, however, it is the skin and the mucous membranes that are involved and that represent the interface between the individual organism and its environment, **Table 2 -3** (**Wahn, *et al*., 2004**).

Table 2 -3: Clinical manifestations of allergic diseases in various organs

Organ	Symptoms[a]	Differential diagnosis
Cardiovascular	Anaphylaxis, vasculitis	Other cases of shock, vasovagal reaction, vascular diseases
Lung	Bronchial asthma, allergic bronchitis, hypersensitivity, pneumonitis	Bronchitis, chronic obstructive pulmonary disease, irritative toxic asthma, pneumonia
Upper airways	Rhinitis, sinusitis, pharyngitis, laryngeal edema, laryngitis	Vasomotor rhinitis, infection
Eye	Conjunctivitis, atopic keratoconjunctivitis, blepharitis, lid edema	Irritation, infectious conjunctivitis rosacea, psoriasis, seborrheic dermatitis, Melkersson-Rosenthal syndrome
Ear	Otitis externa, serous otitis media? tinnitus? vertigo?	Psoriasis, infection, microcirculatory disturbance
Blood	Hemolytic anemia, thrombocytopenia, agranulocytosis	Hematologic disease, toxic reactions
CNS	Fever	Infectious diseases
	(Cramps)	Neurological diseases
	(Migraine?)	
Skin	Urticaria, angioedema	Hereditary angioneurotic edema
	Vasculitis	Non-inflammatory purpura
	Contact dermatitis and atopic eczema	Other forms of dermatitis
	Drug-induced exanthematous eruptions	Viral exanthematous eruptions
	Granulomatous reactions	Infectious or foreign body granuloma
Oral/genital mucosa	Gingivostomatitis, erythema multiforme, vulvovaginitis (aphthae?)	Infection, morbus Behçet
Gastrointestinal	Food allergy with nausea, gastritis, enteritis	Malabsorption syndromes, infectious gastroenteritis, ulcus pepticum, enzyme deficiency
Musculoskeletal	Arthralgia	Other forms of arthritis and myositis
Kidney	Immune complex nephritis	Other kidney diseases

2.3. 2.Classification of Allergic Diseases:

The multitude of symptoms of allergic diseases need a classification. Coombs and Gell **(Coombs & Gell, 1963)** were the first to bring some order to the field of clinical immunology and allergology when in1963 they proposed a classification of pathogenic anaphylaxis.

The pathophysiological principle is the release of vasoactive mediators after the bridging of at least two Ig-E molecules on the surface of mast cells and basophil leukocytes by the allergen, **Figure 2-1**. This reaction does not need complement activation. Atopic eczema is characterized by elevated serum Ig-E levels. (**Johannes, *et al.*, 2019**).

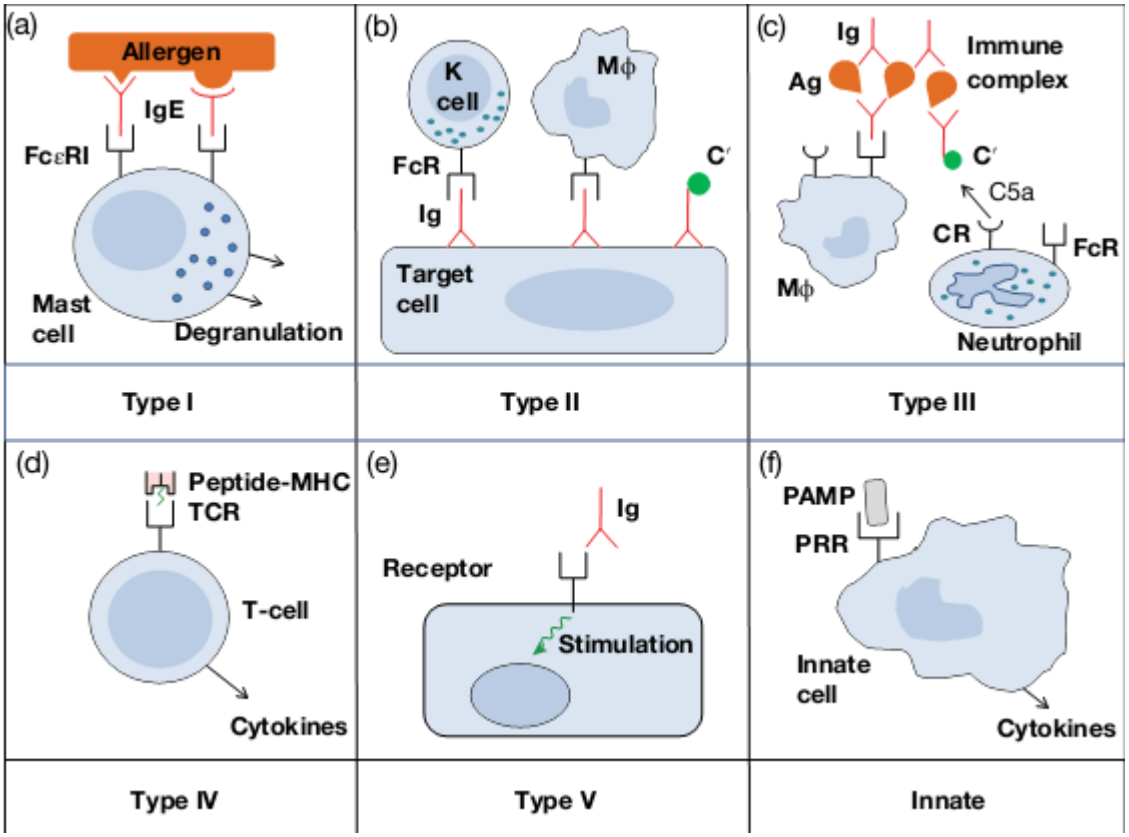

Figure 2-1: Six categories of hypersensitivity (Roitts. I. *et al.*, 2017)

Type-II:

The not so frequent reactions of type-II (mostly hematologic diseases) develop through the action of cytotoxic antibodies directed against surface determinants of cells (after a drug, for instance, has been attached as a hapten to the surface of leukocytes, platelets, or erythrocytes and leads to allergic agranulocytosis or thrombocytopenia) **Figure 2-1.**

anaphylaxis. The pathophysiological principle is the release of vasoactive mediators after the bridging of at least two Ig-E molecules on the surface of mast cells and basophil leukocytes by the **Type-III**:

Circulating immune complexes may activate the complement system as well as neutrophil granulocytes and platelets, **Figure 2-1**. Clinically, one can distinguish two types according to the kinetics: immune complex anaphylaxis as an immediate reaction has been observed in dextran anaphylaxis and xenogeneic serum therapy. A clinically different entity is the condition of serum sickness, which gave rise to von Pirquet's definition of allergy and accompanies fever, vasculitis, nephritis, arthritis, and urticaria because of deposits of circulating immune complexes in moderate antigen excess) (**Johannes, 2019**).

Type-IV.

Reactions mediated through sensitized lymphocytes comprise allergic contact dermatitis, the chronic phase of atopic eczema and many drug-induced exanthematous eruptions, **Figure 2-1**. Some forms of purpura pigmentosa progressiva can perhaps be mentioned here. The tuberculin reaction as well as organ transplant rejection follows similar mechanisms. According to modern immunology, predominantly TH1 cells play a role in delayed-type hypersensitivity (DTH), whereas TH2 reactions are important in the early phase of atopic eczema (**Johannes , 2019**).

Type-V.

The recently suggested type-V category describes granulomatous reactions (such as after injection of foreign material) (e.g., zirconium or soluble bovine collagen) after 2 – 5 weeks characterized histologically by epithelioid cell granulomas. **Figure 2-1**

Type -VI:

Pathogenic hypersensitivity reactions occurring through the specific antibody action have been called "stimulating/neutralizing hypersensitivity" (**Roitts , *et al*., 2017**) and occur in genetically predisposed individuals, an imbalance in the immune autoimmune diseases such as thyroiditis (LATS, long-acting thyroid-stimulating factor) or myasthenia

gravis with antibodies against the acetylcholine receptor in the motoneuron. So-called "reverse anaphylaxis" after injection of antibodies (e.g., anti-Ig-E or antibodies against the Ig-E receptor) might also be mentioned here; there is some overlap with type II reactions, **Figure 2-1**.

Generally, it should be stressed that every classification is predominantly of a didactic nature. In the living organism – unlike in a textbook – different types of reactions occur and influence each other in parallel. In everyday practice, type-I reactions such as allergic rhino-conjunctivitis, allergic asthma, urticaria, and anaphylaxis as well as type-IV reactions such as allergic contact dermatitis are the most important manifestations of allergy. Atopic eczema can be regarded as a mixture between type I and type IV reactions. (**Johannes , 2019** & **Roitts *et al*., 2017**).

2.4. Mechanism of Allergy and Immune System

There are two branches of the immune system, the innate (natural) and the acquired (adaptive) which are dependent of each other. The acquired immune defense cannot function without the innate immune defense and the latter system is more effective operating in conjunction with the acquired immune system (**Turgeon, 2014**).

The role of the immune system is to protect the body against invading pathogens causing different diseases. When the immune system misidentifies a harmless foreign antigen as a pathogen, an allergic reaction occurs (**Calzada, *et al*., 2018**). To protect the organism against exaggerated stimulation signals from harmless antigens, such as environmental and self-antigens, the immune system must be closely monitored. In system's regulatory mechanisms may lead to allergic diseases or autoimmune disorders, depending on the nature of the antigen (**Akdis, & Akdis., 2014**).

During an allergic reaction, the immune system must detect pathogenic stimuli and generate a robust immune response. Specific antigen sensitization is required: naive T and B cells identify specific sections of antigens, which are termed epitopes. First, specific MHC (major histocompatibility complex) class II antigens synthesized on the antigen-presenting cells (APC) surface detect allergens and deliver them to naive T lymphocytes. T cell activation causes T helper type 2 (TH2) cells to proliferate and differentiate. Interleukin IL-5, IL-4, and IL-13 and innate (ILC-2) lymphoid cells that can maintain and enhance local TH2 inflammation caused by the secretion of TH2 cytokines (IL-13 and IL-5) are the primary cytokines responsible for the allergic response (**Shamji, & Durham, 2017)**.

These ILs act on B cells, causing them to switch to the Ig class E (Ig-E). Allergen-specific Ig-E antibodies bind to high-affinity Ig-E receptors (FcRI) on basophils and mast cells. Repeated exposure to the allergen causes FcRI-bound Ig-E to crosslink, boosting the release of other mediators and histamine that generate allergic disease symptoms. Allergen-specific cells are enlarged and reactivated locally after 6–12 h of allergen exposure, culminating in the late phase of an allergic reaction. Effector cells (basophils, mast cells, and eosinophils in particular) release cytokines and inflammatory mediators, prolonging the proinflammatory response, **figure2.2**. The symptoms of allergic disorders are caused by this phase, and persistent allergen exposure causes the disease to become chronic (**Larché, *et al*., 2006**).

Specific antigen sensitization is required for allergic diseases development. Inflammatory cytokines (IL-13, IL-4, and IL-5) are produced as a result of cell expansion and differentiation to TH2 cell subtypes. They regulate the activation and recruitment of pro-inflammatory cells (mast cells and eosinophils) in mucosal target organs, as well as the class switching of Ig-E in B cells. Allergy symptoms and inflammation are triggered by

these activations (**Calzada, D. *et al*., 2018**).

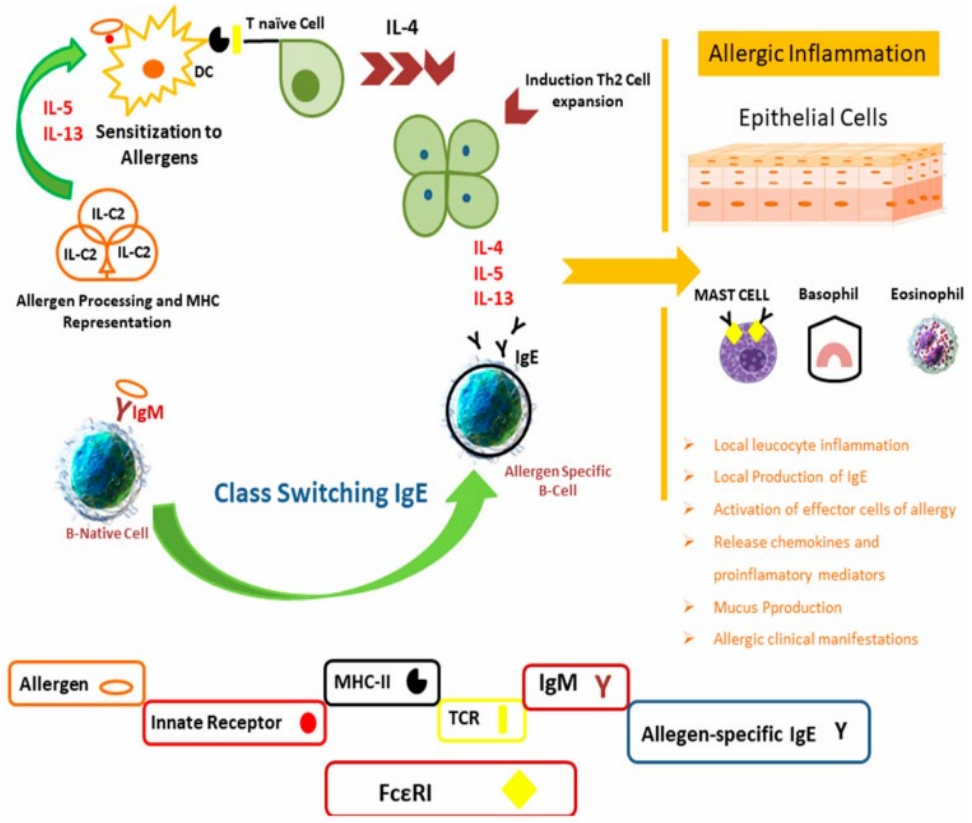

Figure 2-2: Allergic reaction mechanisms (Aldakheel F., 2021).

2.5. Allergy Diagnosis:

For accurate diagnosis of allergies, the factors, such as detailed clinical history, and knowledge about local environment, are crucial. Additionally, the association between allergen exposure and onset of clinical features, periodicity of symptoms (i.e., seasonal/ perennial ,diurnal), animal or insect exposure, the affected body systems, familial atopy and occupational history should be investigated. The diagnosis of allergy comprises **four steps,** which supplement each other: **History**, **Skin tests**, **In vitro allergy tests** & **Provocation tests (Johannes , 2019)**.

2.5.1. History:

The taking of an allergy history requires great experience .Often several visits are necessary (e.g., a young man with nickel allergy and eczema on the left thumb: the elicitor was his bicycle bell). A good allergist has to be like Sherlock Holmes – nothing is unimportant (**Table 2.5 & 2.5**) (**Johannes, 2019**).

Table 2.5. History parameters for and against the appearance of allergy

	Parameter	
	Allergy probable	Allergy unlikely
Onset	Youth	Elderly age
Family history	Positive	Negative
Specific elicitors	Detectable	Unknown
Fever	No	Yes
Improvement after change of milieu	Yes	No
Symptoms	Objective, reproducible	Only subjective, not reproducible

Table 2.6. Relevant questions for allergy history

Symptoms
- Onset (first occurrence, acute complaints)
- Duration
- Timely course (circadian, yearly rhythm)
- Intensity (severity)
- Frequency of relapses
- Response to therapy
- Deterioration through therapy
- Necessity of hospital admission

Other diseases
- Personal history (atopy)
- Family history (atopy)
- Other conditions (gastroesophageal reflux, skin or airway diseases, drug or food reactions)

Elicitors and situations
- Season of the year
- Local conditions (indoor, outdoor)
- Occupation
- Holiday, leisure
- Hobby
- Drugs
- Foods
- Exercise
- Stress, emotional burden
- Infectious disease
- UV radiation
- Hormonal situation (menstruation, pregnancy)

Living conditions
- Animal contact (also passive, "derivative")
- Tobacco smoke (active, passive)
- Housedust mite, mold exposure
- Chemicals
- Plants
- Cosmetics
- Sleeping dyspnea, snoring, mouth breathing

2.5. 2.Skin Tests:

Skin tests include epidermal (patch test, friction test) and percutaneous (prick, scratch, intradermal) test procedures **(Johannes , 2019)**.

2.5. 2.1 Patch Test

Since the first description of a patch test by J.Jadassohn (**Jadassohn .1895**)**,** the patch test has been used for the diagnosis of type IV reactions, mostly allergic contact dermatitis or exanthematous drug eruptions. It will be described in detail in Sect. 5.5 on "Eczema." But also for immediate-type reactions such as contact urticaria, the so-called open patch test has gained importance, which is read after 20 min **(Bandmann & Fregert , 1982)** The "atopy patch test" (APT) with Ig-E-inducing allergens allows the evaluation of the relevance of a sensitization (by the prick or RAST methods) for atopic eczema **(Darsow , *et al*. 1995).**

-Indications for the patch test: (Leelavathi, *et al*., 2021)

1) Suspected contact or occupational dermatitis where the lesion is isolated in the area of contact.
2) Worsening of existing atopic dermatitis despite adequate treatment.
3) Recurrent dermatitis affecting the lips, face, hands, feet and perineum (areas that are frequently exposed to contact allergens).
4) Stasis eczema, discoid eczema and chronic recurrent eczema for which a definite cause cannot be established.

-Precautions and contraindications for the patch test: (Lazzarini , *et al*. 2013).

Pre-test counselling is important because patients must refrain from bathing and exercise during the test period. Sweating and wetting of the patch causes it to dislodge ,leading to test failure. Refraining from bath or ablution may not be

1) acceptable in certain cultures ;hence, informed consent must be obtained. Patients should be counselled regarding side effects such as erythema, pruritus, or hyper- or hypopigmentation at the test site. Occasionally, blisters may appear, and eczema may flare. Any skin discoloration that may occur at the test site will resolve with time.
2) The test should be planned about 6 months from the time of suspected contact to avoid a flare of the existing dermatitis, especially if it is poorly controlled.
3) Patients who are on treatment with a high daily oral steroid (> 10 mg ,(steroid injections, cyclosporin (> 2 mg/kg) or phototherapy, or those who have recent excessive sun exposure (within 1 week) should defer the patch test because it may affect test results. Those on low doses of oral steroids (< 10 mg (and antihistamines may proceed with patch testing because neither substance is known to affect the test.
4) Topical steroid application must be avoided at the test site both 1 week before and during the test.
5) The patch test should be deferred in pregnant women because immunological changes of pregnancy may affect patch results.
6) A positive reaction may spread from a test site, causing a false positive result at adjacent sites. Hence, results need to be interpreted with caution.
7) An irritant reaction to an allergen may cause a false positive result.

2.5. 2. 2 Friction Test

In highly sensitized individuals, the friction test can be recommended (e.g., with animal hair or drugs) **(Fuchs , *et al.* 1981).** In the friction test, the native allergen is rubbed ten times over the skin of the volar forearm (controls with pads). After tape stripping (friction test with strip-ping), the reaction can be enhanced. **(Gronemeyer & Debelic . 1967)**.

2.5. 2.3 Prick Test

A drop of the allergen extract is applied to the skin, which then is briefly pricked using a lancet or a needle (there should be no bleeding!). After 15 min the test solution is wiped off and the reaction is read. New standardized needles allow a defined depth of penetration **(Dreborg & Frew, 1993).**

Skin prick test –SPT- is first described by Charles Harrison Blackley (1860s) in patients of 'hay fever .'SPT, which is the most frequent method for diagnosis of Ig-E mediated allergic diseases (**D'Amato, *et al*., 2002**) should be administrated to patients with either recurrent or persistent symptoms which cannot be adequately controlled by therapy. Generally, clinical conditions where SPT is indicated are asthma, rhinitis, eczema/atopic dermatitis, suspected occupational exposure to selected potential allergens.

In this test, once the allergens are introduced into the skin, dermal mast cells begin to degranulate due to cross-linking of sIg-E bound to their membrane receptors, leading to the immediate release of histamine which can be clinically characterized by wheal erythema (flare) that can be measured to assess the degree of cutaneous sensitivity, hence, SPT represents a surrogate indicator of systemic allergic sensitization (i.e., nose, lungs, eyes, gut) through the presence of cutaneous reactivity to specific allergens.

Since blood vessels and pain receptors are located in deep dermis, SPT is pain -free and associated with minimal risk of bleeding or infection if performed appropriately (**Nitta. 2003**)

Selection of antigens should be based upon patient's clinical and environmental history, occupation and socio - economic factors. Among the most common allergen to be used in SPT, include house dust, house dust mite, relevant pollens (grass, tree or weeds), fungus (Alternaria ,Aspergillus), insects (Cockroach) and pet animals (dog ,cat, buffalo), milk, egg,

peanut, soya, wheat, tree nut, fish and shellfish. Patients on anti-histaminic and immunomodulators, on b -blockers, with unhealthy skin condition, within 4 weeks of anaphylaxis and extremes of age are not suitable for SPT. As positive and negative control, histamine and normal saline ae used, respectively and re ad after 10 minutes and 15 minutes (**Hasunuma , *et al.*, 2014**).

Positive reaction is suggested by appearance of a wheal at the prick site (**Fig. 2. 3**). The maximum diameter of the wheal is measured, and reaction interpreted in millimeters (mm) of wheal diameter (**Wenzel., 2012**). Positive control should be at least 3 mm or more than negative control to establish test validity. Any allergen showing a wheal size of ≥3 mm than the negative control is considered to be positive indicator of hypersensitivity. (**Valavanidis, *et al.*, 2006**).

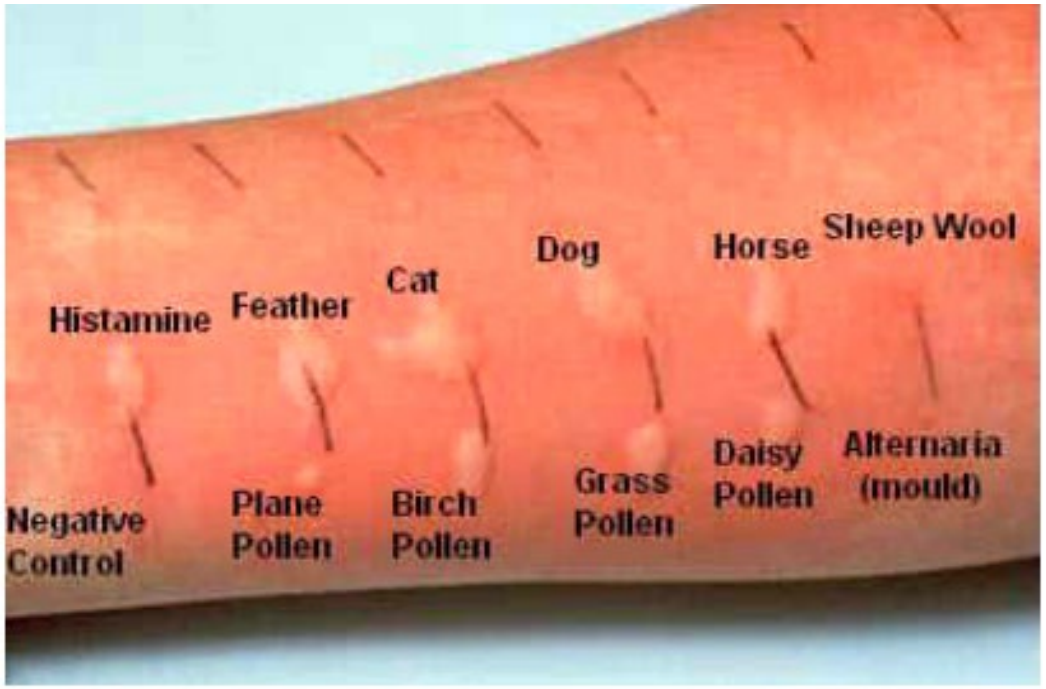

Figure 2.3. An example of skin prick test (SPT) (https://www.aashwas.in/diagnostic -services/skin-prick-test -spt/)

Factors Influencing on SPT result

1) **Medications** – Certain medications such as antihistaminic, Astemizole and long-term systemic steroids may affect the results of SPT **(Hasunuma, *et al*., 2014).**
2) **Age** – SPT is currently practiced beyond 6 months of age though no lower or upper age limit cut -off is recommended **(Hasunuma , *et al.,* 2014).**Skin reactivity declines after 60 years ..
3) **Test area** – Generally, left forearm is the preferred area for this test. The mid and upper back are 33% more reactive than the lower back. The back as a whole is more reactive (53% (than the forearm. An area approximately 5 cm away from the wrist and 3 cm from the antecubital fossa, on the forearm is usually used (**Hasunuma, *et al.,* 2014**).
4) **Distance between two pricks** – A minimum of 2 cm gap should be present between two adjacent test sites .(Figure 1.2. An example of skin prick test SPT) (https://www.aashwas.in/diagnostic -services/skin-prick-test -spt.)
5) **False positives** – Skin conditions such as dermatographism and acute or chronic urticaria ,naturally occurring histamine in some allergen extracts (insect venom, mold, foods), non -standard allergen preparations, cross -reactivity with homologous proteins.
6) **False negatives** – Recent use of (within 4 weeks) anaphylaxis, some medications, and UV exposure.

- Indications for the prick test: https://bpac.org.nz/BT/2011/December/allergy testing.aspx

- Suspected food allergy (e.g. to egg ,peanut, wheat, fish, soy or cow's milk) that cannot be determined from food elimination or challenge.
- Poorly controlled or frequent exacerbation of allergic rhinitis ,rhinosinusitis, eczema or bronchial asthma, where identifying and avoiding allergens (animal dander ,pollen, cockroaches and house dust mites) may improve the condition.

- Suspected or previous allergy to a drug such as penicillin (only when there are limited alternative drugs ,which can be used for treatment).

- Precautions and contraindications for the prick test:

https://bpac.org.nz/BT/2011/December/allergy testing.aspx

- Patients on treatment with oral antihistamine and antidepressants need to defer treatment before the test (3 days for 1st-generation and 10 days for 2nd-generation antihistamines) to avoid wheal dampening.
- Application of topical steroids at the test site should be stopped 2 to 3 weeks prior to testing because it may dampen the results. However ,oral or inhaled steroids may be continued because use of these substances does not affect the results.
- The prick test is contra-indicated in patients who experienced anaphylaxis 4 to 6 weeks prior to the test.
- The prick test in the elderly may not be accurate because skin reactivity declines with age. Serum Ig-E testing may be considered instead.
- It is best to defer the prick test for children below 2 years of age and pregnant women.
- There is a small chance of anaphylaxis during the test. Hence ,testing should be performed where health professionals and emergency resuscitation facilities are available.

2.5. 2.4. Scratch Test

Here the skin is superficially scratched under allergenic material (in the case of powder together with some drops of physiological saline). The scratches are approximately 5 mm, and there should be no bleeding **(Johannes , 2019)**.

2.5. 2.5.Intradermal Test

In this test, 0.02 – 0.05 ml of the allergen solution; commonly 1/100 of the prick test solution's concentration (though this does not hold for individual allergens!) – is injected strictly intra-dermally using a small syringe and needle. A small wheal (approx. 3 mm) will be observed. The interpretation of intradermal test reactions is difficult. Especially for mold, food, and drugs, false-positive reactions are common. Granulomatous reactions (type V) need up to 3 weeks to develop fully. While the Kveim (sarcoidosis) and Mitsuda tests (tuberculoid lepra) have a historical significance, this type of reaction is important prior to treatment with soluble bovine collagen **(Burg, *et al*., 1986).**

In all the above-mentioned skin test procedures, adequate controls (positive with histamine or codeine, negative with saline or sol-vent) need to be performed. The quantitative interpretation of skin test results uses a comparison with the histamine-induced wheal and flare reaction **(Johannes, *et al*., 2019)**.

Complications can occur even in skin testing, either as hyperergic local reactions or as systemic reactions such as anaphylaxis or exacerbation of the underlying disease (asthma, eczema). Therefore, allergy tests should only be performed by experienced physicians trained for possible emergencies. Special caution has to be taken in patients with a history of anaphylaxis; we perform skin tests only under inpatient conditions when there is a history of grade III or IV anaphylaxis. Patients using beta-blockers – possibly also angiotensin-converting enzyme inhibitors – show an increased risk of anaphylaxis **(Johannes, *et al*., 2019)**.

2.5. 2.3.Reading of Skin Tests

The test reaction of percutaneous tests is evaluated using the diameter of the wheal and flare either according to an arbitrary scale from 0 to ++++ **(Kemp & Lockey, 1999)** or in millimeters. For quantification of skin test results, the titration with different concentrations

has given better results than the measurement of wheal and flare areas **(Table 2.7).** Flares under 3 mm in diameter as well as all reactions not significantly exceeding the negative control (saline) are negative. Wheals without flare under 3 mm diameter as well as flares without wheals under 5 mm are questionably positive and are not considered in allergy passports or for forensic questions. A repeat test at a later date can be considered.

In evaluation of immediate-type reactions ,an additional reading after 6 and 24 h can give information on so-called "late cutaneous reactions" **(Dorsch & Ring, 1981)** (not to be confused with delayed-type reactions after 48 or 72 h = type IV), which are Ig-E mediated and occur after very intense immediate-type reactions, which sometimes show a biphasic course ("dual reaction,("reaching a maximum after 6 – 8 h. Arthus-type reactions (type III) caused by circulating immune complexes reach a maximum after 12 – 36 h.

Problems in test reading occur through false positive or false negative test reactions, e.g., through the use of irritating preparations, in patients with urticaria factitia (false positive) or when antigens are diluted too much, under the influence of drugs, in certain neuro-logic diseases or within too short an interval from an anaphylactic reaction (false negative) (**Table 2.7**).

At the time of allergy testing, there should be allergen avoidance if possible. During the pollen season or intense contact with pets, skin tests can induce an exacerbation of symptoms. Skin reactions are subject to fluctuations in intensity according to age, sex, body surface area, season, and allergen exposure. This, however, does not play a major role in allergy practice if the test is otherwise well standardized.

Table 2.7. Reasons for false-negative and false-positive skin test reactions (Johannes, 2019).

False-negative reactions
- Extract (too diluted, too weak, not soluble, wrong vehicle)
- Test procedure (depth of puncture, reading time)
- Test area (premedication, neuropathy)
- Systemic medication (antihistamines, etc.)
- Underlying disease (e.g., nervous disease)

False-positive reactions
- Extract (irritative, direct histamine release)
- Test procedure (irritative, no controls)
- Test area (inflamed skin, "angry back" patch test)
- Underlying disease (e.g., urticaria factitia)
- Artificial reaction (Munchhausen syndrome)

2.5.3 In vitro Allergy Tests

In vitro allergy diagnosis has an independent and equal place besides the three other pillars of allergy diagnosis **(Ring, 1981).** In in vitro allergy investigations, there are separate tests for serologic and cellular diagnosis as well as for allergen-specific and non-specific parameters (markers of allergy or inflammation) (**Table 2.8**).

Table 2.8. In vitro allergy tests (LTT = lymphocyte transformation test) (Johannes , 2019).

Non-allergen-specific (general markers of allergy and inflammation)	
Serologic	**Cellular**
Total IgE	Blood count
Total Ig + subclasses	Lymphocyte subpopulations
Complement factors	Lymphocyte stimulation test (LTT) (mitogens)
Complement activity (CH50)	
Immune complexes	
Mediators in blood, tissue, and urine (histamine, methylhistamine, ECP, EPX, tryptase)	
Allergen-specific	
Serologic	**Cellular**
Specific IgE (e.g., RAST)	Histamine release
• Qualitatively (allergen mixtures, strip tests)	Basophil degranulation
• Semiquantitatively (e.g., RAST)	Basophil activation (CD63)
	Sulfido-leukotriene release (CAST)
	LTT (allergen)
Specific antibodies of other classes (type III)	
• Precipitation/immunodiffusion	
• Passive hemagglutination	
• RIA/EIA	
• Antibodies against specific proteins (immunoblot)	

2.5.3.1. In vitro diagnosis tests (Immunoglobulin (Ig) E antibody levels)

In many routine allergy diagnostics, Ig-E level are used to detect and monitor the reaction of the immune system to the allergen (**Kos and Sanders, 2018**). Ig-E molecules produced against specific antigens are labelled as serum specific Ig-E (sIg-E) (**Ansotegui , *et al.*, 2020**). These can be detected by enzyme conjugated antihuman Ig-E antibodies. However, raised levels of Ig-E may also be due to conditions such as parasitic infestations, immunodeficiency disorders (e.g., AIDS, hyper Ig-E syndromes etc.) and Ebstein Barr virus (EBV) infection (**Alvarez-Alvarez, *et al.*, 2018**). The major downside of sIg-E estimation

is false positivity with high total Ig-E levels (>300 kIU/L) due to non-specific binding to test allergens (**Endara, *et al.*, 2015**).

-Indications for serum Ig E testing: (Leelavathi, *et al*., 2021)

- The skin prick test is not available or the suspected allergen is not available in skin prick test series.
- The patient has extensive dermatitis or dermographism that may cause a false positive with the skin prick test.
- The patient is unable to discontinue oral antihistamines.
- There is a history suggestive of an allergy, but skin prick testing is negative.
- There is a history of anaphylaxis to any allergen.

The advantages of the skin prick test compared to serologic testing are the lower cost and the shorter time to obtain results, while the disadvantages include the facts that fewer allergens can be tested, cooperation from young children is difficult, several essential drugs must be withheld and the procedure has a small risk of anaphylaxis. **(Leelavathi, *et al*., 2021)**

2.5.3.2. Comparison of in vitro test with in vivo test

The main advantages of in vitro tests over in vivo test include no effect of anti-histaminic or steroids, feasibility with any skin condition and no risk of systemic reactions. Furthermore , serum sIg-E has better specificity with higher positive predictive value to identify allergens e.g., pollen and insects) sensitization **(Franck, *et al.*, 2011).,**On the other hand, SPT have an advantage over in vitro tests in terms of faster result (15 -20 minutes), no interference with high IgE levels and cost effectiveness **(Hasunuma, *et al.*, 2014).**

2.5.4 Provocation Tests:

Strictly speaking, skin tests are also “provocation tests,” namely provocation of the skin as the manifesting organ. In modern terminology, however, provocation test means the exposure of an organ involved with the respective allergen. The most important provocation tests in practice are **(Przybilla, *et al*., 2000):**

- **Conjunctival**
- **Nasal**
- **Bronchial**
- **Oral**
- **Parenteral** (e.g., subcutaneous with local anesthetics) provocation**.**

Any provocation test should be performed un-der controlled and emergency conditions.

Provocation tests involve a certain degree of risk for the patient! Naturally, occurring allergic reactions are imitated under control. Therefore, provocation tests should only be performed when indicated, in remission, and when other diagnostic parameters (history, skin test, in vitro test) have not given a clear-cut diagnosis. In allergic bronchial asthma, the performance of bronchial provocation tests with acetylcholine or histamine belongs to the obligatory evaluation of lung function. Allergen provocation tests can only be done as confirmation tests; no large “test series” are possible **(Schultze-Werninghaus, *et al*., 2000).**

The critical evaluation of history, skin test, and in vitro tests can often save the patient from having to undergo a provocation test **(Fig. 2-4)**. Out of all the diagnostic procedures used, skin tests represent the most practical method. Compared to RAST, skin test reactions stay positive over a longer period after allergen contact. In an overview of all the procedures, the predominant place of history is evident **(Fig. 2-5).**

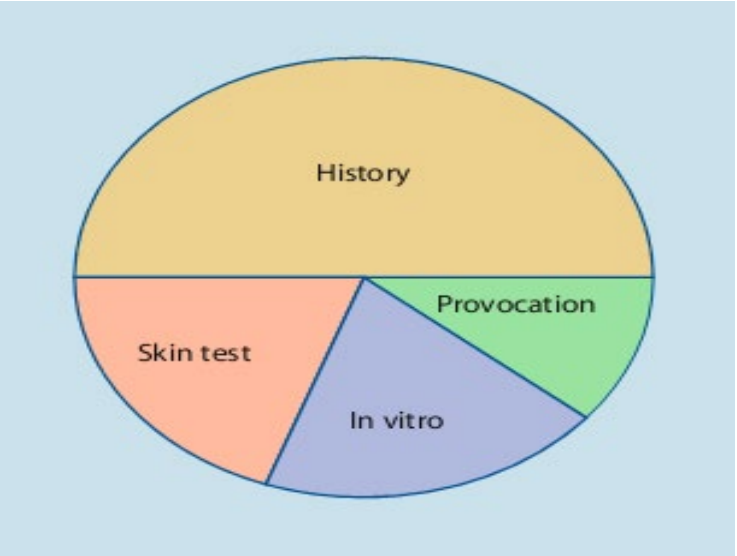

Figure 2-4: Importance of the various methods used for allergy diagnostics (Johannes , 2019)

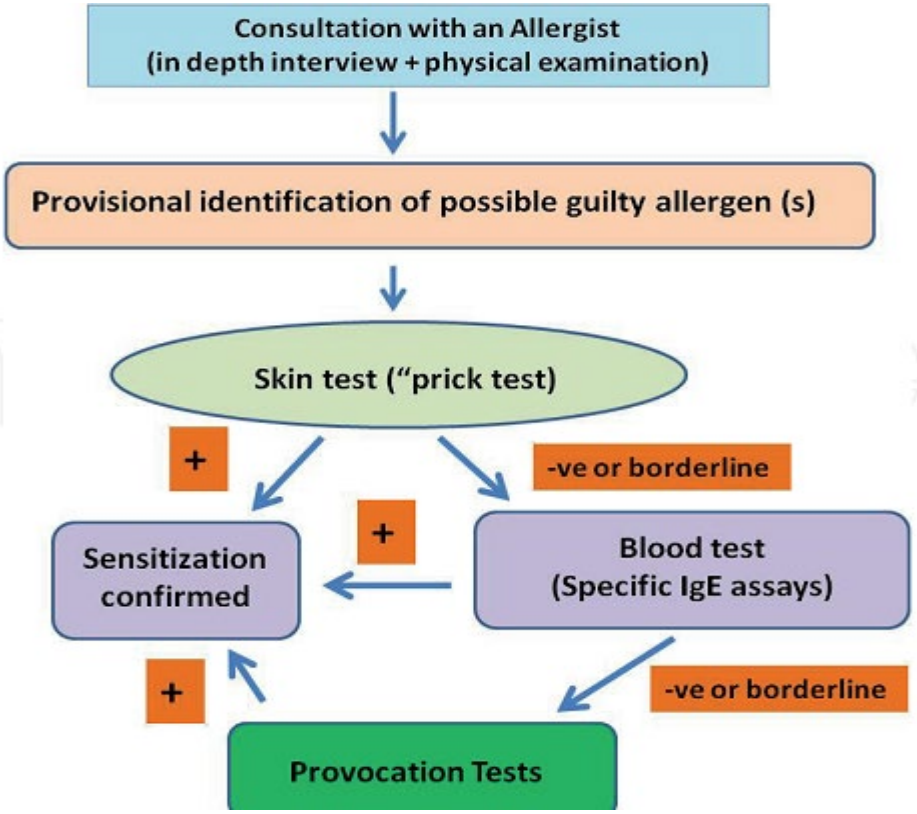

Figure 2-5-: Schematic diagram showing the identification and assessment of atopic status using clinical history, physical examination and laboratory tests

(http://creativecommons.org/licenses/by/3.0)

2.6. Allergy Prevention and Therapy

The most efficient causal method of allergy treatment is the **avoidance of the eliciting allergen**. Allergen avoidance comprises not only the avoidance of pets, sanitizing measures in the apartment, anti-house dust mite strategies, but also the elimination of unspecific irritants, as well as dietetic regimens in food allergy; finally, changes in occupation as well as rehabilitation treatments in an allergen-poor climate (North Sea, high altitude as in Davos, Switzerland) have to be considered.

The next causal therapeutic option is **allergen-specific immunotherapy** (hyposensitization), where it is possible to change the abnormal pathologic immune reaction into normal immunity.

The final aim of any treatment is that the patient will be **free of symptoms**. The single steps in the general concept of allergy treatment do not exclude each other, Also during allergen-specific immunotherapy, symptomatic treatment has to be given. **Table 2.9** shows the most important steps of a treatment strategy ranging from allergen avoidance to psychosomatic counseling or psychotherapy.

Table 2.9. General concept of allergy treatment (Johannes, 2019).

Level of action	Procedure
Allergen exposure	Avoidance (e.g., apartment, mite protection, rehabilitation in occupational allergy, climatic therapy, diet)
Pathogenic immune reaction	Allergen-specific immunotherapy (hyposensitization), immunosuppression, immunomodulation
Inhibition of mediator release	Mast cell stabilizers
Inhibition of inflammation	Glucocorticosteroids
Receptor antagonists	
Histamine	Antihistamines (sedating, non-sedating)
Leukotrienes	Leukotriene antagonists, lipoxygenase inhibitors
Specific therapy at organ level	Bronchodilation, secretolysis, physical therapy, skin care, restoration of disturbed barrier
Psyche	Antidepressives, psychotherapy, psychosomatic counseling

The treatment of allergic diseases in children follows a similar pattern to that of adults. Treatment options include **allergen avoidance** through environmental control, **pharmacotherapy**, and **immunotherapy (Aldakheel, *et al*., 2021)**.

2.6.1. Allergen Avoidance:

The primary focus of allergy treatment should always be the strict avoidance of specific allergens that cause allergic disease. The greatest and best guideline for reducing allergy reactions in sensitive people is to avoid allergen exposure. Food allergies and some stinging insect allergies are treated primarily through avoidance, which can be quite helpful if patients are well trained about preventive measures. However, it is impossible to avoid certain allergens that travel through the air and are easily inhaled without control or notice. Avoidance is impossible in these circumstances, and additional therapeutic procedures are necessary to overcome difficulties **(Pramod, 2021 & Douglass, *et al*., 2006)**.

2.6.2. Pharmacotherapy:

Pharmacotherapy can relieve allergen-induced symptoms when allergen prevention and tracking are impossible and allergy exposure is inevitable. Many drugs are developed that are antagonistic to and block the actions of allergic mediators. Anti-leukotrienes and antihistamines are two common drug targets that prevent the onset of allergic symptoms and inhibit the action of inflammatory mediators **(Bonyadi, *et al*., 2017)**. The FDA has approved adrenaline (epinephrine), antihistamines, glucocorticosteroids, and theophylline, which primarily act as anti-inflammatory molecules. Decongestants, mast cell stabilizers, and eosinophil chemotoxins, along with anti-leukotrienes, such as zafirlukast (Accolate) or montelukast (Singulair), are commonly used as drugs to monitor and prevent chronic and acute allergic diseases. **(Pullerits, *et al*., 2002)**

2.6.3. Immunotherapy:

Allergen-specific immunotherapy entails administering an increasing dose of allergens to a patient over time to ensure immunological and clinical tolerance. Allergen injection immunotherapy induces T cell tolerance through a variety of methods, including alteration in secreted cytokines, decreased allergen-induced proliferation, stimulation of apoptosis, and T regulatory cells production. This results in the reduction of inflammatory mediators and cells in the affected tissues, production of blocking antibodies, and suppression of Ig-E **(Gardner, *et al*., 2004).**

This sort of immune therapy has been demonstrated to be effective in studies, and long-term use has indicated that immunotherapy can help to avoid the development of atopy. The intravenous administration of monoclonal anti-Ig-E antibodies is the second type of immunotherapy. These attach to both B-cell-associated and free Ig-E, signaling and killing them **(Wong & Lomas, *et al*., 2019)**.

Sublingual immunotherapy is a third type of therapy that is given orally and is based on oral immune tolerance to non-pathogens, such as resident bacteria and foods. Allergy shot therapy may become the most effective allergy treatment method in the future. Close supervision and a long-term commitment are required in this therapy for successful individual treatment **(Scurlock, *et al*., 2018)**.

2.6.4. Ineffective and Unproven Treatments:

An enzyme potentiated desensitization (EPD) experimental treatment has been tested in some recent investigations, but no encouraging outcomes have been found. The same method is currently used in many hypoallergenic food preparations. The treatment approach, however, was not convincing, and was not acknowledged as effective. EPD uses allergen dilutions with beta-glucuronidase enzymes to polarize T-regulatory lymphocytes and to change the allergen nature, which down-regulates Ig-E induction, favors desensitization, and prevents allergic reactions **(Astarita, *et al*., 1996).**

Allergy research has progressed quickly in recent years **(Bochner, *et al*., 2013)**. Recent advances in proteomics, analytical methods, and genomics have resulted in massive amounts of allergen-related data. **Allergen bioinformatics** deals with **tools/algorithms** for **allergenicity/allergen prediction**, **allergenic cross-reactivity prediction**, **allergen databases**, and **allergen epitope prediction (Ghosh & Gupta-Bhattacharya, *et al*., 2011)**.

2.7. Epidemiology of allergic diseases

In the recent years, allergic diseases are showed to be a primary cause of morbidity in children and adults under the age of 40, and their prevalence has been on a steady rise globally ,and in low - and middle -income countries (LMICs) in particular as they are moving more and more towards urbanization **(Stróżek, *et al.*, 2019) .** Furthermore, their severity appears to be increasing, especially in children and young adults, who are bearing the highest burden of these trends (**Blaiss, *et al*., 2013)**. It has been estimated that asthma and allergic dis eases affect 30% of the global population **(Stróżek, *et al*., 2019).** Worldwide ,200 to 250 million people suffer from food allergies, and 400 million suffer from rhinitis (**Blaiss, *et al*.**, **2013).**

Allergic diseases include life-threatening anaphylaxis; asthma; rhinitis; drug, food, and insect allergies; eczema; and urticaria (hives); angioedema; and eosinophilic esophagitis . These diseases can cause long -term immune dysfunction and inflammation, which can form an underlying susceptibility for many other non -communicable diseases (NCDs), such as diabetes ,obesity and cardiovascular diseases, **Table 2.10**, (**Pawankar, *et al*., 2014**). In addition to the health complications, such diseases can result in high socio -economic burden to the affected families and countries due to health care costs, morbidity, reduced quality of life and poorer work performance. Every year, asthma and allergic rhinitis alone are estimated to result in a loss of 100 million workdays and missed school days only in the European Union (EU). When these diseases are not treated adequately ,their economic burden is estimated to be between 55 billion and 151 billion euros annually in the EU (**Zuberbier, *et al*., 2014**).

In LMICs, the economic burden of such diseases has even more profound effect on the daily lives of individuals, resulting in poverty due to loss of workdays and wages.

For instance, in India, it has been reported that the monthly cost of medication for an asthmatic child can be as much as one-third of an average family's monthly income (**Pawankar, *et al*., 2014**).

In LMICs, the environmental risk factors, such as outdoor and indoor pollution (e.g .cooking and tobacco smoke), are believed to contribute the most to the rise of prevalence of this category of diseases. Indoor pollution is estimated to be as much as five times more severe in LMICs than in high-income countries **(WHO, 2007).** Furthermore, similar to high-income countries ,other environmental risk factors such as climate change, reduced biodiversity and changes in the weather patterns can have direct and indirect consequences on the population health in LMICs, in part by contributing to allergic disease (**Pawankar, *et al*., 2014**).

Despite the growing burden of allergic diseases, in high-income and low - and middle -income countries, the efforts targeting allergic diseases remain fragmented. Allergic diseases have not been given the same level of public and governmental attention as other chronic diseases, such as cancer and cardiovascular diseases. This is surprising given the burden of allergic diseases even from childhood and onwards. This highlights the need for more epidemiological studies to assess the actual prevalent of these diseases, worldwide, in particular in LMICs, (**Nathan, *et al*., 20 08**).

Table 2. 10. Allergic types and epidemiology (Ebert & Pillsbury. 2011 & Aldakheel. 2021).

Type of Allergy	Symptoms	Prevalence	Affected Organ	Causes
Allergic rhinatisis	Sneezing, itchy, watery, and red eyes, stuffy or runny nose, swelling around the eyes.	Affects 10–30% of the population worldwide	Nose	Genetic and environmental factors
Asthma	Wheezing, coughing, shortness of breath, and chest tightness	Affects 3 to 9% of the population worldwide	Airways of lungs	Genetic and environmental factors
Food allergy	Itchiness, vomiting, swelling of the tongue, hives, diarrhea, low blood pressure, trouble breathing	Affects 8% of the population worldwide	Skin, respiratory system, gastrointestinal tract	Immune response to food
Skin allergy	Rash, itching, swelling, redness, cracked skin, flaking or scaling of skin, raised bumps	Worldwide, lifetime prevalence of above 20%	Skin	Latex, food, drugs, water, sunlight, nickel, chemicals, soap, poison oak or poison ivy
Drug allergy	Itching, rash, fever, facial swelling, hives, shortness of breath, cardiac symptoms	Affects 10% of the population worldwide	Nose, lungs, throat, ear, lining of the stomach, and skin	Reactions to medications
Insect allergy	Itching, pain, and swelling and appearance of redness at the sting/bite or surrounding affected areas	Many allergic severe cases have been documented with insect bites worldwide; however, there has been no systemic report.	Skin, eyes, throat, tongue	Insects bite or sting
Anaphylaxis	Itchy rash, numbness, throat swelling, lightheadedness, shortness of breath	Affects 0.05–2% of the population worldwide	Skin, nose, throat, lungs, gastrointestinal tract	Foods, insects bites, medications

2.7.1. Risk factors

Allergy risk factors are divided into two categories: **host** and **environmental. Host Factors** includes: Race, sex, heredity, and age are the host characteristics that influence the allergy risk ,with heredity being the most important. Host factors are not currently modifiable. **Environmental Factors includes** Smoking, Pollution, Dietary Habits and Infections**. (Aldakheel, *et al*., 2021)**. Allergic diseases are multifactorial and appear to be caused by a combination of genetic and environmental factors. Heritability of allergic disease is estimated to around 60-80% ,and a number of specific gene variants have been

found to increase the risk of disease **(Ullemar, *et al*., 2016).**

One such example is the filaggrin gene, in which loss-of-function mutations have been associated with skin barrier dysfunction and increased the risk of eczema. **(Palmer, *et al*., 2006).** Parental allergy is a strong risk factor for allergic disease. However, the associations have been reported to be somewhat more pronounced for maternal, compared to paternal allergy, indicating that non-genetic factors such as in-utero programming are also important **(Lim, *et al*., 2010).**

Second hand tobacco smoke exposure is one of the most established environmental risk factors for asthma, and may also increase the risk for other allergic diseases. **(Thacher, *et al*., 2014).** Both maternal smoking during pregnancy and second hand smoke exposure during childhood have been associated with wheeze and asthma in children. **(Neuman, *et al*., 2012).** Air pollution and indoor mold and dampness are other environmental risk factors that have been linked to asthma and allergic disease in children **(Thacher, *et al*., 2017).**

The prevalence of allergic disease, including asthma, rhinitis and allergic sensitization are lower among children raised on a farm and in rural, compared to urban areas **(Illi, *et al*., 2012).** In addition, large family size and early day-care attendance have been shown to reduce the risk of asthma and allergic sensitization, although the risk of transient wheeze in early life may be increased **(Rothers, *et al*., 2007).**

These observations have been proposed to be explained by the hygiene hypothesis, which suggests that a diverse exposure to bacteria and parasites in infancy is important for immune function development **(Liu, 2015).** In contrast, some viral infections in infancy such as the respiratory syncytial virus and rhinovirus have been shown to increase the risk of asthma.

However, it is unknown whether these associations are causal or explained by increased susceptibility in these children **(Feldman, *et al*., 2015).**

Factors in early childhood may also contribute to the risk of allergic disease. Breastfeeding has been shown to reduce the risk of asthma symptoms in early childhood, but the protective effect seems to diminish over time **(Dogaru, *et al*., 2014).**

Maternal factors during pregnancy such as obesity, diet ,certain medication and stress have also been suggested to contribute to the risk of asthma **(Castro-Rodriguez, *et al*., 2016).**

Since allergic disease continues to develop throughout childhood, lifestyle and environmental factors beyond infancy or early childhood may also influence the risk of disease. Furthermore, certain dietary factors such as intake of oily fish and antioxidants have been shown to reduce the risk of asthma and rhinitis up to adolescence **(Gref, *et al.,* 2017).**

Chapter three

Subjects & methods

3. Subjects and Methods

3.1 Study design

The study was conducted as retrospective study in records from patients who presented for treatment at Elaj Medical Center, during January to December 2023. **(appendix1).**

3.1.1 Study area

The present study was conducted at Elaj Medical Center, Sana'a City

3.1.2 Sample size

The sample size was statistically calculated for as study by the Epi Info statistical program version 20 (CDC, Atlanta, USA). confidence levels 99%, and the samples size comes to be 82 and will be select by using sample random sampling method (SPSS) Where **(www.dorakmt.tripod.com).**

3.1.3 Inclusion criteria

Patients treated at Elaj Medical Center, Sana'a City, Yemen.

3.1.4 Exclusion criteria

Patients who didn't admitted at Elaj Medical Center, Sana'a City, Yemen.

3.1.5 Data collection

Clinical Laboratory test results for patients and their demographic data was collected from registration records of the Elaj Medical Center by using data extraction format. All data included in the study was retrieve from the records anonymously with no identifications of the donors an extraction sheet will use, and data will be provided only as frequencies of positive results for each test.**(appendix2).**

3.1.6 Statistical analysis

The data was be analyzed by Social Package of Statistical Science (SPSS) version 20 (LEAD Technologies; Inc. USA). 95% confidence interval. *P* values <0.05 will be considered statistically significant. Variables were represented as frequencies and %. in addition, association between variables was assessed by $\mathbf{x^2}$ test and fisher exacted test (https://statpages.info/ctab2x2.html).

4. Ethical Considerations

The protocol of this study and its ethical consideration had approved by the Emirates International University Faculty of Medicine and Health Sciences and from the Elaj Medical Centre, Authorization**. (appendix3).**

5. Interpretation of clinical results:

3.5. 1. Interpretation of Skin Prick Test results:

According to the manufacturing company product:

- Diameter of the allergen bigger than 3 mm.

- Diameter bigger than half diameter of Histamine wheel. **(appendix6).**

3.5. 2. Interpretation of Patch Test results:

According to the manufacturing company product:

- (1+) Weak positive reaction with non-vesicular erythema, infiltration, possible papules

- (2+) Strong positive reaction with vesicular arythema, infiltration and papules

- (3+) Extreme positive reaction with intense erythema and infiltration, coalescing vesicles, bullousreaction . **(appendix7).**

Chapter four

Results

4. Results

The study aimed to detect patterns of Hypersensitivity among Yemeni patients at Elaj Medical Center in Sana'a city, Yemen during 2023.

4.1. Distribution of Hypersensitivity among Yemeni patients in Sana'a city.

A total 82 patient received by Elaj Medical Center during January and December 2023 was interviewed and had diagnosed as Delayed Hypersensitivity (25.6%) & Immediate Hypersensitivity (74.4%), **table-4.1**.

Both Delayed Hypersensitivity& Immediate Hypersensitivity was diagnosed by Skin Prick test and Patch test at Elaj Medical Center.

Table (4.1): Distribution of Hypersensitivity among Yemeni patients in Sana'a city.

Hypersensitivity	Frequency	Percent%
Delayed Hypersensitivity "Contact Dermatitis"	21	25.6%
Immediate Hypersensitivity "Atopic Dermatitis"	61	74.4%
Total	**82**	**100.0%**

4.2. Distribution of Immediate Hypersensitivity among Yemeni patients in Sana'a city.

The study found that Immediate Hypersensitivity, (25.6%), was more prevalent than Delayed Hypersensitivity, (74.4%), among Yemeni patients in Sana'a city, **table-4.1**.

4.2.1. Demographic data of patients with Immediate Hypersensitivity.

The results of this study found that female had, (52.5%), more affected with Immediate Hypersensitivity than male (47.5%) with age group 31-40 YRS, was 24.6%, **table- 4.2**.

Table (4.2): Distribution of Immediate Hypersensitivity among Yemeni patients according to age group and gender

Characteristics	Categories	n	(%)
Sex	MALE	30	47.5
	Female	31	52.5
Age groups	<10YRS	2	3.3
	10-20 YRS	14	24.6
	21-30 YRS	14	21.3
	31-40 YRS	15	24.6
	41-50 YRS	13	21.3
	51-60 YRS	2	3.3
	> 60 YRS	1	1.6
	TOTAL	**61**	**100.00%**

4.2.2. Allergens of Immediate Hypersensitivity.

Table (4.3) showed that most allergens that caused Immediate Hypersensitivity was *D.PT* and *D.farina*, with frequency 41 & 40, while less allergens with *Candida albicans*, *Composite*, and *Hores* with frequency 1 among males and females.

The study found that there was a significant association between allergen (*Mimosa*) and gender with $P = 0.0286$ and $X^2 = 4.792$ among patients with Immediate Hypersensitivity, **table-4.4**.

Table (4.3): Distribution of Immediate Hypersensitivity among Yemeni patients according to allergen and gender

	Allergen	Male (n)	Female (n)	Total (n)
1	D.farina	16	24	40
2	D.PT	17	24	41
3	Storae Mites	7	9	16
4	Alternaria	7	10	17
5	Aspergillus Mix	12	18	30
6	Candida Albicans	0	1	1
7	Penicillinum Mix	7	7	14
8	Cladosporium	1	4	5
9	3GrassesCocksfood.Rye.Timothy	3	4	7
10	Timothy	5	10	15
11	Bermuda Grasses	8	13	21
12	Date Palm	5	7	12
13	Mesquite	5	8	13
14	Mimosa	5	15	20
15	Rough Pigweed	7	10	17
16	Fat Hen	6	9	15
17	Mugwort	8	9	17
18	Plantain	6	9	15
19	Sorrel	7	11	18
20	Chenoppdiaceae(Mixture)	4	11	15
21	Composite	0	1	1
22	Wall Pellitory	1	1	2
23	Salsola Kali	1	1	2
24	Dadelion	1	1	2
25	Cat	13	14	27
26	Hores	1	0	1
27	Dog	9	12	21
28	Coockeoach(Balttela Garmanica	6	9	15
29	Celery	1	1	2
30	Banana	1	1	2

Table (4.4): Distribution of Immediate Hypersensitivity among Yemeni patients according to allergen and gender

Allergen	Categories	Total (n, %)		Male (n, %)		Female (n,%)		Chi-square test	*P value*
D.farina	*Positive*	40	65.57%	16	40%	24	60%	1.844	0.1745
	Negative	21	34.43%	13	62%	8	38%		
D.PT	*Positive*	41	67%	17	41%	24	59%	1.2	0.3
	Negative	20	32.79%	12	60%	8	40%		
Storae Mites	*Positive*	16	26.20%	7	44%	9	56%	0.004	0.95
	Negative	45	73.70%	22	49%	23	51%		
Alternaria	*Positive*	17	27.80%	7	41%	10	59%	0.111	0.7393
	Negative	44	72.10%	22	50%	22	50%		
Aspergillus Mix	*Positive*	30	49.10%	12	40%	18	60%	0.439	0.5075
	Negative	31	50.80%	17	55%	16	52%		
Candida Albicans	*Positive*	1	1.60%	0	0%	1	100%	0.921	0.3371
	Negative	60	98.40%	29	48%	31	52%		
Penicillinum Mix	*Positive*	14	22.90%	7	50%	7	50%	0.044	0.8338
	Negative	47	77%	22	47%	25	53%		
Cladosporium	*Positive*	5	8.10%	1	20%	4	80%	0.672	0.4124
	Negative	56	91.9	28	50%	28	50%		
3Grasses Cocksfood.Rye. Timothy	*Positive*	7	11.40%	3	43%	4	57%	0.07	0.792
	Negative	54	88.60%	26	48%	28	52%		
Timothy	*Positive*	15	24.40%	5	33%	10	67%	0.943	0.3315
	Negative	46	75.60%	24	52%	22	48%		
Bermuda Grasses	*Positive*	21	34.40%	8	38%	13	62%	0.641	0.4234
	Negative	40	65.60%	21	53%	19	48%		
Date Palm	*Positive*	12	19.60%	5	42%	7	58%	0.067	0.795
	Negative	51	80.40%	26	51%	25	49%		
Mesquite	*Positive*	13	21.30%	5	38%	8	62%	0.181	0.6702
	Negative	48	88.70%	24	50%	24	50%		
Mimosa	*Positive*	20	32.70%	5	25%	15	75%	4.792	0.0286
	Negative	41	67.30%	24	59%	17	41%		
Rough Pigweed	*Positive*	17	27.80%	7	41%	10	59%	0.111	0.7393
	Negative	44	72.70%	22	50%	22	50%		
Fat Hen	*Positive*	15	24.50%	6	40%	9	60%	0.141	0.7071
	Negative	46	75.50%	23	50%	23	50%		
Mugwort	*Positive*	17	27.80%	8	47%	9	53%	0.002	0.9626
	Negative	44	72.20%	21	48%	23	52%		
Plantain	*Positive*	15	24.50%	6	40%	9	60%	0.141	0.7071
	Negative	46	75.50%	23	50%	23	50%		
Sorrel	*Positive*	18	29.50%	7	39%	11	61%	0.353	0.5522
	Negative	43	70.50%	22	51%	21	49%		
Chenoppdiaceae (Mixture)	*Positive*	15	24.50%	4	27%	11	73%	2.454	0.1172
	Negative	46	75.50%	25	54%	21	46%		
Composite	*Positive*	1	1.60%	0	0%	1	100%	0.921	0.3371
	Negative	60	98.40%	29	48%	31	52%		

Wall Pellitory	*Positive*	2	3.20%	1	50%	1	50%	0.005	0.9436
	Negative	59	96.80%	28	47%	31	53%		
Salsola Kali	*Positive*	2	3.20%	1	50%	1	50%	0.005	0.9436
	Negative	59	96.80%	28	47%	31	53%		
Dadelion	*Positive*	2	3.20%	1	50%	1	50%	0.005	0.9436
	Negative	59	96.80%	28	47%	31	53%		
Cat	*Positive*	27	44.20%	13	48%	14	52%	0.007	0.9326
	Negative	24	55.80%	16	67%	18	75%		
Hores	*Positive*	1	1,6%	1	100%	0	0%	0.002	0.9604
	Negative	50	98.40%	28	56%	32	64%		
Dog	*Positive*	21	34.40%	9	43%	12	57%	0.068	0.7941
	Negative	40	65.60%	20	50%	20	50%		
Coockeoach (Balttela Garmanica	*Positive*	15	24.50%	6	40%	9	60%	0.141	0.7071
	Negative	46	75.50%	23	50%	23	50%		
Celery	*Positive*	2	3.20%	1	50%	1	50%	0.005	0.9436
	Negative	59	96.80%	28	47%	31	53%		
Banana	*Positive*	2	3.20%	1	50%	1	50%	0.005	0.9436
	Negative	59	96.80%	28	**47%**	31	53%		

4.3. Distribution of Delayed Hypersensitivity among Yemeni patients in Sana'a city

4. 3.1. Demographic data of patients with Immediate Hypersensitivity.

The results of this study found that female had, (57%), more affected with Delayed Hypersensitivity than male (43%) with age group 31-40 YRS, was 33%, **table- 4.5**.

Table (4.5): Distribution of Delayed Hypersensitivity among Yemeni patients according to age group and gender

Characteristics	Categories	n	(%)
Sex	MALE	9	43%
	Female	12	57%
Age groups	<10YRS	0	0%
	10-20 YRS	6	29%
	21-30 YRS	6	29%
	31-40 YRS	7	33%
	41-50 YRS	2	10%
	51-60 YRS	0	0%
	> 60 YRS	0	0%
	TOTAL	**21**	**100.00%**

4.3.2. Allergens of Delayed Hypersensitivity.

Table (4.6) showed that Paraphenylenediam, and Potassium bichromate was the most allergen and Neomycin Sulphate was the least allergen that caused Delayed Hypersensitivity among males and females, **figure 4-1**.
The study found that there was not association between allergen and gender with among patients with Delayed Hypersensitivity, **table-4.8**.

Table (4.6): Distribution of Delayed Hypersensitivity among Yemeni patients according to allergen and gender

	Allergen	Male (n)	Female (n)	Total (n)
1	Paraphenylenediam	4	5	9
2	Formaldehyde	2	0	2
3	Epoxy Resins	1	0	1
4	Benzocaine	1	2	3
5	Balsm of Peru	2	1	3
6	Parabens mix	3	3	6
7	Chlorocresol	0	1	1
8	Chobalt Sluphate	4	3	7
9	Mercapto benzothiazole	2	2	4
10	Pottassium bichromate	4	5	9
11	Parthenium	2	1	3
12	Black Rubber mix	1	1	2
13	Thiuram mix	3	2	5
14	Wool Alcohol (Lanolin)	0	1	1
15	Vaseline	4	1	5
16	Colophony	2	3	5
17	Nickel Sulphate	3	6	6
18	Neomycin Sulphate	0	0	0
19	Nitrofuro Zon	4	0	4
20	Fragrance mix	3	3	6

Table (4.7): Association between allergen and Gender.

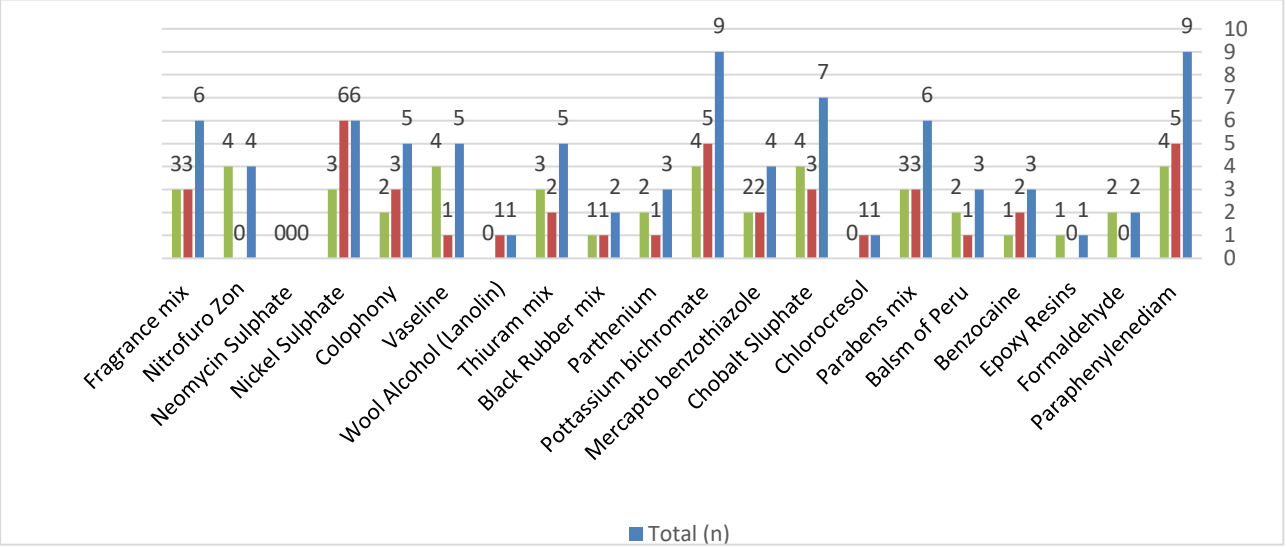

Figure (4.1): Distribution of allergens of Delayed Hypersensitivity among Yemeni patients according to gender

Table (4.8): Distribution of Delayed Hypersensitivity among Yemeni patients according to allergen and gender

Allergen	Categories	Total (n, %)		Male (n, %)		Female (n,%)		Chi-square test	P value
Paraphenylenediam	Positive	9	43%	4	44%	5	56%	0.016	0.8987
	Negative	12	57.1%	5	42%	7	58%		
Formaldehyde	Positive	2	28.6%	2	100%	0	0%	0.933	0.3342
	Negative	19	90%	7	37%	12	63%		
Epoxy Resins	Positive	1	4.76%	1	100%	0	0%	0.022	0.8824
	Negative	20	95.24%	8	40%	12	60%		
Benzocaine	Positive	3	14.29%	1	33%	2	67%	0.13	0.7188
	Negative	18	85.71%	8	44%	10	56%		
Balsm of Peru	Positive	3	14.29%	2	67%	1	33%	0.073	0.7871
	Negative	18	85.71%	7	39%	11	61%		
Parabens mix	Positive	6	28.57%	3	50%	3	50%	0.175	0.6757
	Negative	15	71.43%	6	40%	9	60%		
Chlorocresol	Positive	1	4.76%	0	0%	1	100%	0.788	0.3749
	Negative	20	95.24%	9	45%	11	55%		
Chobalt Sluphate	Positive	7	33.33%	4	57%	3	43%	0.219	0.64
	Negative	14	66.67%	5	36%	9	64%		
Mercapto benzothiazole	Positive	4	19%	2	50%	2	50%	0.103	0.7483
	Negative	17	81%	7	41%	10	59%		
Pottassium bichromate	Positive	9	42.9%	4	44%	5	56%	0.016	0.8987
	Negative	12	57.1%	5	42%	7	58%		
Parthenium	Positive	3	14.3%	2	67%	1	33%	0.073	0.7871
	Negative	18	85.7%	7	39%	11	61%		
Black Rubber mix	Positive	2	9.5%	1	50%	1	50%	0.046	0.8301
	Negative	19	90.5%	8	42%	11	58%		
Thiuram mix	Positive	5	23.8%	3	60%	2	40%	0.137	0.7116
	Negative	16	76.2%	6	38%	10	63%		
Wool Alcohol (Lanolin)	Positive	1	4.8%	0	0%	1	100%	0.788	0.3749
	Negative	20	95.2%	9	45%	11	55%		
Vaseline	Positive	5	23.8%	4	80%	1	20%	1.974	0.16
	Negative	15	71.4%	5	33%	11	73%		
Colophony	Positive	5	23.8%	2	40%	3	60%	0.022	0.8824
	Negative	16	76%	7	44%	9	56%		
Nickel Sulphate	Positive	6	28.57%	3	50%	6	100%	0	1
	Negative	15	71%	5	33%	10	67%		

Neomycin Sulphate	*Positive*	0	0%	0	0%	0	0%	0	0
	Negative	21	100%	0	0%	0	0%		
Nitrofuro Zon	*Positive*	4	19%	4	100%	0	0%	3.649	0.0561
	Negative	15	71%	5	33%	11	73%		
Fragrance mix	*Positive*	6	28.57%	3	50%	3	50%	0.175	0.6757
	Negative	15	71%	6	40%	9	60%		

Chapter five

Discussion

5. Discussion

The study was a retrospective study and provides a comprehensive evaluation of the prevalence and characteristics of Delayed Hypersensitivity-contact dermatitis- and Innate Hypersensitivity-atopic dermatitis- in Sana'a city, Yemen, and compares the findings with relevant studies conducted in Saudi Arabia, Egypt, and other countries.

The results of this study indicated that Innate Hypersensitivity -atopic dermatitis- was more prevalent than Delayed Hypersensitivity-contact dermatitis- in Sana'a, with 74.4% and 25.6% respectively. This finding aligns with the results of a similar study conducted in Saudi Arabia, which reported a 68.3% prevalence of Innate Hypersensitivity-atopic dermatitis- and 31.7% prevalence of Delayed Hypersensitivity-contact dermatitis **(Al-Asmari, *et al*., 2019).** In contrast, a study in Egypt found a higher prevalence of Delayed Hypersensitivity (57.1%) compared to Innate Hypersensitivity (42.9%) **(Abdel-Hafez, *et al*., 2003).** In the United States, the National Health and Nutrition Examination Survey (NHANES) reported a 7.3% prevalence of Innate Hypersensitivity and 5.7% prevalence of Delayed Hypersensitivity in the general population **(Silverberg, *et al*., 2013).**

The variations in prevalence across these regions may be attributed to differences in environmental exposures, genetic predispositions, and lifestyle factors. The higher prevalence of Innate Hypersensitivity-atopic dermatitis in Sana'a and Saudi Arabia, compared to the higher prevalence of Delayed Hypersensitivity-contact dermatitis in Egypt, highlights the importance of regional epidemiological studies to inform targeted prevention and management strategies **(Aldakheel, *et al.,* 2021).**

The current study found a relatively even distribution of Delayed and Innate Hypersensitivity across different age groups in Sana'a city. This was consistent with the findings from study conducted in Saudi Arabia, where the prevalence of both conditions remained stable across age **(Al-Asmari, *et al*., 2019).**

In contrast, the Egyptian study reported a higher prevalence of Delayed Hypersensitivity-contact dermatitis in older age groups **(Abdel-Hafez *et al*., 2003).** While the NHANES data from the United States showed a higher prevalence of Innate Hypersensitivity-atopic dermatitis in younger individuals **(Silverberg, *et al*., 2013).**

These regional differences may be influenced by factors such as occupational exposures, access to healthcare, and cultural practices that influence skin care and management.

The skin prick test results for atopic dermatitis from this study highlighted the significant role of dust mite allergens (D.PT) in the development of allergic skin conditions in Sana'a. This was consistent with findings from Saudi Arabia and Indonesia where dust mite allergens were also identified as a prominent trigger-allergen **(Al-Asmari*, et al*., 2019 & Nopriyati, *et al.* 2022).**

In Egypt, the most common allergens associated with delayed hypersensitivity-contact dermatitis were Nickel sulfate, Fragrance mix, and Potassium dichromate **(Abdel-Hafez**, ***et al*., 2003).** The NHANES data from the United States showed that Nickel, Neomycin, and Cobalt were the most prevalent innate hypersensitivity-contact allergens **(Silverberg**, ***et al*., 2013).**

These regional differences in allergen profiles emphasize the importance of local and context-specific assessments to guide the identification and management of triggers for delayed-contact and innate hypersensitivity-atopic dermatitis.

The present study found that females was more affected than males with delayed hypersensitivity- contact dermatitis and equal affected in case of innate hypersensitivity-atopic dermatitis. This finding disagree with study conducted in India **(Gopinath VPK, *et al* 2019).** This may be due to the fact that females have a more outgoing nature in this society than males and have a greater tendency to seek medical care by being

the primary earning member in the family with significant exposure to allergens in workplaces.

The current study results found a significant association between gender and positive skin prick test results for Mimosa, suggesting a potential gender-specific susceptibility to certain allergens as a risk factor. A similar gender-based association was not observed in the Saudi Arabian & Egyptian studies **(Al-Asmari, *et al*., 2019 & Abdel-Hafez, *et al.*, 2003).**

The varying gender associations across these regions highlight the complex interplay between biological, environmental, and cultural factors that may influence the development and presentation of skin conditions.

This study is limited by its focus on a single city in Yemen, which may not be representative of the broader national context. Expanding the research to include larger and more diverse populations across Yemen, as well as conducting longitudinal studies, would provide a more comprehensive understanding of the epidemiology and trajectories of contact and atopic dermatitis.

Additionally, incorporating in-depth investigations of environmental, genetic, and socioeconomic factors that may contribute to the observed regional differences would help elucidate the underlying mechanisms and inform tailored prevention and management strategies **(Gref, *et al*., 2017).**

Chapter Six

Conclusion & Recommendation

6.1 Conclusion

1) Innate hypersensitivity-atopic dermatitis more prevalent than delayed hypersensitivity-contact dermatitis.

2) The study highlighted the significant role of dust mite allergens (D.PT) in the development of allergic skin conditions among Yemeni patients in Sana'a city.

3) The study highlighted the significant role of Paraphenylenediam, and Pottassium bichromate was the most allergen caused Delayed Hypersensitivity among Yemeni patients.

4) The findings highlight the varying prevalence, age distributions, allergen profiles, and gender associations across these regions, emphasizing the need for context-specific approaches to diagnosis, management, and prevention.

5) Continued research and collaboration across diverse settings will be crucial in addressing the global challenge of delayed-contact and innate hypersensitivity-atopic dermatitis.

6.2 Recommendations

1. Further studies should be conducted to include a larger and more diverse population across Yemen, not just limited to Sana'a city.

2. Develop educational campaigns and resources to help patients and healthcare providers recognize and avoid relevant allergens.

3. Train healthcare professionals, including general practitioners and pediatricians, on the accurate diagnosis and evidence-based management of contact and atopic dermatitis.

4. Implement public awareness campaigns to educate the community on the prevention, early recognition, and appropriate management of contact and atopic dermatitis.

5. Investigate the potential role of genetic, socioeconomic, and cultural factors in the development and presentation of contact and atopic dermatitis in Yemen and the broader region.

References

Akdis, C.A.; Akdis, M. (2014): Mechanisms of immune tolerance to allergens: Role of IL-10 and Tregs.J. Clin. Investig. 124,4678–4680.

Aldakheel F.M. (2021): Allergic Diseases: A Comprehensive Review on Risk Factors, Immunological Mechanisms, Link with COVID-19, Potential Treatments, and Role of Allergen Bioinformatics, Int. J. Environ. Res. Public Health, 18, 12105. https://doi.org/10.3390/ijerph182212105

Alinaghi F, Bennike NH, Egeberg A, Thyssen JP, Johansen JD. (2019): Prevalence of contact allergy in the general population: A systematic review and meta-analysis. Contact Dermatitis;80 (2):77-85.

Alshaiby S. (2021): Clinical presentation of allergic fungal sinusitis in Aden, Yemen Clinical presentation of allergic fungal sinusitis in Aden, Yemen. Hadhramout University Journal of Natural & Applied Science, 18.

Alvarez-Alvarez I, Niu H, Guillen-Grima F, *et al* . (2018): Meta-analysis of prevalence of wheezing and recurrent wheezing in infants. Allergologia et Immunopathologia; 46:210 – 7. doi:10.1016/j.aller.2016.08.011

Ansotegui IJ, Melioli G, Canonica GW, *et al*. (2020): Ig-E allergy diagnostics and other relevant tests in allergy, a World Allergy Organization position paper. World Allergy Organ J; 13:100080. doi:10.1016/j.waojou.2019.100080.

Astarita, C.; Scala, G.; Sproviero, S.; Franzese, A. (1996): Effects of enzyme-potentiated desensitization in the treatment of pollinosis: A double-blind placebo-controlled trial.J. Investig. Allergol. Clin. Immunol., 6, 248–255.

Avenberg KM, Harper DS, Larsson BL **(1986):** Foot notes on allergy. Pharmacia, Uppsala.

Baldacci, S.; Maio, S.; Cerrai, S.; Sarno, G.; Baïz, N.; Simoni, M.; Annesi-Maesano, I.; Viegi, G.; Study, H. (2015): Allergy and asthma: Effects of the exposure to particulate matter and biological allergens.Respir. Med. 109, 1089–1104.

Bandmann H-J, Fregert S (1982): Epikutantestung, 2nd edn. Springer, Berlin Heidelberg New York. USA.

Blackley C **(1873):** Experimental researches on the cause and nature of hay fever.

Balli`ere, Tindall & Cox, London.

Blaiss, MS, Canonica, GW, Holgate, ST, Lockey, RF and Pawankar R. White (2013): Book on Allergy (Update: 2013).

Bochner, B.S.; Rothenberg, M.E.; Boyce, J.A.; Finkelman, F. (2013): Advances in mechanisms of allergy and clinical immunology in 2012. J. Allergy Clin. Immunol, 131, 661–667.

Bonyadi, M.; Hassanzadeh, D.; Seyfizadeh, N.; Borzoueisileh, S. (2017): Assessment of allergen-specific IgE by immunoblotting method in atopic dermatitis. Eur. Ann. Allergy

Clin. Immunol., 49, 213–219.

Burg G, Przybilla B, Bogner J (1986): Contact-allergy time. In: Ring J, Burg G (eds) New trends in allergy II. Springer, Berlin Heidelberg New York, pp 230–-239.

Calzada, D.; Baos, S.; Cremades, L.; Cardaba, B. (2018): New treatments for allergy: Advances in peptide immunotherapy.Curr. Med.Chem., 25, 2215–2232.

Calzada, D.; Baos, S.; Cremades-Jimeno, L.; Cárdaba, B. (2018): Immunological mechanisms in allergic diseases and allergen tolerance: The role of treg cells. J. Immunol. Res. 2018, 6012053.

Castro-Rodriguez JA, Forno E, Rodriguez-Martinez CE, Celedon JC. (2016): Risk and Protective Factors for Childhood Asthma: What Is the Evidence? J Allergy Clin Immunol Pract. 4(6):1111-22.

Coombs PR, Gell PG. (1968): Classification of allergic reactions re-sponsible for clinical hypersensitivity and disease. In: Gell RR, ed. Clinical Aspects of Immunology. Oxford University Press;:575-596.

Coombs RRA, Gell PGH. (1963): The classification of allergic reactions underlying disease. In: Coombs RRA and Gell PGH, eds. Clinical Aspects of Immunology Philadelphia: Davis;317.

D'Amato G, Liccardi G, D'Amato M, *et al.* (2002): Outdoor air pollution, climatic changes and allergic bronchial asthma. European Respiratory Journal; 20:763 –76. doi:10.1183/09031936.02.00401402

Darsow U, Vieluf D, Ring J (1995): Atopy patch test with different vehicles and allergen concentrations:

An approach to standardization. J Allergy Clin .Immunol 95:677 – 684

De Weck **A (1997):** A short history of allergological diseases and concepts. In: Kay B (ed) Allergy. Blackwell, Oxford, pp 3 – 22.

Delves PJ. **(٢٠١٩):** Overview of Allergic and Atopic Disorders - Immunology; Allergic Disorders. Merck Manuals Professional Edition.;:1–13.https://www.merckmanuals.com/professional/immunology–allergic disorders/allergic,-autoimmune,-and-other-hypersensitivity disorders/overview-of -allergic -and-atopic-disorders.

Descotes, J. & Choquet-Kastylevsky, G. **(2001):** Gell and Coombs's classification: is it still valid? Toxicology, 158, 43-9.

Dogaru CM, Nyffenegger D, Pescatore AM, Spycher BD, Kuehni CE. (2014): Breastfeeding and childhood asthma: systematic review and meta-analysis. Am J Epidemiol;179(10):1153-67.

Dorsch W, Ring J (1981): Induction of late cutaneous reactions (LCR) by skin blister fluid (SBF) from allergen-tested and normal skin. J Allergy Clin. Immunol 67:117 – 125.

Douglass, J.A.; O'Hehir, R.E. 1. (2006): Diagnosis, treatment and prevention of allergic disease: The basics.Med. J. Aust., 185, 228–233.

Dreborg S, Frew A (eds) (1993): Allergen stan-dardization and skin tests. Position Papers

Aller-gy 48 [Suppl]:48 – 82

Ebert Jr CS, Pillsbury HC (2011): Epidemiology of Allergy. Otolaryngol. Clin North Am.;44:537-548.

Endara P, Vaca M, Platts-Mills TAE, *et al*. (2015): Effect of urban vs. rural residence on the association between atopy and wheeze in Latin America: Findings from a case-control analysis. Clinical and Experimental Allergy; 45:438 –47. doi:10.1111/cea.12399

Feldman AS, He Y, Moore ML, Hershenson MB, Hartert TV. (2015): Toward Primary Prevention of Asthma. Reviewing the Evidence for Early-Life Respiratory Viral Infections as Modifiable Risk Factors to Prevent Childhood Asthma. Am J Respir Crit Care Med 191(1):34-44.

Franck U, Herbarth O, Röder S, *et al*. (2011): Respiratory effects of indoor particles in young children are size dependent. Science of the Total Environment; 409:1621–31. doi:10.1016/j.scitotenv.2011.01.001

Fuchs E, Gronemeyer W, Bandilla K (1981): Reib-test und Tierhaarallergie, zugleich ein klinischer Beitrag "Zum Problem der Rasse-Spezifität". All-ergologie 4:241 – 248

Gardner, L.M.; Thien, F.; Douglass, J.A.; Rolland, J.M.; O'Hehir, R.E. (2004): Induction of T 'regulatory'cells by standardized house dust mite immunotherapy: An increase in CD4+ CD25+ interleukin-10+ T cells expressing peripheral tissue trafficking markers.Clin. Exp. Allergy, 34, 1209–1219.

Ghosh, D.; Gupta-Bhattacharya, S. (2011): Allergen bioinformatics: Recent trends and

developments. Sel. Work. Bioinform., 49, 1–14.

Gref A, Rautiainen S, Gruzieva O, Hakansson N, Kull I, Pershagen G, et al. (2017): Dietary total antioxidant capacity in early school age and subsequent allergic disease. Clin. Exp. Allergy; 47(6):751-9.

Gronemeyer W, Debelic M (1967): Der sog. Reib-test, seine Anwendung und klinische Bedeutung. Dermatologica (Basel) 134:208

Grosvenor, M. B. & Smolin, L. A. **(2015):** Visualizing nutrition: Everyday choices (3rd ed.). Hoboken, NJ: Wiley.

Hasunuma H, Ishimaru Y, Yoda Y, *et al*. (2014): Decline of ambient air pollution levels due to measures to control automobile emissions and effects on the prevalence of respiratory and allergic disorders among children in Japan. Environmental Research; 131:111 –8. doi:10.1016/j.envres.201 4.03.007

https://bpac.org.nz/BT/2011/December/allergy at 3-4-2024

Illi S, Depner M, Genuneit J, Horak E, Loss G, Strunz-Lehner C, et al. **(2012):** Protection from childhood asthma and allergy in Alpine farm environments-the GABRIEL Advanced Studies. J Allergy Clin Immunol;129(6):1470-7.e6.

Jadassohn J (1896): Zur Kenntnisse der Arzneie-xantheme. Arch Derm Syph 34:103 Bericht V. Kon-greß D. derm. Ges., Graz, 23 – 25 September 1895

Jeffrey K. (2012): Integrated review immunology and microbiology. 2nd ed. USA.

Johansen JD, Aalto-Korte K, Agner T, Andersen KE, Bircher A, Bruze M, et al. (2015):

European Society of Contact Dermatitis guideline for diagnostic patch testing - recommendations on best practice. Contact Dermatitis;73(4):195-221.

Johansson SG. **(1967):** Raised levels of a new immunoglobulin class (IgND) in asthma. Lancet.;2(7523):951-3.

Kemp SF, Lockey R (eds) (1999): Diagnostic methods in allergy. CRC Press, Boca Raton. USA.

Lazzarini R, Duarte I, Lindmayer FA. (2013): Patch tests. An Bras Dermatol. Nov; 88(6): 879-888.

Leelavathi Muthupalaniappen, Adawiyah Jamil (2021): Prick, patch or blood test? A simple guide to allergy testing. Malays Fam Physician.;16(2). https://doi.org/10.51866/rv1141.

Lei, D.K.; Grammer, L.C. (2019): An overview of allergens. Allergy Asthma Proc. 40, 362–365.

Li JT. (2002): Allergy testing. Am Fam Physician . Aug; 66(4): 621-624.

Lim RH, Kobzik L, Dahl M. (2010): Risk for asthma in offspring of asthmatic mothers versus fathers: a meta-analysis. PloS One;5(4):e10134.

Liu AH. (2015): Revisiting the hygiene hypothesis for allergy and asthma. J Allergy Clin Immunol;136(4):860-5.

McKinley, M. P., O'Loughlin, V. D. & Bidle, T. S. (2016): Anatomy and Physiology: An integrative approach. New York, NY: McGraw Hill Education.

Murphy K, Travers P, Walport M. (2008): Janeway's Immunobiology. Seventh ed.

Abingdon: Garland Science.

Nathan RA, Meltzer EO, Derebery J, *et al.* (2008): The prevalence of nasal symptoms attributed to allergies in the United States: Findings from the burden of rhinitis in an America survey. Allergy and Asthma Proceedings; 29:600 –8. doi:10.2500/aap.2008.29.3179

Neuman A, Hohmann C, Orsini N, Pershagen G, Eller E, Kjaer HF, et al. (2012): Maternal smoking in pregnancy and asthma in preschool children: a pooled analysis of eight birth cohorts. Am J Respir Crit Care Med;186(10):1037-43.

Nosbaum A, Vocanson M, Rozieres A, et al. (2009): Allergic and irritant contact dermatitis. Eur J Dermatol . Jul; 19(4): 325-332.

Obaid J. & Waheed A. (٢٠١٩): Sensitization Pattern to common Inhalant allergens among patients with Allergic Rhinitis in Taiz, Yemen. AL - Saeed Journal of Humanities and Applied Sciences 3 ,2.

Obaid J. et al., (2022): Early infant feeding and allergic respiratory diseases in Ibb city, Yemen. European Journal of Medical Research 27:35. https://doi.org/10.1186/s40001-022-00662-7

Palmer CN, Irvine AD, Terron-Kwiatkowski A, Zhao Y, Liao H, Lee SP, et al. (2006): Common loss-of-function variants of the epidermal barrier protein filaggrin are a major predisposing factor for atopic dermatitis. Nature Genet;38(4):441-6.

Pawankar R. **(٢٠١٤):** Allergic diseases and asthma: A global public health concern and a call to action. World Allergy Organization Journal;7:1 –3. doi:10.1186/1939-4551-7-12

Pawankar R. (2014): Allergic diseases and asthma: A global public health concern and a call to action. World Allergy Organization Journal;7:1 –3. https: //doi:10.1186/1939-4551-7-12.

Phil. Johannes Ring (2019): Johannes Ring · Allergy in Practice. Springer-Verlag Berlin Heidelberg New York. http://www.springeronline.com.

Pirquet C (1906): Allergie. Munchener Medizinische Wochenschrift. ; 53:1457-8.

Pomés A. (2008): Common structures of allergens. Revue Française d'Allergologie et d'Immunologie Clinique.;48(3):139-42.

Pramod, S.N. (2021): Immunological Basis for the Development of Allergic Diseases-Prevalence, Diagnosis and Treatment Strategies. In Cell Interaction-Molecular and Immunological Basis for Disease Management; Intech Open: London, UK.

Pramod, S.N. (2021): Immunological Basis for the Development of Allergic Diseases-Prevalence, Diagnosis and Treatment Strategies. In Cell Interaction-Molecular and Immunological Basis for Disease Management; IntechOpen: London, UK.

Przybilla B, Bergmann K-C, Ring J (eds) (2000): Praktische Allergologische Diagnostik. Stein-kopff, Darmstadt.

Pullerits, T.; Praks, L.; Ristioja, V.; Lötvall, J. (2002): Comparison of a nasal glucocorticoid, antileukotriene, and a combination of antileukotriene and antihistamine in the treatment of seasonal allergic rhinitis. J. Allergy Clin. Immunol. 109, 949–955.

Ring J (1981): Diagnostic methods in allergy. Behring Inst Mitt 68:141 – 152

Roitt, I. et al., (2016): Roitt's Essential Immunology. Thirteenth edition www.wiley.com/wiley-blackwell.

Rothers J, Stern DA, Spangenberg A, Lohman IC, Halonen M, Wright AL. (2007): Influence of early day-care exposure on total IgE levels through age 3 years. J Allergy Clin Immunol;120(5):1201-7.

Schultze-Werninghaus G, Merget R (2000): Asthma bronchiale. In: Praktische Allergologische Diagnostik. Steinkopff, Darmstadt, pp 165 – 182

Scurlock, A.M. (2018): Oral and sublingual immunotherapy for treatment of Ig-E-mediated food allergy.Clin. Rev. Allergy Immunol.55, 139–152.

Shamji, M.H.; Durham, S.R. (2017): Mechanisms of allergen immunotherapy for inhaled allergens and predictive biomarkers.J. Allergy Clin. Immunol. 140, 1485–1498.

Stróżek J, Samoliński B, Kłak A, *et al.* (2019): The indirect costs of allergic diseases. International Journal of Occupational Medicine and Environmental Health 32:281 –90. doi:10.13075/ijomeh.1896.01275

Thacher JD, Gruzieva O, Pershagen G, Melen E, Lorentzen JC, Kull I, et al. (2017): Mold and dampness exposure and allergic outcomes from birth to adolescence: data from the BAMSE cohort. Allergy;72(6):967-74.

Thacher JD, Gruzieva O, Pershagen G, Neuman A, Wickman M, Kull I, et al. (2014): Pre- and postnatal exposure to parental smoking and allergic disease through adolescence. Pediatrics;134(3):428-34

Turgeon M. L, (2014): Immunology & Serology in Laboratory Medicine, 5th ed. http://evolve.elsevier.com/Turgeon/immunology/

Turnbull, J.; Adams, H.; Gorard, D. (2015): The diagnosis and management of food allergy and food intolerances.Aliment. Pharmacol.Ther, 41, 3–25.

Ullemar V, Magnusson PK, Lundholm C, Zettergren A, Melen E, Lichtenstein P, et al. (2016): Heritability and confirmation of genetic association studies for childhood asthma in twins. Allergy;71(2):230-8.

Valavanidis A, Fiotakis K, Vlahogianni T, *et al.* (2006): Characterization of atmospheric particulates, particle -bound transition metals and polycyclic aromatic hydrocarbons of urban air in the center of Athens (Greece). Chemosphere 65:760 –8. doi:10.1016/j.chemosphere.2006.03.052

Wahn U, Seger W, Wahn V (eds) **(2004):** Allergien imKindesalter,4th edn. Fischer, Stuttgart.

WHO (2007): Chronic Respiratory. WHO Library 2007;:1–37. doi:ISBN 978 92 4 156346 8.

WHO (2007): Chronic Respiratory. WHO Library:1–37. doi:ISBN 978 92 4 156346 8.

Wong, A.G.; Lomas, J.M. (2019): Allergy testing and immunotherapy.Pediatr. Rev., 40, 219–228.

Y. Nitta MAMS. (2003): Air Pollution and Respiratory in Chiba Prefecture, Japan Symptoms in Children Living along Trunk Roads. Journal of Epidemiology; 13:108 –19.

Zuberbier T, Lötvall J, Simoens S, et al. **(٢٠١٤):** Economic burden of inadequate management of allergic diseases in the European Union: A GA2LEN review. Allergy: European Journal of

Allergy and Clinical Immunology ;69:1275–9. doi:10.1111/all.12470.

Zuberbier T, Lötvall J, Simoens S, *et al*. (2014): Economic burden of inadequate management of allergic diseases in the European Union: A GA2LEN review. Allergy: European Journal of Allergy and Clinical Immunology; 69:1275–9. doi:10.1111/all.12470

(http://creativecommons.org/licenses/by/3.0) at 5-4-2024

(http://dx.doi.org/10.1016/B978-0-12-385245-8.00018-2) at 28-3-2024.

(https://www.aashwas.in/diagnostic -services/skin-prick-test -spt/**)** at 1-4-2024 .

Appendix


مركز
علاج
للتداوي الطبيعي
عيادة الحساسية
عيادة التغذية العلاجية
مختبر الحساسية


عيادة الحساسية
ALLERGY CLINIC
EIU
الجامعة الإماراتية الدولية
EMIRATES INTERNATIONAL UNIVERSITY

Some of the reagent used in skin prick test, patch test and vaccine


Test
Mugwort
Timothy
Ryegrass
Cat dand
D. farina
Silver
Conc.: 50 HEP
Glycerol 50%
0.9%, Phosph
Batch:A23J03
Store between
inmunotek


SB 2
CREDISOL
BD


Ramla Abdul Qawi Radman
Strength 4

مركز علاج لإزالة التحسس
نموذج استبيان خاص بالمريض

معلومات شخصيه

الاسم : ..... الجنس :.....

العمر:..... الحالة الاجتماعية :..... العمل :.....

العنوان: ..... المدينة :.....

اعراض الحساسية ● الجلد ● الصدر ● الأنف ● العين

ماهي الاعراض الشائعة لديك: .....

.....

بداية ظهور الاعراض لأول مرة: .....

تظهر الاعراض طوال السنة نعم ☐ لا ☐

هل تزداد الاعراض ليلا نعم ☐ لا ☐

هل تزداد الاعراض داخل المنزل نعم ☐ لا ☐

هل تزداد الاعراض خارج المنزل نعم ☐ لا ☐

هل توجد تهويه كافيه في المنزل نعم ☐ لا ☐ قليلا ☐

هل يوجد لديك حيوانات اليفه نعم ☐ لا ☐

ماهي ؟.....

هل توجد حشائش او أشجار في البيئة المحيطة بك نعم ☐ لا ☐

هل تعاني من الحساسية في الاماكن الرطبة نعم ☐ لا ☐

هل تعاني من الحساسية للغبار او الأتربة نعم ☐ لا ☐

هل يعاني أحد افراد الاسرة من الحساسية نعم ☐ لا ☐

هل تعاني من ازمة في التنفس او أي احد من العائلة نعم ☐ لا ☐

هل اصبت بنوبة حساسيه شديده من قبل استدعت دخول الطوارئ نعم ☐ لا ☐

ماهي الأسباب؟ ....

.....

ماهي الأدوية التي تم استخدامها مسبقا .....

Date: اسم المريض

Sex: العمر

اسم الطبيب

Patch Test

S	Allergen	result
1	Paraphenylenediam	
2	Formaldehyde	
3	Epoxy Resins	
4	Benzocaine	
5	Balsm of Peru	
6	Parabens mix	
7	Chlorocresol	
8	Chobalt Sluphate	
9	Mercapto benzothiazole	
10	Pottassium bichromate	

S	Allergen	result
11	Parthenium	
12	Black Rubber mix	
13	Thiuram mix	
14	Wool Alcohol (Lanolin)	
15	Vaseline	
16	Colophony	
17	Nickel Sulphate	
18	Neomycin Sulphate	
19	Nitrofuro Zon	
20	Fragrance mix	

Note :

(1+) weak positive reaction with nonvesicular erythema, infiltration, possible papules

(2+) Strong positive reaction with vesicular arythema , infiltration and papules

(3+) Extreme positive reaction with intense erythema and infiltration, coalescing vesicles, bullous reaction

Signature:

.....

Date:	التاريخ	**Name:**	اسم المريض
Sex:	الجنس	**Age:**	العمر
Lab. No.:	الرقم المخبري	**Doctor**	اسم الطبيب

Skin Prick Test Report

CODE	Allergen	wheat diameter (mm)
	MITES	
1	D.farina	Non Reactive
2	D.PT	Non Reactive
3	Storae Mites	Non Reactive
	Mould &Yeast	
4	Alternaria	Non Reactive
5	Aspergillus Mix	Non Reactive
6		
7	Penicillinum Mix	Non Reactive
8	Cladosporium	Non Reactive
	Grasses	
9	**3Grasses Cocksfood.Rye. Timothy**	Non Reactive
10	Timothy	Non Reactive
11	Bermuda Grasses	Non Reactive
	Trees	
12	Date Palm	Non Reactive
13		
14	Mimosa	Non Reactive
15	Rough Pigweed	Non Reactive

CODE	Allergen	wheat diameter (mm)
	Weeds	
16	Fat Hen	Non Reactive
17	Mugwort	Non Reactive
18	Plantain	Non Reactive
19	Sorrel	**Non Reactive**
20	Chenoppdiaceae (Mixture)	Non Reactive
21	Composite	Non Reactive
22	Wall Pellitory	Non Reactive
23		
24		
	Epithelia	
25	Cat	Non Reactive
26		
27	Dog	Non Reactive
28	Coockeoach (Balttela Garmanica	**Non Reactive**
29	Negative control	
30	Positive control (Histamine)	
	Food	

Notes:

*** Positive result :**

1)Diameter of the allergen bigger than 3 mm .

2) Diameter bigger than half diameter of Histamine wheel

Signature:

.....

Arabic summary

الجمهورية اليمنية
وزارة التعليم العالي والبحث العلمي
الجامعة الإمارات الدولية
كلية الطب والعلوم الصحية
قسم المختبرات الطبية

أنماط فرط الحساسية بين المرضى اليمنيين المترددين على مركز علاج الطبي في مدينة صنعاء، اليمن

مشروع تخرج مقدم لكلية الطب والعلوم الصحية كاستيفاء جزئي لمتطلبات نيل درجة البكالوريوس في طب المخبري

مقدم من

١. آية العسولي
٢. آيات االمشدلي
٣ إيمان الغرباني
٤. دعاء الفقيه
٥. هاجر حميد
٦. غدير العطاب
٧. جوهرة بابعير
٨.هناء الحلك
٩. سامح الأديب
١٠. رشا القودري
١١. لولة العامري
١٢. ليث الشيباني
١٣. ولاء صابونة

مشرف البحث

أستاذ مشارك دكتور/عبدالباسط الغوري

دكتوراه في طب الإحياء الدقيقة (رئيس قسم المختبرات الطبية، كلية الطب والعلوم الصحية، الجامعة الإمارات الدولية)

٢٠٢٤م
١٤٤٥هـ

الملخص العربي

الخلفية: أمراض الحساسية هي رد فعل فرط الحساسية ضد عوامل الاتصال الخارجية وتستمر في الزيادة في جميع أنحاء العالم. إذا تركت دون علاج يمكن أن يسبب أعراض التهاب الأنف التحسسي، والربو، والشرى المزمن، وحساسية الدواء، والتهاب الجلد التأتبي / التماسي، والتهاب الملتحمة التحسسي، والتهاب الجيوب الأنفية المزمن ، بحيث يمكن أن يتداخل مع نوعية الحياة. أجريت هذه الدراسة للتحقيق في أنماط تفاعل فرط الحساسية بين المرضى اليمنيين في مركز علاج الطبي في مدينة صنعاء، اليمن خلال عام ٢٠٢٣.

الأساس المنطقي: تسليط الضوء على أهمية الفحص الروتيني اختبارات تشخيص الحساسية اختبار وخز الجلد أو مصل Ig-E واختبار رقعة الجلد قبل أي إدارة وعلاج محددين للحساسية.

المرضى والطرق: دراسة بأثر رجعي للتحقيق في اختبار البقعة وتفاعل اختبار وخز الجلد بين المرضى الذين يعانون من التشخيص السريري لتفاعلات فرط الحساسية المتأخرة أو الفورية - الاتصال / التهاب الجلد التأتبي الذين تمت إحالتهم إلى مركز علاج الطبي في مدينة صنعاء ، اليمن خلال عام ٢٠٢٣. جميع المرضى الذين خضعوا لاختبار البقعة واختبار وخز الجلد. وقد قرأت النتائج وفسرت وحللت.

النتائج: من بين ٨٢ حالة تفاعلت بشكل إيجابي مع واحد أو أكثر من مسببات الحساسية ، تفاعلت ٦١ (٧٤,٤٪) بشكل إيجابي مع اختبارات وخز الجلد التي تفاعلت مع فرط الحساسية الفورية - التهاب الجلد التأتبي. في حين أن ٢١ (٢٥,٦٪) تفاعلوا بشكل إيجابي مع اختبارات البقعة قد أخرت تفاعل فرط الحساسية - التهاب الجلد التماسي. كانت الإناث أكثر تأثرا من الذكور الذين يعانون من تفاعلات فرط الحساسية المتأخرة والفورية مع الفئة العمرية ٣١-٤٠ سنة ، وهو ما يمثل ٣٣ ٪.

الاستنتاج: في حالة تفاعلات فرط الحساسية الفورية ، كانت مسببات الحساسية الأكثر شيوعا في دراستنا هي D.farina و D.PT بتردد ٤١ و ٤٠ ، في حين أن مسببات الحساسية الأقل مع المبيضات البيض ، المركب ، و Hores مع التردد ١ بين الذكور والإناث. وجدت الدراسة أن هناك ارتباطا كبيرا بين مسببات الحساسية (الميموزا) والجنس مع P = 0.0286 و X2 = 4.792 بين المرضى الذين يعانون من فرط الحساسية الفورية. فيما يتعلق بتفاعلات فرط الحساسية المتأخرة ، كانت أكثر مسببات الحساسية شيوعا

هي Paraphenylenediam و Pottassium bichromate ولكن كبريتات النيومايسين كانت الأقل إثارة للحساسية. وجدت الدراسة أنه لا يوجد ارتباط كبير بين مسببات الحساسية والجنس بين المرضى الذين يعانون من فرط الحساسية المتأخرة.