ALLERGIC FOODS: A CASE STUDY IN KHARTOUM STATE

By

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Dedication

To my Parents

My Husband

My Family

With best wishes

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ABSTRACT

A case study was conducted in Khartoum state (Khartoum, Khartoum North and Omdurman) to investigate foods causing allergy for 50 patients differed in age, occupation, location and gender. The results obtained showed that most vulnerable groups were those of age ranged between 31 and 40 years followed by those of age more than 40 years and those of age between 1 and 10 years. Results also showed that among patients studied, students were the most vulnerable group followed by government officials and house wives. Labors were the most resistant groups. Regarding the location, Omdurman was the most invaded area compared to Khartoum and Khartoum North. Results also showed that there were different types of allergy such as skin, abdominal pain, diarrhea, eye pain and digestion stress. For all patients (50) studied, eggplant was the most food caused allergy (30%) especially skin allergy followed by egg (16%). The duration of allergy symptoms differed between patients from one day to more than 3 days even after treatment.

خلاصة الأطروحة

تم عمل مسح في ولاية الخرطوم (الخرطوم- بحري- ام درمان) لمعرفة الأغذيـة المـسببة للحساسية. تم اختيار ٥٠ حالة على حسب العمر والوظيفة والموقع والجـنس. النتـائج التـي حصل عليها توضح أن اكثر المجموعات المعرضة للحساسية أعمارهم تتراوح بين ٣١ إلـي ٤٠ عام وتليهم المجموعات التي أعمارهم أكثر من ٤٠ عام ثم بعد ذلك تلك المجموعات التي تتراوح أعمارهم بين سنة و١٠ سنوات. النتائج توضح أن معظم المصابين بالحساسية كـانوا من الطلاب يليهم الموظفين ثم ربات المنازل. لوحظ أن العمال هـم أكثـر الفئـات مقاومـة للحساسية. لاحظت الدراسة أيضاً أن منطقة ام درمان هي أكثر المناطق التـي تنتـشر فيهـا الحساسية مقارنة بالخرطوم والخرطوم بحري. أوضحت الدراسـة أيـضاْ أن أهـم أنـواع الحساسية المنتشرة هي الجلدية والآلام المعوية والاسهالات وآلام في العيون وعدم انتظام في عملية الهضم. اوضحت الدراسة أن الباذنجان هو أكثر الخضروات المسببة للحـساسية يليـه البيض. اتضح أن فترة الحساسية تختلف بين المصابين من يوم إلي أكثر من ثلاثة أيام حتـى بعد العلاج.

CHAPTER ONE
INTRODUCTION

1.1. Introduction:

Food allergy is recognized as an important public health problem. It can have severe and sometimes fatal consequences for a minority of sufferers and impairs the quality of life of other sufferers and their families. In addressing the issue the food industry has faced many challenges. Meeting these challenges has required a systematic consideration of all the elements that contribute to a product from the initial concept to the point at which it reaches the consumer (Crevel, 2005). In particular, much closer links have been developed with suppliers and manufacturing processes have been re-thought to reduce the risk arising from allergens. Nevertheless, gaps remain that place limits on the assessment of allergenic risks, including a lack of information about thresholds of reactivity and of good predictive tools to assess the allergenicity of novel proteins (Crevel, 2005). Food allergy is an immune system response to a food that the body mistakenly believes is harmful. Once the immune system decides that a particular food is harmful, it creates specific antibodies to it called IgE antibodies to that food (Adam, 1994). An allergen is defined as either the source of an allergy-producing substance, the allergy-producing substance itself, or one or more of the specific proteins that make up the substance and provoke the immune response (Katz, 1996). The next time the individual eats that food, the immune system release massive amounts of chemicals, including histamine, in

order to protect the body (Katz, 1996). Therefore, the only way to avoid a reaction is to eliminate ingestion of the food protein even in small amount. Several manifestations of allergy may appear in some individuals verging from a minor reaction to severe symptoms (Smith and Taylor, 2005). Common milder symptoms can sometimes rapidly progress to more severe, life threatening symptoms. Skin manifestations are hives, swelling, itchy, red rash, eczema flare, itching or swelling of lips. Gastrointestinal symptoms like cramps, nausea, vomiting, and diarrhea. Respiratory symptoms are itchy, water eyes, runny nose, stuffy nose, sneezing, coughing, and wheezing. More severe life-threatening symptoms are: for respiratory: shortness of breath, difficulty swallowing, tightness of chest, itching or swelling of tongue, throat, change in voice: and for cardiovascular are: drop in blood pressure, fainting, shock (Spregel and Fiedler, 2005). A person may become allergic to food or other allergen at any age. However, children are frequently attacked and there is a higher incidence in adults than in children (Hatpern *et al*., 1998). The sensitiveness may wear off or the patient may become desensitized. In later life individuals may be entirely free from the disturbance that affected them in childhood (Hatpern *et al*., 1998). Foods that belong to the same botanic group may produce a similar allergic reaction: for example, cabbage and cauliflower, orange and grape fruit (Warren *et al*., 1982). Furthermore, an allergic individual who has experiences reaction to a given food may on another day eat the same food without reactions (Spies *et al*., 1995). The response may be due to general physical condition, an allergic response may occur only when the individual is fatigued or emotionally upset (Spies *et al*., 1995). Any food

can produce the allergic manifestations. However it is believed that protein is the important factor in food allergy, although the offending food may contain only a minute amount of protein (Holland *et al*., 1992). Among the most common offenders are: wheat, milk, eggs, fish, shellfish, strawberries, tomatoes and chocolate. Other offenders considered are: pork, orange, spices, condiments, nuts, corn, asparagus, spinach, cabbage, celery, onions, garlic (Holland *et al*., 1992). The ingestion of the smallest quantity of it as offending food, may produce symptoms or reaction, therefore, it's necessary for the allergic individual to analyze prepared foods and food combinations before eating them (Holland *et al*., 1992). The removal of the offending food or foods from the diet or desensitization are two possible methods of treatment for allergy (Holland *et al*., 1992). In patients with severe allergic manifestations, the hormones, corticotropin and cortisone have been found to be highly efficient drugs for the symptomatic control of all types of allergy, but to relieve severe symptoms (May,1980). The treatment may be by avoidance of the causative food, denaturation of protein or by using drugs (May, 1980).

1.2 Objectives of the research:

1. General:

The high prevalence of allergic disease in our society and the existence of numerous case of sensitivity in Khartoum State, these may simply reflect the conditions in which we live. Therefore, knowledge and attention to allergic foods should be considered.

2. Specific:

1. To study and evaluate the prevalence of allergy in dermatology departments in hospitals of Khartoum, Khartoum north and Omdurman teaching hospitals.
2. To make a rough inventory of the food expected to be the main reason for the allergy in Khartoum State hospitals.
3. To develop knowledge to avoid the allergic foods.

CHAPTER TWO

LITERATURE REVIEW

2.1. Background of Food Allergy

Food allergy has been long recognized as a clinical phenomenon, with numerous reports in the 20th century medical literature (Bielory, 2000a). Over the last two decades, however, this perception has changed and food allergy is now recognized as a public health problem. A major factor in this increased concern is probably the rise in the prevalence of a topic disease of which it can be considered a manifestation (Bielory, 2000b). The prevalence and incidence of food allergy and the number of severe reactions also appear to be increasing, although the lack of sound baseline epidemiological data still precludes firm conclusions (Smith and Taylor, 2005). The increasing interest has driven action by food manufacturers, retailers and regulatory bodies to ensure that the risk to individuals who have food allergies is minimized (Crevel, 2005). It has also helped to shape the regulatory requirements for the introduction of new proteins to the market; particularly, but not exclusively, those proteins produced by modern biotechnology (Crevel, 2005). Food allergy has affected the food industry and it has met the challenges posed. However, while it was known that patients could suffer extremely severe and sometimes fatal reactions following ingestion of minute amounts of the offending food, food allergy was perceived as a problem for the individual sufferers (Crevel, 2005). Adverse reactions to food have been recognized since ancient times. Today they have acquired dimensions of controversy and distortion. Some physicians (who usually care for children) as cribs a staggering array of symptoms to foodstuffs, others

(who usually care for adults) seem unwilling to consider any food reactions "Allergic" except for a cute anaphylactic reactions (Feingold, 1989). The subject of food allergy is usually referred to as confusing and controversial. Confusion among professionals and the public can be traced in part lack of rational integration of existing knowledge with basic concepts that could aid in the care of patient with suspected adverse reactions to food (Feingold, 1989).

2.2. Hypersensitivity Reaction

In most instances hypersensitivity may be defined as a state in which the introduction of an antigen into the body elicits and unduly severe reaction. The reaction occurred between the antigen and products of the immune response produce the lesions of the hypersensitivity diseases processes (Adam, 1994). Hypersensitivity reaction may be localized to the site of the entry of the antigen or generalized the local reactions of inflammatory nature, but may also include spasm of sooth muscle. The generalized effects include fever, shock, gastrointestinal and pulmonary collapse. One of the earliest example of hypersensitivity showed that, intravenous injection of small amounts of extracts of sea anemone into dogs was harmless, but a second injection some week later was quickly followed by a violet and sometimes fatal reaction with vomiting, abnormal defecation and collapse. Since this early report which illustrates the acute and severe nature of some hypersensitivity a great deal has been learned, and hypersensitivity reactions may now be classified into four major types (Adam, 1994). The definition of hypersensitivity given above refers solely to foreign antigen entering the body from outside. However, the term includes also the condition

commonly known as the auto-immune diseases, in which antibodies and sensitized lymphocytes appear which are capable of reacting with a normal cell or tissue constituent. Hypersensitivity reaction may be resulted also from passive immunizations, for example when antibody produced in the mother by active immunization by fatal red cells, and crosses the placenta in a subsequent pregnancy to gain entrance to fetal circulation. Another special example of hypersensitivity of increasing importance is the rejection process in allergenic or heterogenic tissue transplants. The increasing diversity and use of drugs has also provided an important group of drug hypersensitivity and the same applied to the expanding number of chemicals used domestically or in industry (Adam, 1994). Hypersensitivity reactions in man whether they occur naturally as result of transplantation or from administration of a drug or a food tend to be complex and often involve more than one of the types (Adam, 1994). A topic, anaphylactic or type 1 reactions occurred in individuals who are predisposed to develop increased amounts of IgE class antibodies in responses to antigenic stimuli. IgE antibody binds to mast cells and subsequent union of the corresponding antigen triggers off release of histamine from the sensitized mast cells giving rise to a local inflammatory reaction and sooth muscles spasm, or to a more generalized reaction. Example includes hay fever, asthma (Adam, 1994). Cytotoxic antibody or type 2 reactions occur when antibody develop which is capable of reacting with surface antigens of cells. As a result the cells is injured by subsequent compliment activation, phagocytosis, example include destruction of red cells and platelets by auto-antibodies to their surface components (Adam, 1994). Immune-complex, arthus-type or

type 3 reactions are caused by the reaction of antibody, usually of IgG class, with the corresponding soluble antigen. This can occur locally (Arthus reaction) or in the blood. In either case, immune complexes are deposited in the walls of blood vessels, where they activate complement and induce vascular injury (Adam, 1994). Delayed hypersensitivity or type 4 reactions occur when primed T lymphocytes, which develop during the cell-mediated immune response, encounter the corresponding antigen. The specifically reactive T lymphocytes transform blast cells secrete a number of factors (lymphokiness) which mediate and a cute inflammatory reaction, aggregations of more lymphocytes monocytes, and sometimes necrosis. The tuberculin skin reaction is a good example (Adam, 1994).

2.3. Definition of Food Allergy:

Food allergy will refer to any adverse reaction, anywhere in the interaction of a food antigen and specific antibody or sensitized lymphocytes. If the reaction occurs shortly after ingestion of the food (minutes to hours) the term "immediate food allergy" will be used "immediate reaction" are often IgE related events reaction involves guide dramatic symptoms are after IgE related events (Golant, 1994). If the reaction is delayed (occurring within hours to days after ingestion) antibodies other than IgE and sensitized lymphocytes may be involved, or an IgE reaction requiring time to develop could be responsible; such reactions will be termed "delayed food allergy" (Golant, 1994). If specific food antibodies appear to be the "result" and not the "cause" of symptoms or problems associated with foods, the term "food intolerance"

will be used. Such reactions to food may be enzyme defect e.g. (milk-induced diarrhea in patients with lactose deficiency) or reactions to natural pharmacological agents in food (e.g. hypersensitive crisis from cheese in patients receiving amineoxidase inhibitors) represents especially diagnosable forms of food intolerance (May, 1980).

2.4. Spectrum of Food Allergy:

Food-related reaction encountered in infants, children and adolescents fall into five group.

2.4.1 Allergic Diseases Confined to Gastrointestinal Tract:

Three food protein sources have been proven to cause gastrointestinal disease in infants and children. These are cow milk, wheat gluten and soybean protein. Cow milk protein allergy has been incriminated as cause of many symptoms in the gastrointestinal tract, such as diarrhea, vomiting, colic and regurgitation (Golant, 1989). It is clear that at least five clinical syndromes can be related to cow milk protein allergy. These are: Intractable diarrhea of early infancy, allergic gastroentropathy, primary malabsorption syndrome (celiac sprue like syndrome), gastrointestinal blood loss (Willsonlahey Hiener syndrome), and cow milk protein included colitis. Celiac sprue, also known as celiac disease and gluten-sensitive enteropathy, is characterized by malabsorption resulting from inflammatory injury to the mucosa of the small intestine after the ingestion of wheat gluten or related rye and barley proteins. (Farrell and Kelly, 2002). Intractable diarrhea of early infancy is seen in the first three months of life with severe diarrhea and failure to thrive. Reintroduction of cow milk protein results in exacerbation of the disease.

A similar disease may occur in infants fed soy protein (Golant, 1989). A protein-losing entropathy has been described with symptoms consist of growth retardation, edema, hypoaluminemia eosinophilia and allergic symptoms of skin and respiratory tract. This type of allergy as astronenteropathy responded to milk elimination but symptoms retained with reintroduction of milk into the diet (Golant, 1994). An increasing number of reports documents a "celiac sprue like syndrome" in which infants have severe fat malabsorption, abdominal distention, peripheral wasting, and failure to thrives small bowel biopsy can be really normal or reveal a flat mucosa with increased number of IgE plasma cells. One infant studied in a metabolic unit showed this reaction when10 mg of B-lacto globulin was added to the formula (Conners *et al*., 1997). Infants fed cow milk may also have bloody diarrhea and mucus in their stools. Sigmoidoscopy reveals colitis and acute inflammation and rectal biopsy shows crypt abscesses. The condition clears when milk is eliminated from the diet, even when IgE antibodies to cow milk are not present (Golant, 1989).

2.4.2. Allergic Diseases Involving Organs Remote from Gastro-intestinal Tract:

Acute immediate reaction to food or foods is encountered frequently and the foods responsible are often obvious such as egg white, milk, peanut, nut or cottonseed which expected to cause swelling of the lips, itching, vomiting, urticaria, and diarrhea. On examination the child is flushed, often with swatter eye lids, the uvula is oedematous, and breath sounds are punctuated with course rhonchi or wheezing. The childhood may

persist, but further sensitization to fish, shellfish, nuts and bears may develop (Feingold, 1989). In patients with a topic dermatitis, involved areas may become inflamed, specially infants and young children. In some instances, shortly after ingestion of the food to which the patients is allergic, curiously, there may be no oral or gastrointestinal reaction, this suggests either that antigenic macromolecules have to be absorbed from the gastrointestinal tract and carried to the target organ by the blood or that the child is reacting to the fraction of food the antigencity of which has been "unmasked" by digestion. Cow milk antigenicity has been shown to change with digestion. Allergic rhinitis and asthma may occur in young children as result of food allergy. The reactions has been confirmed by challenge, and may occur (rarely) even in adults. In general food allergy plays a more important role before, a year of age, and because less as a child and adult age (Golant, 1994).

2.4.3. Diseases That May be Exacerbated by Allergy to Foods:

The role of IgE-mediated allergy in celiac sprue is uncertain, but delayed or cell mediated allergy reactions may play a role in gut damage. Positive delayed skin tests to a sub-fraction of gluten have been reported to patients with celiac disease, but it is not clear whether this is a cause or a result of disease. Allergy may also coexist, because of easy penetration via a damaged gut wall. This is also the case in chronic ulcerative colitis. In patients with Heiner syndrome milk allergy, pulmonary hemosiderosis and milk precipitins have been demonstrated. Elimination of milk may result in clinically improvement. Some children with IgA deficiency may develop precipitating antibody to bovine IgM a long with gastrointestinal

symptoms (Golant, 1994). Lactose deficiency is being recognized as a condition that may occurs secondary to foods allergy as well as a primary condition that must be differentiated from food allergy. The mechanism of secondary lactose deficiency appears to be similar to that which occurs after acute gastroenteritis. Since disaccharide enzyme is located at the lips of villi, any villous damage may result in enzyme deficiency (Golant, 1989).

2.4.4. Reactions to Natural Pharmacological Agents in Food:

It is important to note that adverse reaction to foods considered by many researchers to be "allergy" which may in reality represent an annually sensitivity to natural occurring pharmacological agents or to interaction of there agents with other dietary product e.g. development of violet gastrointestinal symptoms on consuming a wild mushroom with wine, because of the trace amount of allergic like substance found in mushrooms (AAPCD, 1996).

2.4.5 Controversial Disease:

The allergic tension fatigue syndrome may be a mixture of psychologic and secondary effect of allergy. It is an allergic condition. It is mediated by a mechanism not involving IgE antibody. Frick (1980) has summarized the evidence for and against it is allergic etiology. The prevalence is not higher in a topic persons and allergic therapy has not been shown to be effective in any controlled study. Hyperactivity from food additives, coloring, agent sugar, or salicylates is an example of such reactions (Dannaeus *et al*., 1989).

2.5. Development of Food Allergy:

The digestive process breakdown complex foods into basic nutrients, but proteins or digestive product of many foods are often absorbed in larger than "elemental" structural form. These identifiable protein or polypeptides can be detected in the blood of even normal a symptomatic children. An adverse reaction can not depend solely upon penetration of foreign protein (Dannaeus *et al*., 1989).

2.5.1. Factors Affecting Passage of Antigen in Systemic Circulation:

Absorption from the gastrointestinal tract is dependent upon the degree of completeness of protein digestion, the consequent size and steric structure of food and antigen, and perhaps "uncovering" of important antigenic sites by incomplete digestion. In all children the permeability of the gut is highest in infancy, decreasing noticeable after 6 months of age. Local immunologic barriers such as secretory IgA are particularly important in infancy (Manzi and Shannon, 2005). In children with gastrointestinal inflammatory or other disease states (such a gastroenteritis or gluten enteropathy) permeability is increased because of damage of cells and mucin (Feingold, 1989).

2.5.2. Processing of Penetrated Antigen:

In normal infant and children, food antigen is either processed by macrophage action, or is "neutralized" by specific IgG, IgM or IgA antibodies. Mediators release or tissue damage does not take place and the antigen is cleared promptly from the circulation. In children genetically predisposed to allergic reaction, an IgE mechanism may develop, so that on subsequent exposure to food antigen IgE reaction can

occur, with harmful mediator release from mast cells and basophiles. Occasionally none a topic child can also develop the same reactivity (Spies, 1995).

2.5.3. Mechanism of Allergic Reaction to Food:

Food allergies and particularly cow milk allergy often appear to be familiar which owing to a genetic tendency to form IgE reaction, rather than to an inherited "milk allergy". In these persons, milk allergy is common since cow milk formulas are usually the first and the most prevalent food in infants diet (Hill *et al*, 2004). *In vitro* immunologic tests have helped to clarify the mechanism involved. Studies on biosynthesis of IgE have demonstrated that the most common defects associated with topic responsiveness are lack of T-suppressor cell activity and unbridled S-cell function. Leukocyte migration inhibition factors have recently been implicated in cow milk allergy, showing that a cell mediated function may account for delayed food allergy (May, 1990). A topic and none topic children may develop food allergy because of IgA deficiency during the age of high permeability of the gut. Secretary IgA has a protective role in gastrointestinal exposure to antigen so that seven transient deficiencies can allow large amounts of food antigen to stimulate the immune system. This mechanism of "antigen overload" is also operative in such predisposing diseases as gastrointestinal disease or chronic aspiration (May, 1990). Antibodies are more a consequence of the predisposing disease. Another mechanism affecting both a topic and none topic children is viral introduction of abnormal IgE responsiveness, whether this affects food allergy is uncertain (May, 1990).

2.5.4. General Characteristics of Food Antigen:

Food allergens are glycoprotein with molecular weights between 18,000 and 36,000, such antigens are resistant to heat and proteolytic action (Frick, 1980). Not all of the proteins of single food are important in allergic reactions. Protein that have been particularly characterized as antigens include egg with, ovomucoid, allergen of fish, bovine serum albumin, v-globulin and kunitz soybeans tyrosine inhibitor in soybeans. There are important antigens that have yet to be characterized, such as proteins other than that allergen of fish which cause allergic symptoms to patients (Frick, 1980). As would be expected food within the same animals or botanical family often share proteins responsible for allergic reaction. Thus a cow milk allergic child may also react to goat milk because there are at least eight cross reacting protein (Frick, 1980). It has been observed that a person allergic to one food is usually allergic to related foods, peanut for example belongs to pea family, and people who can not eat peanuts usually can not eat beans and peas. They are not necessarily allergic nuts. Patient allergic to wheat are often allergic to rice and barley but not to buck wheat, a member of another family (Frick, 1980).

2.6. Chemical and Drugs:

Artificial foods colors, fruit acids, aspirin, antibiotics drugs (any drug may cause allergy) (AAPCD, 1996).

2.6.1. Adverse Reactions to Food additives:

There are thousands of additives used by the food industry for a variety of purposes in the foods we eat. However, only a small number have

been implicated in causing adverse reactions in humans. Although there are reported cases of individuals who have reactions to single additives, most of the medical literature involves patients with asthma or chronic idiopathic urticaria/angioedema whose conditions are exacerbated after ingestion of food additives. Many of these reports are characterized by poorly controlled challenge procedures. Recent studies performed under properly controlled conditions imply that sensitivity to food additives in patients with chronic urticaria/angioedema is very uncommon (Simon, 2003). A child resulting from alteration of living patterns produced by special shopping trips, special food preparation, and change in families perception of the affected child from being "behaviorally disturbed" to nutritionally damaged. This second variable is well known in behavioral research as a "placebo effects", namely the repeated demonstration of measurable effects by the administration of placebo that the patient perceives as an active therapeutic agent (Shapiro, 1990). In order to control the factors first patients were to be placed on a separate food additives free direct with an attempt to disguise this treatment variable. Then, the children who demonstrated measurable behavioral improvement was to be fed "challenge foods" prepares to contain either an artificial food, nor one half of the drolly estimated average amount of food. These two challenge foods were to be indistinguishable from each other and were to be administered on double-blind fashion. If the artificial food colorings improved, the child will eat the additive free challenge food and will deteriorate when he ate food that contains artificial food colorings (Shapiro, 1990). Brief decrease in attention were noted in children receiving the additive containing food that were not

seen when the challenge was additive–free, suggesting transient pharmacological action of food colorings. Orange, apples and tomatoes for example, are eliminated while grapefruit, lemons, and lime are allowed. Unless care is taken, such a diet could result in vitamin deficiency, otherwise the diet appears to be nutritionally sound and even superior since most so-called junk foods are eliminated. One should be alert, however, to families who employ dietary treatment enthusiastically while trained professionals note a persistence of behavioral or learning problems that need treatment. In this instance, endorsement of special diet may help the family avoid other treatments (such as psychotherapy or medication).

2.7. Diagnosis and Therapy of Food Allergy:

2.7.1. History and physical examination

The clinical history should include an accurate description of the adverse food event in order to determine precisely its clinical features and it should provide sufficient information that can be used in the design of a diagnostic oral challenge procedure, which, if positive, reproduces the reported reaction. The main issues of the food reaction to include in the clinical history comprise a description of the specific symptoms, the timing of the reaction, and food suspected of causing the reaction. Specific questions should address the food suspected of provoking the reaction, the amount and the food processing procedure, such as boiled or dry roasted, as the oral challenge should be designed employing the implicated food in the same way as reported by the patient (Hefle and Taylor, 2002). Symptoms produced by allergic reactions to foods may include, alone or in combination, gastrointestinal manifestations with or

pharyngeal pruritus and/or local angioedema, acute gastric and abdominal pain, nausea, vomiting, and diarrhea. Skin symptoms are commonly pruritus, urticaria, angioedema, and worsening of a topic dermatitis. Airway symptoms may include rhinitis and/or asthma. Cardiovascular manifestations such as hypotension and anaphylactic shock may take place during a reaction. If one or more of these symptoms is present, information should be obtained regarding the time relationship and the reproducibility of the symptom with regard to the consumption of the suspected food and whether any other circumstances were involved. Associated factors, e. g., ingestion of medications, such as non steroidal anti-inflammatory drugs (NSAIDs), and exercise should also be identified (Aihara *et al*, 2002). It is worthy to ask about his/her history of other a topic diseases, such as asthma and a topic dermatitis, both of which are risk factors for food allergy (Burks *et al*, 1998). A comprehensive medical history should be obtained in patients suspected of having food allergy-induced respiratory tract symptoms or anaphylaxis (Sampson, 2004). The history should include questions about the timing of the reaction in relation to food ingestion, the minimum quantity of food required to cause symptoms, specific upper and lower respiratory signs and symptoms, and the reproducibility of the symptoms. A family history positive for allergy and/or asthma can be a useful historical point. When there is a history of an unexplained sudden asthma exacerbation, details about preceding food ingestion should be elicited. A history of a severe or anaphylactic reaction following the ingestion of a food may be sufficient to indicate a causal relationship. Finally, documentation of the specific treatment received and its response should be documented. Diet

diaries can be a useful supplement to a medical history, especially in chronic disorders. Moreover, elimination diets, which are typically implemented for 7–14 days, can be used both for diagnostic and therapeutic purposes. Their success depends on identifying the correct allergen and completely eliminating it in all forms from the diet. All efforts should be made to prevent complications from unnecessary dietary restrictions such as poor weight gain and failure to thrive (Roesler *et al*, 1994). In evaluating patients with suspected allergic reactions that may be induced by food allergy, the physical examination is mandatory. Helpful findings include the assessment of overall nutritional status, growth parameters, and any signs of allergic disease, especially atopic dermatitis. Moreover, this examination will help rule-out other conditions that may mimic food allergy (Taylor, 1993). Attention should be directed toward detecting the presence of a topic features, particularly dermatitis, asthma, and rhinitis (Sampson, 2003). If the patient has asthma, an objective evaluation of airway obstruction prior to an oral challenge is mandatory (Sampson, 2003).

2.7.2. Initial Laboratory Test:

Initial laboratory tests depend in large part on the patients' illness or problem, tests such as a complete blood count, urine analysis, quantitative immune globulins and stool guaiac will be usefully in most infant, in evaluating the presence or absence of anemia, and in ruling out chronic infection and for renal disease. A sweat test may be necessary to exclude cystic fibrosis, and examinations will initiate a trial examination diet before ordering more expensive and more specialized laboratory procedures (May, 1980).

2.7.3. Diagnostic Tests for IgE

When an IgE-mediated allergic reaction to food is suspected, skin testing and in vitro tests are useful in establishing if the patient possesses IgE antibodies to specific foods. These tests indicated the presence of an immune IgE-mediated response. Several studies using the double-blind, placebo-controlled, food challenges (DBPCFCs) to establish the diagnosis of clinical allergy revealed that only 40% of medical histories of food adverse reactions can be verified (Parker *et al*, 1993). .

2.7.3.1. Skin Testing:

Percutaneous skin testing remains a primary tool in the diagnosis of food allergy (Sampson, 2004). While the patient is off antihistamines for an appropriate length of time, it is performed with an appropriate skin testing device (e. g., lancet) which punctures the skin through a drop of a glycerinated food extract and appropriate positive (histamine) and negative controls (saline). Skin prick tests (SPTs) are judged positive if there is a mean wheal diameter of 3 mm or greater than those induce by the negative control. These tests have a negative predictive value generally greater than 95% (assuming the disorder being evaluated is IgE-mediated), however, the test has in general a relatively low specificity (approximately 50%). The positive predictive value is only 20–50%, depending on the history. Thus, a positive skin test merely indicates allergic sensitization. Positive tests cannot be considered absolute proof of clinically relevant hypersensitivity and must be interpreted in the context of the clinical history. Negative skin test responses essentially confirm the absence of IgE-mediated allergic reactivity (negative predictive accuracy of a 95%) and are very helpful in

excluding IgE-mediated food allergies (Ballmer-Weber *et al*, 2001). Fruits and other foods of vegetable origin are frequently reported by young and adult patients as the cause of allergy. However, as noted early in 1942 by Tuft and Blumstein, commercially prepared extracts from many fruits and vegetables frequently do not induce positive skin responses in clinically sensitive patients, because of the presence of labile proteins responsible for IgE-mediated sensitivity. Dreborg and Foucard (1983) introduced the prick-prick technique with fresh fruits and vegetables which improved the ability of skin testing to detect immunological IgE-mediated hypersensitivity. In this procedure the skin is punctured after pricking the fresh food. In a study of 100 adults with a history of oral allergy syndrome (OAS) after ingestion of fruits and vegetables, Ortolani *et al.* (1989) demonstrated that skin testing with the prick-prick technique was very sensitive for fruits and vegetables, such as carrot, celery, cherry, apple, tomato, orange, and peach. As observed during skin testing with commercial allergenic extracts, the accuracy of the results of the prick by prick technique with plant-derived foods to predict true clinical allergy is limited. In addition, the extensive immunologic cross-reactivity among different plant proteins implies that skin testing with different fresh fruits and vegetables may produce a high number of positive skin responses which are not clinically relevant. Intradermal skin tests with food extracts have an unacceptably high false-positive rate. These tests have been associated with systemic reactions and should not be used in the workup of food allergy. Finally, well-designed and medically supervised oral food challenges are critical for the confirmation of food allergy (Sampson, 2004).

2.7.3.2. Food-specific IgE Antibodies:

In vitro tests for specific IgE (RAST) are also helpful in evaluating IgE-mediated food allergy. For example, quantitative measurements of food-specific IgE antibodies (e. g., CAP System FEIA, Pharmacia-Upjohn Diagnostics) have been shown to be very useful in predicting symptomatic IgE-mediated food allergy. These tests for specific IgE antibody can be used while the patient is taking an antihistamine and do not depend on having an area of rash-free skin for testing. The general concepts for interpretation are the same as for prick skin tests: a negative result is reliable in ruling-out an IgE-mediated reaction to a particular food and while a positive result does not absolutely prove clinical reactivity, it can be very helpful in implicating a specific food allergy. To some extent, the greater the concentration of a food-specific IgE antibody, the higher the chance of true clinical reactivity. As mentioned above with skin testing, positive tests cannot be considered absolute proof of clinically relevant hypersensitivity and must be interpreted in the context of the clinical history (Ballmer-Weber *et al*, 2001).

2.7.3.3. Optimal Performance of Diagnostic Tests for IgE for Clinical Food Allergy:

In the last years, it has become apparent that a global assessment of the performance (e.g., receiver-operating characteristic plots) of the diagnostic tests for IgE could be useful in selecting the best cut off (optimal operating) point to differentiate actual food allergy. Sporik and colleagues (Sporik *et al.,* 2000). designed an investigation to determine the specificity of the allergen wheal diameter to help identify children who react on formal open food challenges (OFCs). Over a 9-year period,

children referred to a tertiary allergy clinic for the evaluation of suspected food allergy were prospectively studied. Allergen skin prick testing to commercial extracts of cow milk, egg white, and peanut extracts was undertaken using a lancet technique. All children underwent OFCs to the relevant food(s) in a hospital clinic. Challenges were classified as positive if objective signs were seen; negative if the child could tolerate normal quantities of the food, daily, for one week; or inconclusive if none of the former criteria were met. Five hundred and fifty-five challenges were undertaken in 467 children (339 challenges to cow milk, 121 to egg, and 95 to peanut). Fifty-five percent of challenges were positive, 37% negative, and 8% inconclusive. For each food it was possible to identify a skin wheal diameter at, and above, which positive reactions occurred: egg: 7 mm; cow milk: 8 mm; peanut: 8 mm. These investigators proposed that the utilization of these measurements may reduce the need for formal food challenges in patients being assessed for allergic reactions to egg, cow milk, and peanut. Another recent investigation compared the results of skin prick testing to in vitro measurements of specific IgE to food allergens (Hill *et al*., (2001). These investigators reported SPT wheal diameters to cow milk, egg, and peanut above which infants and young children referred for investigation of suspected food allergy showed an adverse reaction on food challenge. These were termed the "100% diagnostic SPT levels". In vivo and in vitro measurements of IgE antibody levels to three common food allergens, cow milk, egg, and peanut, were compared in infants and young children with suspected food allergy, in order to reduce the need for food challenges. SPT (from 1992 to 1998) and CAP values (from

1999 to 2000) were performed in 820 children a 2 years of age with suspected allergy to cow milk and/or egg and/or peanut. SPT levels previously shown to be diagnostic of challenge-proven allergy to cow's milk, egg, and peanut were used as the "100% diagnostic SPT levels" and compared with SPTs and CAP values associated with IgE-mediated food allergy. Statistical analysis showed a significant difference between the "100% diagnostic SPT levels" and positive SPT in identifying patients who did not require food challenge for cow milk (P = 0.01), egg (P a10–6) and peanut (P a10–6), and a significant difference between the "100% diagnostic SPT levels" and positive CAP (P a10–6) for egg and peanut but not cow milk. Overall, 23% of the food challenges were avoided by the use of the "100% diagnostic skin prick test levels". The use of these levels compared with in vitro measurement of IgE antibody to cow milk, egg, and peanut reduced the need for food challenge in young children with suspected food allergy. Two recent studies have attempted to define the risks of clinical reactions as they relate to food-specific IgE antibody (i. e., Pharmacia Diagnostics termed the CAP-RAST FEIA that measures the antibody concentration as kU/L). In the initial study, stored sera from 196 children and adolescents (mean age 5.2 years, 60% male) with a topic dermatitis were analyzed for specific IgE antibodies to foods commonly causing allergy in children, and the results compared to blinded food challenges and "convincing" history of anaphylactic reactions (Sampson and Ho, 1997). When compared with the outcome of DBPCFCs, results of CAP System FEIA are generally comparable to those of SPTs in predicting symptomatic food hypersensitivity. Furthermore, by measuring the concentrations of food-

specific IgE antibodies with the CAP System FEIA, it is possible to identify a subset of patients who are highly likely (A95%) to experience clinical reactions to egg, milk, peanut, or fish. The performance characteristics of the CAP System FEIA for soy and wheat were poor. The follow-up to this study involved a prospective investigation in a patient population of children (median age = 3.8 years) with only about 60% having a topic dermatitis gave similar results (Sampson, 2001). Serum samples from 100 consecutive children and adolescents referred for evaluation of food allergy were analyzed for specific IgE antibodies to egg, milk, peanut, soy, wheat, and fish by using the Pharmacia CAP System FEIA. Food-specific IgE values were compared with history and the results of skin prick tests and food challenges to determine the efficacy of previously established 95% predictive decision points in identifying patients with increased probability of reacting during a specific food challenge. The diagnosis of food allergy was established by means of history or oral food challenge. On the basis of the previously established 95% predictive decision points for egg, milk, peanut, and fish allergy, greater than 95% of food allergies diagnosed in this prospective study were correctly identified by quantifying serum food specific IgE concentrations. Previously established 95% predictive decision points of food-specific IgE antibody concentrations for four major food allergens were effective in predicting clinical reactivity. Therefore, these two studies demonstrate that quantification of food-specific IgE is a useful test for diagnosing symptomatic allergy to egg, milk, peanut, and fish in the pediatric population and could eliminate the need to perform double-blind, placebo-controlled food challenges in a significant number of

children. It has become apparent that adjustments in interpreting these diagnostic cutoff values must be made for disease and age. Forty patients with symptomatic immediate hypersensitivity to egg who did not have a topic dermatitis were evaluated to determine if they continued to remain clinically symptomatic (Crespo *et al*., 1994). . Individual patients had specific IgE in vitro and positive PST to egg. All patients were on an egg elimination diet. During the follow-up period, an open egg re-challenge was performed along with a determination of egg white-specific IgE by CAP System. The egg white-specific IgE values were higher in the positive challenge group than in the negative challenge group (P a 0.01, Mann-Whitney test). There was a direct proportional relationship between the levels of egg white-specific IgE and the likelihood of positive challenge. Specific IgE values above 1.20 KUA/L could be adequate grounds for delaying the follow up of egg challenge. Overall, the study showed that increasing concentrations of egg-specific IgE antibody indicated a higher likelihood of clinical reactivity on re-challenge. The likelihood ratios for a positive oral challenge with egg white IgE level equal to or above 0.35, 0.70, and 1.20 kU/L were 2.2, 3.0, and 6.3, respectively. Another example of the adjustments for age and disease that are needed in the interpretation of these values was demonstrated in a study of infants with possible acute reactions to milk but without a topic dermatitis or gastrointestinal allergy (Garcia-Ara *et al*., 2001). A prospective study was carried out on 170 patients a 1 year old (mean, 4.8 months) with histories suggesting immediate hypersensitivity after ingestion of cow milk formula. Prick test with cow milk and its proteins (a-lactalbumin, b-lacto globulin, and casein),

determination of specific IgE antibodies with the CAP system FEIA for the same allergens as for the prick test, and a challenge test according to the diagnostic protocol were performed for all of the children. A study of validity of the prick test (cutoff point, 3 mm) and CAP system by using different cutoff points in the specific IgE values for cows' milk and its proteins were also analyzed. Prevalence of immediate symptomatic hypersensitivity to CMP in this study was 44%. When both the whole milk and its principal milk proteins were used in the prick test, the negative predictive value was very high, and a negative value excluded allergy in 97% of the patients. When the different cutoff points of the specific IgE for milk were analyzed, 2.5 KU (A)/L had a positive predictive value of 90% and 5 KU (A)/L had a positive predictive value of 95%. When diagnosing immediate hypersensitivity to CMP in infants, negative skin test responses exclude allergy in most of the patients. If the prick test response is positive, specific IgE levels for cows' milk may be helpful. If these values are 2.5 KU (A)/L or greater, the challenge test should not be performed because of its high positive predictive value (90%). Comparing results of food-specific IgE by skin prick testing and in vitro measurements should help to provide better predictive information regarding whether or not to subject a patient with possible food allergy to an oral food challenge. Hopefully, there will be more published data in the future regarding predictive values for other food allergens and comparisons of in vivo and in vitro measures of food-specific IgE. This type of information will be useful to the clinician in the overall decision-making process with food-allergic patients.

2.7.3.4. Oral Food Challenges:

Before carrying out any challenges the patient should be placed on an elimination diet of the suspected food for at least two weeks. In many cases the patient is already avoiding the food at the moment of consultation, especially in the case of several acute, clear-cut episodes. If the patient reports chronic symptoms with several possible culprit foods an elimination diet is advised. If a large number of foods is suspected it is practical to give the patient a list of "safe" foods to be taken and then introduce the suspected foods one by one every week watching for the appearance of symptoms. Whether the re-introduction of the food is carried out at home or in a clinical setting depends on the severity of symptoms; non acute reactions and symptoms probably not due to an IgE-mediated reaction may allow adding the food at home. When there is a clinical suspicion of an allergic reaction to a food and the test for specific IgE antibody to the food is positive, an elimination diet may be implemented to see if there is a resolution of clinical symptoms. Confirming this association, however, can be difficult in many cases. Therefore, food challenges can be a useful and reliable procedure in the diagnostic evaluation of a patient with suspected food allergy. Open or single-blind food challenges are often utilized to screen foods unlikely to provoke food-induced allergic reactions. Of the different type of oral food challenge procedures, the DBPCFC is the best method and remains the gold standard to diagnose and confirm food allergy and other adverse food reactions (Sampson, 1999). An excellent publication has reviewed the combined clinical experience of six centers doing food challenges (Bock *et al*., 1988). These challenges should be conducted in a medical

clinic or hospital setting with available personnel and equipment for treating systemic anaphylaxis. The DBPCFC is considered the state of the art for diagnosis of actual clinical reactivity after food ingestion. With the exception of severe reactions on ingestion of an isolated food it is the only method to exclude bias from patient and physician. Other modalities of oral challenge are performed in the clinical setting, OFCs in which the patient consumes the food without masking and single-blind challenges (SBFC) in which food masking only applies to the patient. In the diagnostic algorithm proposed by the European Academy of Allergy, Asthma, and Immunology, OFC are carried out prior to blinded challenges (Bruijnzeel-Koomen *et al.*, 1995). Patients having a positive OFC undergo a subsequent DBPCFC. If the result of the blinded challenge is negative, it must be confirmed by means of an open feeding under observation to rule out the rare false negative challenge result. The design of all oral challenges with food is determined by the facts of the clinical history. The food for challenge should be administered in the same form as previously ingested, raw or processed. The initial dose should be a fraction of the minimum quantity to produce symptoms reported in the history. Successive increasing doses should reach a cumulative quantity equivalent to a normal amount of the food consumed in everyday life. The time interval between doses should be longer than that reported by the patient in the history and enough for symptoms to develop. OFCs are very useful for evaluating reactions to many foods with a high probability of a negative outcome. SBFCs are time-saving and may prove useful for patients with a high subjective concern about their symptoms to refute doubtful histories. Double-blind challenges are

the final procedure for diagnosis. Assignation for active food (verum) or placebo doses must be randomized by personnel not related to the administration of doses to ensure proper blinding. The number of placebo and verum doses is usually the same in most protocols. Masking may be carried out employing vehicles to hide the flavor, color, and texture of the food. It is preferable to use liquid or semisolid vehicles. Masking with capsules is effective but it may be misleading and dangerous; as no contact of the food with the oral mucosa is allowed, oral symptoms are not detected and severe symptoms may appear only after a high dose has been administered. Solid vehicles, such as fish for crustacean challenges may be good maskers of flavor and texture in some cases. After a negative outcome of a DBPCFC an open administration of the food in usual amounts under observation is mandatory to exclude any concern regarding preparation of the food. Causes of final positive open feedings after a negative DBPCFC include an insufficient amount of food administered in the challenge and loss of allergenic activity of the food due to preparation of the challenge. If capsules have been employed as the vehicle to evaluate oral symptoms by DBPCFC, the lack of contact of the food with the oral cavity during the challenge may produce false-negative results. Also, subjective aversive symptoms in some patients may cause a positive final OFC. So far there are many different challenge protocols and sometimes it is not possible to compare the results of DBPCFC carried out in different centers. A recent study has developed and validated several recipes for milk, soy, egg raw and cooked, peanut, hazelnut, and wheat for DBPCFC in children (Vlieg-Boerstra *et al*., 2004). Further studies are needed to develop validated

protocols for adult patients and different foods. An important issue is the threshold dose, which should be safe and also the cumulative dose which should be enough as some patients need higher doses of a food to elicit a reaction.

2.7.4. Managing Food Allergy:

Once an objective diagnosis is established, the treatment for food allergy is to strictly avoid the ingestion of the food. Patients, parents, and personnel in care of children should have precise instructions about the identification of the food in labels, as the many different names under which a food is labeled may not be recognized by consumers. It is also mandatory to list all sub-ingredients and specify the source of ingredients previously listed as “natural flavors”. Highly sensitive individuals may react to minimum traces of the food due to cross-contamination of food products elaborated in production lines where traces of allergenic food may still be present. In some countries such as the UK, Australia, New Zealand, and Canada labeling includes the term “may contain” particularly for peanut and nuts. Even with appropriate instructions, the risk of an accidental ingestion is present in high-risk situations, with food consumption out of home such as in restaurants, buffets, fairs, and summer camps. It also can happen when a local manufacturer changes the components of a food being consumed locally (Foucard, and Malmheden, 1999). In a recent study analyzing the circumstances of a series of fatal reactions to food, most of them happened to individuals who were known to have food allergy, most subjects had active asthma and most individuals did not have epinephrine available at the time of the reaction (Bock *et al*., 2001).. In school settings, the patient and/or the

caregivers should have precise instructions for treatment in the case of an allergic reaction. All patients with previous severe reactions to a food, especially asthmatic patients should receive or self-administer epinephrine immediately and should be treated as soon as possible in an emergency department. In the case of small children, unable to self-inject, teachers or personnel in charge should be instructed in the use of epinephrine, which should always be present in first-aid kits in schools. Children allergic to food should not be excluded of any school activity, therefore the school should be provided with written information of the food implicated and written instruct instructions on what to do in case of a reaction (Rhim and McMorris, 2001). .

2.7.5. New Therapies for Food Allergy:

After the diagnosis of food allergy has been made the suspected food or foods should be eliminated from the diet. A child with cow milk sensitivity should be given a diet free of cow milk until symptoms clear off. Introduction of small quantities of milk results in exacerbation symptoms, the child should avoid not only cow milk but also processed foods that contain casein lactobumin, whey or those foods prepared from cow milk such as cheese and yoghurt. Young children often develop clinical tolerance to food allergies as they grow older. Accordingly, such foods may be introduced cautiously into the child's diet, after the basic symptoms have been controlled for 6 to 12 months, to determine whether such tolerance has developed. Children are more likely develop tolerance to milk, eggs, wheat and vegetables than to fish and nuts. If the infant or child has reacted to soy, the parents must be a ware that it is commonly found in baby junior foods and cereals, and they must develop a practice

of reacting all labels when allergy to multiple foods exists, the child's diet may become complicated and the physician should be a ware that many food families cross react. For instance, a child may react only to peanut, or to entire legume family. In counseling parents regarding diet, the physician must assume that the diet is adequate in protein, calorie, essential minerals and vitamins. A nutritionist or dietician can often be at tremendous help in working out specific detail of such a diet (Christie, 1990). Major or common foods should not be excluded for long periods of time solely on basis of a positive skin test or RAST tests. The specific foods should be clinically challenged, preferably by blind techniques before to be removed from the diet for long periods of time (except for those had induced anaphylaxis) (Christie, 1990). Over the past several years, there has been a significant amount of research in the area of potential new therapies for food allergy. Conventional subcutaneous allergen immunotherapy has been attempted for peanut allergy. In a double-blind placebo-controlled trial of rush (rapidly increasing doses) peanut immunotherapy, increased tolerance to oral feeding with peanut was observed in four of six patients receiving the active immunotherapy but in none of the six control patients. The rate of serious adverse reactions, however, was unacceptably high, even during the maintenance phase of immunotherapy (39%) (Nelson *et al*., 1997). This important clinical investigation suggested that immunomodulation might eventually be used to induce oral tolerance in food allergic patients if the overall safety profile was improved. Some studies have addressed the use of immunotherapy with birch pollen extracts in birch-sensitive subjects with OAS to apple with promising results (Bolhaar *et al*., 2004). Attempts at

hypo sensitization with food have demonstrated good results in some cases, but schedules are time-consuming and the patients must consume the food regularly to maintain the tolerance (Patriarca *et al*., 1998). Allergen-specific IgE antibodies play a central role in the pathophysiology of a topic disorders, including food allergy. IgE binds to high affinity receptors on the surface of mast cells and basophiles. Cross-linking of IgE molecules on the surface of mast cells by allergen leads to release of preformed mast cells mediators (early phase of allergic reaction) as well as synthesis of pro-inflammatory cytokines and chemokines that result in late phase reaction (Fahy *et al*., 1997). Humanized monoclonal anti-IgE antibodies bind to the constant region (third domain of the Fc region) of the IgE molecule and prevent its binding to the receptor on mast cells and basophiles. In addition, anti-IgE down regulates the expression of the high affinity receptor on mast cells and decreases basophile histamine release (MacGlashan *et al*., 1997). In clinical trials of anti-IgE for the treatment of asthma and allergic rhinitis, symptomatic improvement was observed when circulating levels of IgE antibodies were significantly reduced (Milgrom, et al., 1999). . Recently, a multicenter, randomized, double-blind, placebo- controlled clinical trial evaluated humanized monoclonal anti-IgE antibody (Tannox 901) in the treatment of peanut anaphylaxis (Leung *et al*., 2003). The investigators were interested in determining if treatment with anti-IgE therapy would reduce the sensitivity of patients with peanut allergy following the ingestion of peanuts. The study included 84 adolescents and adults (12–60 years) with a history of immediate hypersensitivity following peanut ingestion. The patients had histories of urticaria, angioedema, lower

respiratory symptoms and hypotension and their reactions were confirmed by DBPCFCs. In addition, they had positive skin tests to peanut, serum IgE levels between 30 and 1000 IU/mL and no prior exposure to monoclonal antibodies. The study design included four dose cohorts of 28 patients each randomized 3:1 (Tannox 901: placebo), including 150, 300, and 450 mg of Tannox 901 or placebo. Injections were administered subcutaneously every four weeks for four doses. The primary endpoint was a change in the threshold dose of peanut that elicited symptoms during an oral food challenge 15–30 days after the last day of study drug. Tannox 901 increased the threshold sensitivity to peanut flour in a dose responsive manner. The effect was highly significant at the 450 mg dose level. The anti-IgE was well tolerated with no evidence of treatment-related systemic adverse events and no evidence of treatment-related laboratory abnormalities (e.g., complete blood counts, urinalysis and blood chemistry). Local adverse events including mild erythema, burning, and edema were noted for at least one injection in 13–14 patients in each dose cohort. Finally, there was no evidence of anti-drug antibodies. An average accidental peanut exposure is believed to be approximately one to two peanuts or less (i.e., approximately 325–650 mg of peanut). Thresholds achieved in the 300 and 450 mg dose groups, 2083 and 2805 mg, respectively (i.e., 6–8 peanuts) should provide substantial protection for most patients. Moreover, 21% and 24% of patients at these respective dose levels were able to ingest at least eight grams of peanut (i.e., 24 peanuts) before experiencing an allergic reaction. Keep in mind, this therapy has not been approved for actual clinical use on patients with peanut allergy.

Further studies, including the investigation of other preparations of humanized monoclonal anti-IgE antibodies need to be conducted. If ultimately successful, anti-IgE could potentially be used for patients with any food allergy, although the protection against anaphylaxis would require continued therapy at regular time intervals indefinitely.

2.8. Prevention of food allergy:

2.8.1. Identification of infant "at risk":

In families with a high prevalence of a topic disease such as allergic rhinitis, asthma and topic dermatitis, the infant appears to be at increase risk of developing similar disease. IgG type sensitization is likely to occur to any of a number of foreign food proteins to which the infant is exposed in early life. Although an occasional clinical history suggests that a family may have a single inherited food allergy, such as to cow mil, the evidence that this often occurs is not convincing. Infant "at risk" also may include those born into families with a high incidence of chronic gastrointestinal disease. In as much as sensitization of gastrointestinal tract (Holland, 1972).

2.8.2. Methods of prevention:

Two major techniques of dietary prevention have been proposed for infant and children:

1. Exclusive breast feeding for at least four to six months, and
2. Substitution to soy formula for cow milk formula.

Several studies have indicated that nursing without supplementation may reduce the incidence of eczema of other allergy of respiratory disease,

although one study suggests that it may not prevent but rather postpone the onset of food allergy. It is important that the mother not drink accessible quantities of milk or eat excessive quantities of eggs white nursing because allergic sensitization may occur in breast milk (Schwchman, 1973). Using only glucose water to give additional water requirements or alternatively, feeding soy formula when the mother is unable to nurse, supplement foods should be with held until four to 6 months of age, then individuals single-grain cereals could be introduced, followed by single fruits, vegetables and meats one at a time[24]. In addition it would seem prudent to withdraw low milk, eggs, and wheat until nine month of age (Taylor, 1993). For adults the only way of prevention is the avoidance of suspected food or foods.

CHAPTER THREE

RESEARCH METHODS

3.1 Time dimensions:

Descriptive study started on April 2007 and ended on October 2007.

3.2 Source of data:

Primary data were collected at the time of study using structured questionnaires. Secondary data were obtained from books, magazines and internet as bases for the literature review.

3.3 Study area:

Hospitals in Khartoum state: Khartoum Teaching Hospital, Khartoum North Teaching Hospital, Omdurman Teaching Hospital, Departments of Dermatology.

3.4 Study population:

Fifity patients from both sexes attending at dermatology departments of different hospitals.

3.5 Study Design:

This is across-sectional, descriptive study.

3.6 Sample Selection:

Every patient came to dermatology department of the hospital at that day was selected for the study.

3.7 Sample Size:

Fifty patients: 15 men, 15 women, 10 boys and 10 girls.

3.8 Data Collection:

The main method used for data collection was direct interview using structured questionnaire format. The questionnaire contains both open

ended and close ended questions. The questionnaire contains social, health and nutrition information.

3.9 Data analysis and Presentation:

The data were statistically analyzed using SSPS and was presented in the form of tables and graphs.

3.10 Study limitation and difficulties encountered:

Limitation and difficulties encountered the study include:

a) Unavailability of records about allergic patients at the hospitals under investigation several years ago.
b) Unavailability of previous and relevant researches on this field in Sudan.

CHAPTER FOUR

RESULTS AND DISCUSSION

Figure 1 showed the distribution of allergic patients (out of 50) in Khartoum State Hospitals. As shown the number of patients in Omdurman (20) were more than those in Khartoum (15), 22% were found to live in Khartoum, 32% Omdurman, 24% in Khartoum North, 2% in East Nile, 12% in Karari and 8% in Gabal Aolea (Fig. 2). Results obtained showed that about 44% of patients were living in Omdurman followed by Khartoum (30%) and finally Khartoum North (26%). The results indicated that Omdurman province was the most invaded area in Khartoum State, this could be due to climatic conditions, type and nature of food and living state of citizens which may contribute to variation between the provinces. Moreover, the data obtained in Figure 3 showed that gender had no effect on the distribution of allergic patients in Khartoum State. Figure 4 showed the distribution of allergic patients (50) according to age. The data showed that most susceptible persons were those of age range from 31 to 40 years (13) followed by those of age >41 year (12) and those of age ranged from 1 to10 years (11). Generally it has been reported that most susceptible persons were those of age below 5

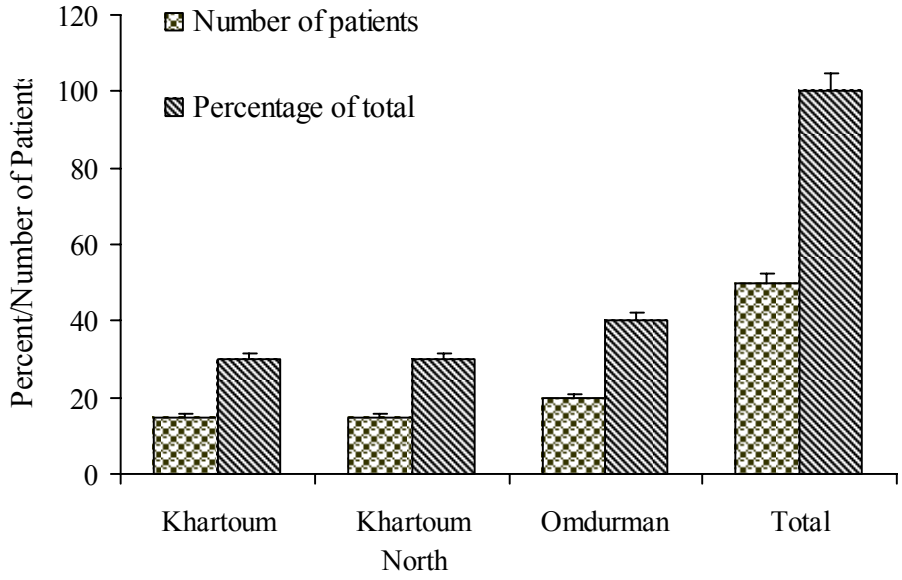

Figure 1. Distribution of allergic patients in Khartoum State.

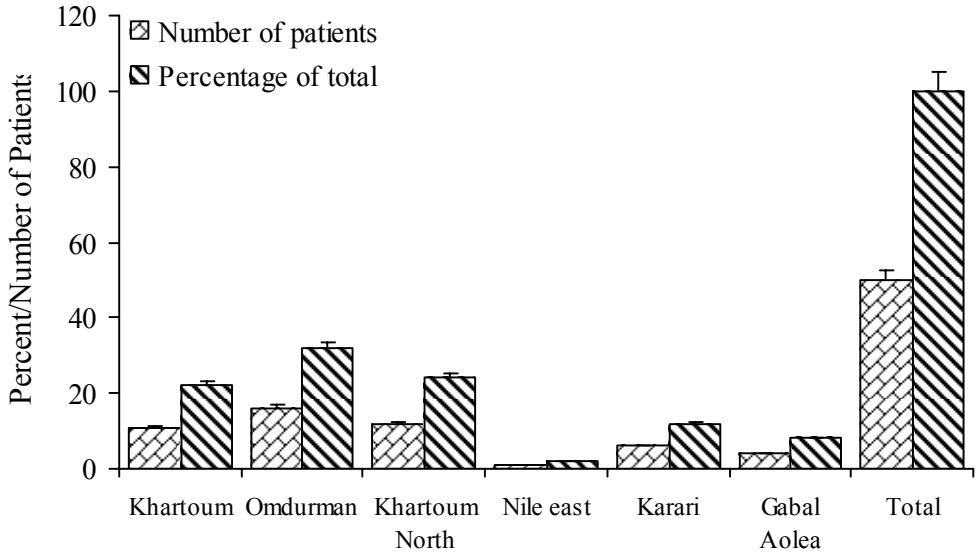

Figure 2. Distribution of allergic patients versus living area of allergic patients in Khartoum State.

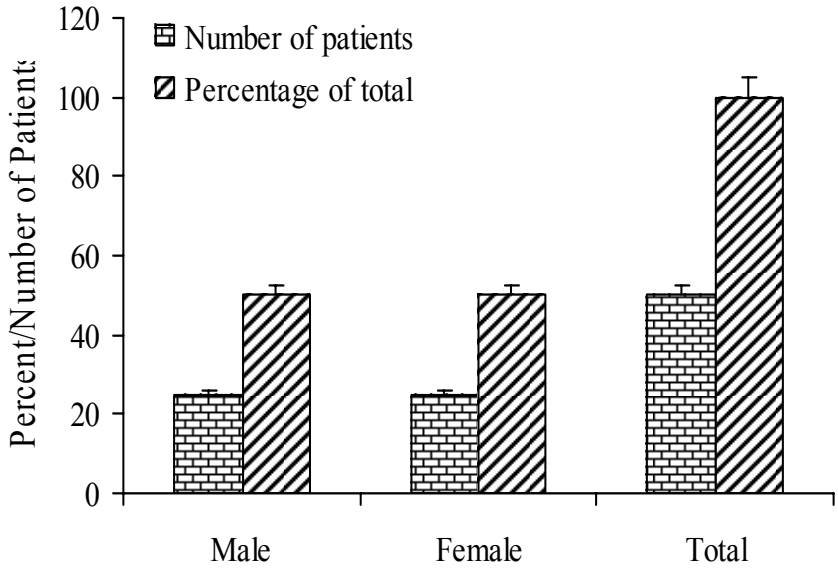

Figure 3. Distribution of allergic patients versus gender of allergic patients in Khartoum State.

years old (Luneta *et al*., 2005). However, our finding was a departure from an otherwise good correlation between age and the existence of allergy, this may be due to many factors such as avoidance of suspected foods by children in this study because most of the allergic foods consumed were not palatable for children such as eggplant, the other factor was that the amount of suspected food taken by children was too small to cause allergy. The later factor was likely to be the key factor that enhances the development of allergy because the food stays for long time before to be absorbed by the body (Luneta *et al*., 2005). A person may become allergic to food or other allergen at any age. However, children are frequently attacked and there is a higher incidence in adults than in children (Hatpern *et al*., 1998). The sensitiveness may wear off or the

patient may become desensitized. In later life individuals may be entirely free from the disturbance that affected them in childhood (Hatpern *et al*., 1998). Also this study indicated that increased intake of suspected food enhanced susceptibility to allergy and increased the number of allergic patients to 21 (out of 50) i.e. 42% of the total patients. Moreover, the response may be due to general physical condition and an allergic response may occur only when the individual is fatigued or emotionally upset (Spies *et al*., 1995).

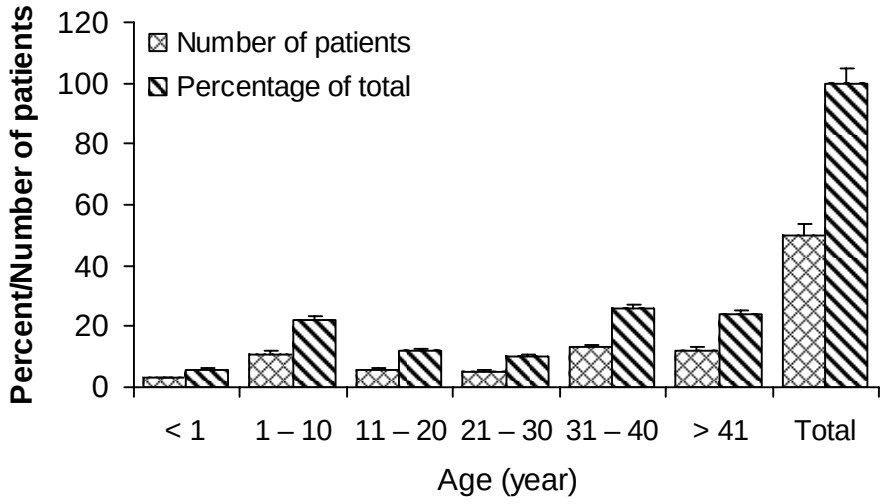

Figure 4. Distribution of allergic patients versus age of allergic patients in Khartoum State.

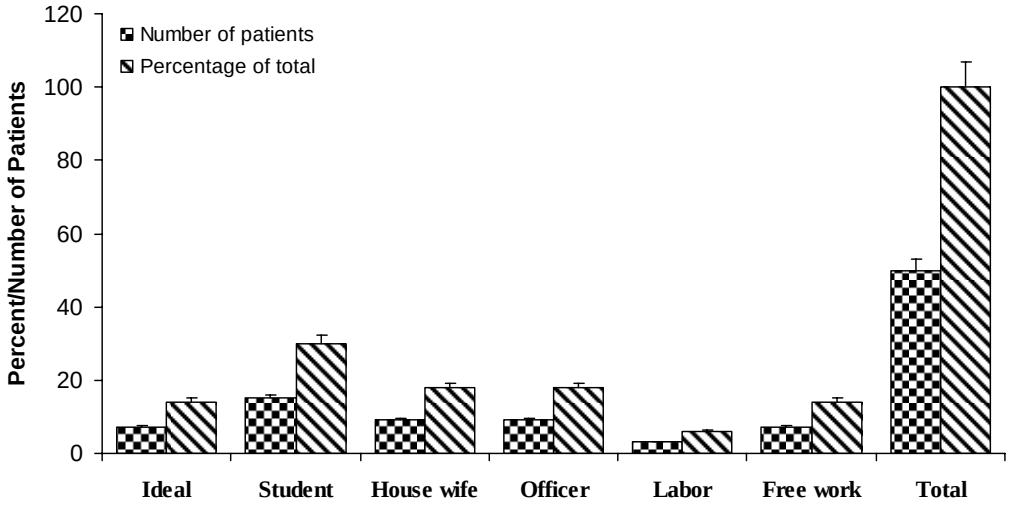

Figure 5. Distribution of allergic patients versus occupation of allergic patients in Khartoum state.

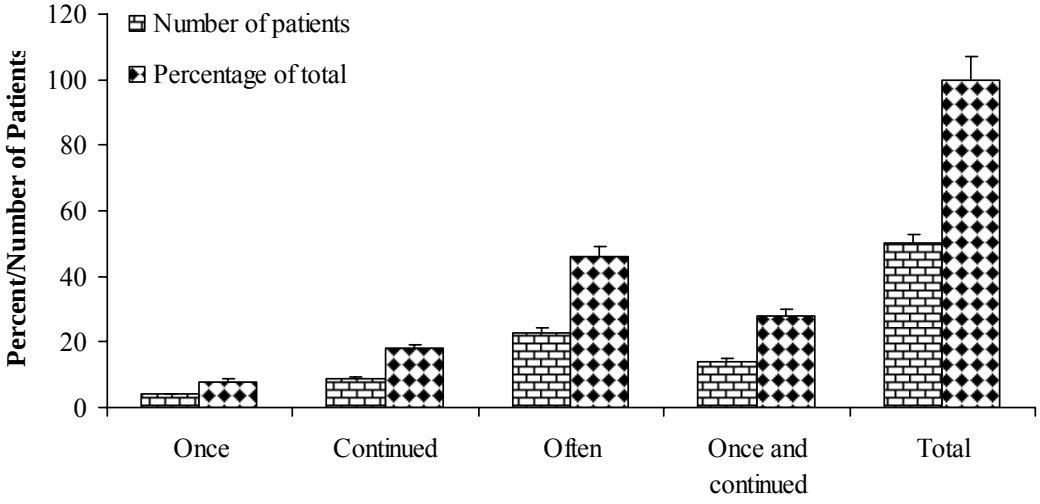

Figure 6. Distribution of allergic patients versus allergy frequency in Khartoum State.

Figure 5 showed that most vulnerable groups were students (30 %) followed by both government officials and housewives (18%) and most resistant were the labors (3%). The data indicated that hard working labors were more resistant to allergy. Out of 50 patients about 23 (46%) were found to suffer from allergy often (Fig. 6) and 14 patients (38%) suffered once, however, the symptoms continued, while others (9) suffered continuously (Fig. 6). Also the occurrence of allergy symptoms during the year was studied as shown in Fig. 7. Results showed that 74% of the patients (50) suffered from allergy when taken suspected foods at any time during the year i.e. the seasons of the year had no effect as suspected food did. Also results showed that 18% of the patients suffered

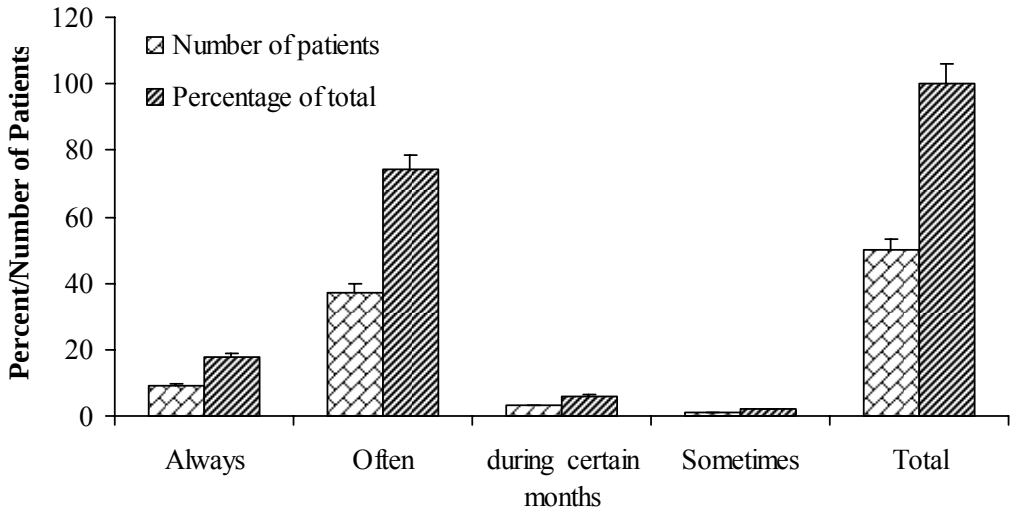

Figure 7. Distribution of allergic patients during the year in Khartoum State.

from allergy throughout the year even if they did not take the suspected food. The only way to treat allergy was the avoidance of suspected food.

However, sometimes treatment lessens the severity of it and still 1% of the patients were found to suffer from allergy symptoms. Table 1 showed that the distribution of patients (50) according to suspected foods showed 30% of the total patients suffered from eggplant allergy followed by egg (16%). Other foods such as cocoa, milk and milk products, carbonated water also significantly caused allergy to 6% of the total patients. Fortunately the harmful food which affected 30% of the patients was not common i.e. not all people take it and was not used as an ingredient for prepared foods. Therefore, it was possible to avoid it. It has been reported that any food can produce the allergic manifestations. However it is believed that protein is the important factor in food allergy, although the offending food may contain only a minute amount of protein (Holland *et al*., 1992). Among the most common offenders are: wheat, milk, eggs, fish, shellfish, strawberries, tomatoes and chocolate. Other offenders considered are: pork, orange, spices, condiments, nuts, corn, asparagus, spinach, cabbage, celery, onions, garlic (Holland *et al*., 1992). The ingestion of the smallest quantity of it as offending food, may produce symptoms or reaction, therefore, it's necessary for the allergic individual to analyze prepared foods and food combinations before eating them (Holland *et al*., 1992). The removal of the offending food or foods from the diet or desensitization are two possible methods of treatment for allergy (Holland *et al*., 1992). Table 2 showed the distribution of patients according to allergy duration and severity. The data obtained showed that 38% of the patients suffered from allergy for only 1 to 2 days, 22% of the patients suffered for one day. However, another 22% suffered from allergy for more than 3 days. The difference between the

two groups may be related to sensitivity to foods as well as the amount of food taken. Allergy last for long time can be classified as intermediate or severe because 60% of patients were found to suffer from intermediate type of allergy and 24% of them suffered from severe allergy (date not shown). Table 3 showed the distribution of allergic patients according to type of allergy. As shown half of the patients suffered from skin allergy and 12% suffered from abdominal pain and diarrhea and few numbers suffered from asthma and eyes pain. Table 4 showed the duration of allergy versus type of food taken by patients. As shown the data obtained revealed that one person suffered from peanut cream allergy with symptoms last for 1 – 2 days while in others the symptoms last for a period more than 3 days. The results obtained reflected the difference in degree of susceptibility between different individuals. Most types of foods had allergy duration varied as in case of peanut cream. However, other types of foods had a fixed duration such as fish which last for 1 – 2 days. Variations in allergy duration between foods were likely due to variations between patients as well as the quantity of food taken. Table 5 showed the degree of symptoms versus type of foods of allergic patients. As shown, the data revealed that most types of food gave medium symptoms for most patients except eggplant which caused severe allergy for 5 patients (out of 15 suffered from eggplant allergy). Also eggs caused severe allergy for two patients (out of 8 patients suffered from egg allergy). Other types of foods such as egg and milk, okra, dates, canned foods and green and hot pepper also caused severe allergy for patients. Results indicated that most types of foods caused allergy with medium symptoms to 60% of the total patients (50) and few caused slight

symptoms to 16% and other caused severe symptoms to 24% of the total patients. Results also indicated that eggplant was the harmful food that caused allergy to 30% of the total patients. Table 6 showed the distribution of patients according to type of food and type of allergy. The data obtained showed that skin allergy was the most prevailing one followed by stomach pain and diarrhea. For eggplant, 12 patients (out of 15) suffered from skin allergy. Cocoa and okra allergic patients suffered from skin allergy. Out of the total patients (50), 25 suffered from skin allergy (50%), 10% of the patients suffered from digestive stress and also 10% suffered from chest and hands pain and 12% from stomach pain and diarrhea. Also the study showed that about 80% of the patients suffering from eggplant allergy had skin allergy as well as those suffering from faba beans, tomatoes and okra. The results obtained indicated that, the most prevailing type of allergy was the skin allergy followed by stomach pain and diarrhea.

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Table 1. Percent patients suffer from allergy versus type of food.

Foods	Number of allergic Patients	Percentage of patients
Peanut cream	2	4
Cocoa	3	6
Eggplant	15	30
Eggs	8	16
Milk or milk products	3	6
Carbonated water	3	6
Canned food	2	4
Eggs or milk	2	4
Eggs or carbonated drinks	1	2
Faba beans	1	2
Tomatoes	1	2
Egg , milk , eggplant or okra	1	2
Dates	1	2
Fish	2	4
Meat	2	4
Green or hot pepper	1	2
Okra	2	4
Total	50	100

Table 2. Percent patients suffer from allergy versus duration of allergy.

Duration (days)	Number of patients	Percentage of patients
Not specified	2	4
1	11	22
2	19	38
3	7	14
> 3	11	22
Total	50	100

Table 3. Percent patients suffer from allergy versus type of allergy.

Type of allergy	Number of patients	Percentage of patients
Skin	25	50
Diarrhea	1	2
Abdominal Pain	2	4
Indigestion	5	10
Asthma	4	8
Lack of appetite	1	2
Abdominal pain and diarrhea	6	12
Chest and hands pain	5	10
Eyes pain	1	2
Total	50	100

Physician at the hospitals under investigation diagnosed allergic types.

Table 4. Type of food versus duration of allergy.

Type of food	Duration (days)					Total of patients
	Not specified	1	2	3	> 3	
Peanut cream	0	0	1	0	1	2
Cocoa	0	2	1	0	0	3
Eggplant	0	1	6	3	5	15
Eggs	1	1	3	3	0	8
Milk or milk products	0	2	1	0	0	3
Carbonated water	0	2	1	0	0	3
Canned foods	1	1	0	0	0	2
Egg or milk	0	1	0	1	0	2
Egg or carbonated water	0	0	1	0	0	1
Faba beans	0	0	1	0	0	1
Tomatoes	0	0	0	0	1	1
Egg or milk or eggplant or okra	0	0	0	0	1	1
Dates	0	0	1	0	0	1
Fish	0	0	2	0	0	2
Meat	0	1	1	0	0	2
Green or hot pepper	0	0	0	0	1	1
Okra	0	0	0	0	2	2
Total	2	11	19	7	11	50

Table 5. Type of food versus level of allergy.

Type of foods	Level			Total of patients
	Slight	Medium	Severe	
Peanut cream	0	2	0	2
Cocoa	0	3	0	3
Eggplant	3	7	5	15
Eggs	2	4	2	8
Milk or milk products	1	2	0	3
Carbonated water	1	2	0	3
Canned foods	1	0	1	2
Egg or milk	0	1	1	2
Egg or carbonated water	0	1	0	1
Faba beans	0	1	0	1
Tomatoes	0	1	0	1
Egg, milk, eggplant or okra	0	0	1	1
Dates	0	0	1	1
Fish	0	2	0	2
Meat	0	2	0	2
Green or hot pepper	0	0	1	1
Okra	0	1	1	2
Total	8	30	12	50

Physician at the hospitals under investigation diagnosed allergic types.

Table 6. Type of food versus specific types of allergy.

CHAPTER FIVE
CONCLUSION AND RECOMMENDATIONS

5.1. Conclusion:

* The majority of patients suffered from allergy are from Omdurman Province (40%) followed by Khartoum Province and Khartoum North (20%).
* The sex distribution among the patients indicates that there is no significant difference in patients sex with regard to food sensitivity.
* Students are the most susceptible group to food allergy (30%) followed by the house wife and the officers (18%).
* Free workers have the lowest susceptibility to food allergy (14%).
* There is a direct proportion between the level of allergy symptoms and the amount of food taken.
* Eggplants is the most type of food responsible for the allergic disease (30%) especially skin allergy followed by egg (16%).

5.2. Recommendations:

* The strict avoidance of the suspicious foods is the only way to avoid allergenic reaction.
* The consumer should read the ingredients of all processed foods to maintain control over the allergic ones.

* It is recommended to give alternative foods in order to maintain the nutritional status of the individuals suffering from food-induced allergic conditions.

* Food allergy or food hypersensitivity is a disease that is not only of concern to the individual who is affected but also to those involved directly and indirectly in supplying and preparing food for the food-allergic individual, and its impact on society should be evaluated on this basis.

* Most of mothers in this study were from lower social and educational classes therefore, we have to improve:
  - Δ The level of patients awareness.
  - Δ The standard of living.
  - Δ Knowledge of appropriate medical treatments.

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Appendix I
Questionnaire
Khartoum State

1- Data location:

i- Khartoum ( ) ii- Khartoum North ( ) iii- Omdurman ( )

2- Patient gender:

i- Male ( ) ii- Female ( )

3- Patient age:

i- Less than 1 year ( )

ii- 1- 10 years ( )

iii- 11-20 years ( )

vi- 21- 30 years ( )

v- 31-40 years ( )

iv- More than 41 year ( )

4- Patient occupation:

i- Student ( )

ii- Housewife ( )

iii- Officer ( )

vi- Lab our ( )

v- Free work ( )

iv- Not identified ( )

5- Patient living area:

i- Khartoum ( ) ii- Khartoum North ( ) iii- Nile East ( )

vi- Omdurman ( ) v- Ombadda ( ) iv- Korari ( )

iiv- Gabal Aolea ( )

6- Allergy frequency:

i- First time ( )

ii- Fixed rate ( )

iii- When eating allergic food oftenly ( )

iv- When eating allergic food repeatedly ( )

7- Allergy persistence:

i- Continued ( )

ii- When avoiding allergic foods ( )

iii- Disappear in certain months ( )

iv- Disappear After treatment ( )

8- Type of foods taken by patient:

i- Ordinary foods ( )

ii- Children's food ( )

iii- not mentioned ( )

9- Duration of allergy:

i- One day ( )

ii- 1-2 days ( )

iii- 2-3 days ( )

iv- More than 3 days ( )

v- not mentioned ( )

10- Level of allergy:

i- Slight ( ) ii- Medium ( ) iii- Severe ( )

11- Type of allergy:

i- Skin ( ) ii- Diarrhea ( ) iii- Abdominal pain ( )

iv- Indigestion ( ) v- Asthma ( ) vi- Chest hands pain ( )

vii- Eye complaints ( )

12- Expected foods for allergy:

i- peanut cream	( )	ii- Cocoa	( )	iii- Eggplant	( )
iv- Eggs	( )	v- Milk	( )	vi- Milk products	( )
vii- Carbonated water	( )	viii- Canned food	( )	ix- Beans	( )
x- Tomatoes	( )	xi- Okra	( )	xii- Date	( )
xiii- Fish	( )	xvi- Meat	( )	xv- Peppers	( )

13- Relation ship to climatic factors:

i- Yes ( ) ii- No ( )